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Editorial

Değerli Meslektaşlarımız

Tüm dünyanın özellikle de sağlık camiasının çok olağanüstü şartlardan geçtiği bir zaman dilimindeyiz. Adeta kartlar yeniden karılıyor. Bu olağanüstü koşullarda en çok yük alan ve sürekli ön cephede mücadale eden sağlık çalışanları olarak başkalarının temastan kaçtığı kişilerle yakın temas kurmak zorunda kaldık. Kimi hastalara santral kateter açtık, kimi hastaları mekanik ventilasyona bağladık,kimisini entube ettik kimine kalp masajı yaptuık hep yakın kalmak zorundaydık. Mümkün olduğunca korumalara rağmen maalesef ciddi sayıda kayıplarımız var. Bu dönem eğitim süreçlerini çok etkiledi, özellikle mezuniyet sonrası eğitimin ana unsurları olan kongreler ve sempozyumlar ertelendi, iptal edildi şimdilerde e kongre olarak varlığını sürdürmeye çalışıyor. Yayınlar da bu koşullardan etkilendi. Bu kadar yoğun çalışma temposu içinde ön cepheden acil servislerden yaptığımız çalışmalar aslında geleceğe not düşmektir. 2. yılımızda 5 Sayımızla karşınızdayız. Artık uluslar arası endekslerde taranan, yurt dışından da rağbet gören ileriye yönelik umutları yükselen dergimizi bu pandemi dönemimde dahi zamanında yayın hayatına kazandırmış olmaktan çok mutluyuz. Tıp kritik hastalarda başarılı olduğu kadar başarılıdır.

Saygılarımızla

Tüm editöriyal kurul adına editör;
Prof. Dr. Başar Cander

Dear Colleagues,

We are at a time when the whole world, especially the health community, is going through extraordinary conditions. It is as if the cards are shuffled again. In these extraordinary conditions, as healthcare workers who were the most burdensome and constantly fighting at the front, we had to establish close contact with those whom others avoided. We opened a central catheter for some patients, connected some patients to mechanical ventilation, we intubated some of them, and others performed heart massage, and we always had to stay close. Despite as many protections as possible, unfortunately we have a significant number of casualties. This period affected the educational processes a lot, especially the congresses and symposiums, which are the main elements of post-graduation education, were postponed, canceled, and now it is trying to survive as e-congress. Broadcasts were also affected by these conditions. The work we do from the frontline emergency services in such a busy schedule is actually a note for the future. We are with you in our 2nd year with our 5th issue. We are very happy to have brought our magazine, which is now scanned in international indexes and attracted abroad, with its prospective hopes, to its publishing life in time, even during this pandemic period. Medicine is as successful as it is in critically ill patients.

Regards

Editor on behalf of the entire editorial board;
Prof. Dr. Başar Cander

Contents

Review Article
Eurasian Journal of Critical Care

Ventilatory Management Strategies For Acute Respiratory Distress Syndrome (Ards) Due To Covid-19 Disease

Turgut TEKE[1], Taha Ulutan KARS[2], Korhan KOLLU[2]

[1]Professor, MD, Department of Chest Disease, Division of Intensive Care, Necmettin Erbakan University, Meram School of Medicine, Konya, Turkey

[2]Consultant, MD, Department of Internal Medicine, Division of Intensive Care, Necmettin Erbakan University, Meram School of Medicine, Konya, Turkey

Abstract

Acute Respiratory Distress Syndrome (ARDS) is a life-threatening diffuse inflammatory condition in the lungs and result in the oxygen treatment-refractory hypoxemic respiratory failure. ARDS is not a disease and is the result or complication of an underlying disease. COVID-19 pneumonia-related ARDS is a specific condition with unique phenotypes. Although patients had very severe hypoxemia in the early stages of respiratory distress due to COVID-19 disease, there was relatively well-preserved lung compliance. This phenotype is named as "atypical ARDS" or "ARDS type L". In advanced stage, some patients (20-30%) can return to a clinical picture more characteristic of typical ARDS progressively. This phenotype is called "typical ARDS" or "ARDS type H". Different types of ARDS that develop due to COVID-19 pneumonia require different ventilation strategies, depending on the underlying pathophysiology. In patients with early-stage atypical ARDS phenotype higher TVs and lower PEEP may be preferred, as opposed to the lung protective mechanical ventilator strategy. Nowadays, in the typical ARDS phenotype, the lung protective ventilation strategy used in classical ARDS is widely preferred. Refractory patients (a small number of patients) need to additional applications which are including prone ventilation and exorcoral membrane oxygenation (ECMO).

Keywords: COVID-19 disease, ARDS, Ventilatory management strategies, Prone ventilation, ECMO

Introduction

Acute Respiratory Distress Syndrome (ARDS) is a life-threatening acute diffuse inflammatory condition in the lungs. ARDS is result in the oxygen treatment-refractory hypoxemic respiratory failure[1]. ARDS is not a disease and is the result or complication of an underlying disease. In ARDS, hypoxemia occurs as a result of different mechanisms. Alveolar edema and collapse resulting from diffuse alveolar damage (DAD), which is considered the morphological hallmark of the lung in ARDS, decreases lung volumes and results in a decrease in compliance[2]. Disruptions in the resulting intrapulmonary shunt and ventilation/perfusion (VA/Q) ratio cause hypoxemia. In addition, surfactant deficiency, the loss of hypoxic pulmonary vasoconstriction and impaired regulation of pulmonary blood flow also contribute to the development of hypoxemia. DAD may be due to pulmonary or extra-pulmonary causes. Pulmonary ARDS is a direct insult to the lung affecting alveolar epithelium whilst extra-pulmonary ARDS is an indirect lung injury caused by inflammatory mediators acting on the vascular endothelium[3]. Pulmonary ARDS is noticeably more common than extra-pulmonary ARDS, and its most common cause is pneumonia (about 60% of cases)[4]. Extra-pulmonary ARDS is more common amongst postoperative and trauma patients.

In ARDS due to COVID-19 pneumonia, thrombosis and associated ischemic events are very common[5,6]. COVID-19 is a systemic disease that mainly causes damage to the vascular endothelium. The disproportionate endothelial injury plays a major role in the deterioration of pulmonary vasoregulation, the deterioration in the VA / Q ratio (possibly the primary cause of severe hypoxemia at the beginning) and thrombogenesis. COVID-19 has a highly activated coagulation cascade that goes through diffuse micro and macro thrombosis in the lung and other organs and very high D-dimer levels are associated with badly results. Most deaths from ARDS due to COVID-19 pneumonia have evidence of a thrombotic disseminated intravascular coagulation (DIC)[7].

The current definition of ARDS is the Berlin defination at the international American-European Consensus Conference in 2012 (Table 1). The Berlin definition, ARDS is classified according to the degree of hypoxemia. Treatments and ventilator management strategies have also been proposed according to the degree of hypoxemia. In the LUNG SAFE study performed using Berlin criteria in 2014 among 459 intensive care units (ICUs) in 50 countries patients with ARDS represented 10% of all ICU admissions and 23% of all intubated patients in ICU were due to ARDS[4]. Among them, 30% had mild, 47% had moderate and 23% had severe ARDS. It was also stated that 59% of these ARDS developed due to pneumonia, 14% to aspiration, 16% to sepsis and 7.5% to non-cardiogenic shock. ARDS develops in 42% of patients presenting with COVID-19 pneumonia and 61-81% of those who require hospitalization in the ICU[8].

Corresponding Author: Turgut TEKE **e-mail:** turgutteke@hotmail.com
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Table 1. ARDS Berlin Diagnostic Criteria

Timing	New or increased respiratory symptoms starting within a week
Chest Radiography	Bilateral diffuse infiltrations: completely effusion, atelectasis, no lobar collapse or nodule
Cause of Edema	Clinical findings should not be explained by the presence of heart failure or fluid load. If there is no risk factor, echocardiography should be performed to exclude hydrostatic edema.
Oxygenation	
Mild	When PEEP ≥5 cmH2O: 300 ≥ PaO2/FiO2 > 200
Moderate	When PEEP ≥5 cmH2O: 200 ≥ PaO2/FiO2 > 100
Severe	When PEEP ≥5 cmH2O: PaO2/FiO2 ≤ 100

Even though it can meet the Berlin criteria, COVID-19 pneumonia-related ARDS is a specific condition with unique phenotypes[9]. Although patients had very severe hypoxemia in the early stages of respiratory distress due to COVID-19 pneumonia, there was a relatively well-preserved lung compliance[10,11]. The median respiratory system compliance is usually around 50 ml/cmH_2O. In the early stage, ground-glass pattern on chest tomography (CT) suggesting interstitial involvement rather than alveolar edema and generally peripheral involvement are noteworthy. Many of these patients do not appear overtly dyspneic. This phenotype is named as "atypical ARDS" or "ARDS type L", which has low lung elastance (relatively high compliance) and high lung gas volume, thus low response to the application of extrinsic positive end-expiratory pressure (PEEP)[9,12,13]. High PEEP administration does not improve oxygenation, as severe hypoxemia primarily results from deterioration in the VA / Q ratio rather than alveolar collapse. For many patients, the disease may stabilize at this stage without worsening or progressing. In advanced stage, some patients (20-30%) can return to a clinical picture more characteristic of typical ARDS progressively, depending on disease severity and host's response or suboptimal management. This phenotype is called "typical ARDS" or "ARDS type H". At this stage, there are widespread consolidations in chest CT, high lung elastance (low compliance), low lung gas volume and high response to to the application of extrinsic PEEP. However, it should be kept in mind that intermediate forms can be found in which the features of these two types with different pathophysiology may coincide[9,12,13].

Regardless of the condition that causes ARDS, most severe ARDSs require invasive mechanical ventilation. Unlike spontaneous breathing, invasive mechanical ventilation delivers positive pressure throughout the breathing cycle. If the lung-protective mechanical ventilator strategy is not followed (eg. tidal volume (TV): >12ml/kg and PEEP: about 5cmH2O), invasive mechanical ventilation itself can worsen existing lung damage. It is known that ventilation with 6 ml/kg TV significantly reduces mortality (9%) compared to ventilation with 12 ml/kg TV[1,14]. Therefore, it should be aimed to prevent the occurrence of ventilator induced lung injury (VILI) in mechanical ventilation application. VILI consists of many different components such as volutrauma, barotrauma, atelectrauma and biotrauma. The most important is volutrauma. Atelectotrauma is caused by repeatedly opening and closing small airways and alveoli over the breathing cycles. Biotrauma is a general biological response that results in cytokine release due to the effect of stress and strain at the cellular level. The cellular toxicity of oxygen is another component of VILI[14].

It is not clear whether different types of ARDS that develop due to COVID-19 pneumonia require different ventilation strategies. The key treatment strategy is to maintain oxygenation[9,12,13]. Different ventilation strategies are required, depending on the underlying pathophysiology (Table 2). In patients with early-stage atypical ARDS phenotype with good lung compliance, higher TVs (7-8 mL/kg ideal body weight) and lower PEEP (8-10 cmH_2O) may be preferred, as opposed to the lung protective mechanical ventilator strategy. Today, in the typical ARDS phenotype associated with COVID-19, the lung protective ventilation strategy used in classical ARDS is widely preferred[9,15]. In this section, ARDS, which develops due to COVID-19 pneumonia, will refer to lung protective low tidal volume ventilation (LTVV), which is the basic mechanical ventilation strategy.

LOW TIDAL VOLUME VENTILATION (LTVV)

As with all ARDS patients, the recommended mechanical ventilation strategy in patients with COVID-19 pneumonia that develops ARDS and needs a ventilator is lung protective mechanical ventilation which low TV, optimal PEEP and plateau pressure (Pplat) are monitored tightly. The main purpose is to adjust the ventilator settings in a way that ensures sufficient gas exchange without causing VILI (by maintaining Pplat <30 cmH_2O and driving pressure <14 cmH_2O). The most common practice is to target at least 55 mmHg for partial arterial oxygen pressure (PaO_2) and at least 88% for arterial oxygen saturation (SaO_2). More conservative oxygenation strategies that target SpO_2 with pulse oximeter between 88-92% may also be possible in patients undergoing mechanical ventilation[16].

Table 2. Ventilation Strategies in ARDS Associated with COVID-19 Pneumonia[9]

Time Period	Purpose	Respiratory Support Options
Before Intubation	• Ensuring adequate gas exchange • To prevent P-SILI formation	- Oxygen therapy - CPAP, NIMV, HFNC - Keep in pron position - Ensure inspiratory effort is not severe
Mechanical Ventilation	• Preventing increased lung damage • Preventing VILI	- Minimize TV, breathing frequency and PEEP - Make settings to ensure proper gas exchange - Adjust the fluid balance - Reduce tissue oxygen consumption - Keep in mind the need for ECMO
After Intubation	• Minimizing pulmonary stress • Preventing VILI	**Atypical ARDS**: - Use lower PEEP (<10 cmH_2O) - Use more liberal TV (7-9 ml/kg) when needed - Reduce tissue oxygen consumption - Keep in mind the prone positioning
	• To reduce and distribute pulmonary and vascular stresses equally • Optimizing oxygen • Preventing VILI	**Typical ARDS**: - Use higher PEEP (<15 cmH_2O) - Use low TV (5-7 ml/kg)ü - Reduce tissue oxygen consumption - Prone positioning
Weaning	• Preventing return to VILI or lung damage	- Make the transition carefully - Avoid sudden changes - Perform spontaneous breathing trial at the end of the weaning process

ARDS: *Acute Respiratory Distress Syndrome*, P-SILI: *Patient Self-Induced Lung Injury*, VILI: *Ventilator-Induced Lung Injury*, CPAP: *Continious Positive Airway Pressure*, NIMV: *Non-Invasive Mechanical Ventilation*, HFNC: *High Flow Nasal Cannula*, TV: *Tidal Volume*, PEEP: *Positive End Expiratory Pressure*, ECMO: *Extracorporeal Membrane Oxygenation*

In patients with ARDS with COVID-19 pneumonia, LTVV ≤6 mL/kg should be targeted according to the ideal body weight. Initially, tidal volume 6 mL/kg with volume limited assist control mode should be preferred and Pplat should be ≤30 cmH_2O. PEEP adjustment should be made according to the inspired oxygen fraction (FiO_2), keeping PaO_2 in the range of 55 to 80 mmHg or keeping SaO_2 in the range of 88% to 95% (Table 3). In situations such as severe hypercapnia or patient-ventilator dyssynchronies, there may be a need to change this ventilation strategy. LTVV reduces the development of VILI which can cause additional lung injury and mortality in patients with ARDS.

TV, Pplat and compliance values, which are standard variables in mechanical ventilator management, are used in patients with ARDS. Driving pressure is also used in the management of severe or refractory cases with a lung that has the flexibility to benefit from high PEEP values. Lung protective ventilation strategies are associated with limited driving pressure (driving pressure = Pplat measured with ventilator-applied PEEP or TV/respiratory system compliance).

Application and Adjustment

When starting LTVV, typically volume or pressure limited assist control mode selection, TV and breathing frequency adjustments, and PEEP and FiO_2 levels are adjusted. Worldwide volume-limited assist control ventilation is most commonly used mode of ventilation in ICU[17]. Pressure limited mode is also a viable option as long as a consistent and stable TV is provided in accordance with the LTVV strategy. There are no clinical data demonstrating a difference in outcomes between these two modes[18]. In most patients with ARDS, pressure limited mode provides good patient tolerance and stable airway pressure, while volume limited mode provides a stable TV. The main advantage of volume limited mode in

Table 3. FiO_2 and PEEP Combinations

FiO_2	0,3	0,4	0,5	0,6	0,7	0,8	0,9	1,0
PEEP*	5	5-8	8-10	10	10-14	14	14-18	18-24

* The initial PEEP value should be set at the lowest value shown in the table according to FiO_2.

terms of respiratory mechanics is that it allows continuous monitoring of Pplat pressure. Regardless of whether volume limited or pressure limited ventilation mode is selected, fully supported control modes (eg. assist control) are preferred over partial assisted control modes (eg. synchronous intermittent mandatory ventilation [SIMV]).

The initial TV should be adjusted to 6 mL/kg based on predicted body weight and to meet the minute ventilation needs of the patient, provided that the initial respiratory rate is ≤35 breaths/min (usually 14-25 breaths/min). The reason for setting the respiratory rate relatively high (by increasing the minute ventilation) is to prevent the occurrence of respiratory acidosis, which can be caused by low TV. However, there is some experimental evidence that mild respiratory acidosis can protect the lungs[19]. In the next 1 to 4 hours, the patient's clinical response, gas exchange, and Pplat can be used to adjust the TV and breathing rate as needed. TV adjustments should be made to ensure that lung-protective ventilation is properly applied and to evaluate the response in real time before taking arterial blood gases. Simultaneous adjustments are typically made to adapt the clinic, gas exchange and Pplat parameters. Pplat target should be ≤30 cmH_2O and TV should be adjusted according to Pplat. If Pplat ≤30cmH_2O and TV is 6 mL/kg according to ideal body weight, no further adjustment is required. If Pplat >30 cmH_2O, it can be planned to decrease up to 4 mL/kg with decreases of 1 mL/kg on TV. The breathing frequency should be increased to ensure proper minute ventilation at any decrease in TV. In cases where patient-ventilator dyssynchronies, Pplat <25 cmH_2O and TV <6 mL/kg, Pplat should be increased between 25 and 30 mmH_2O or TV to 6 mL/kg in 1 mL/kg increments. If dyssynchronization is serious, the TV can be increased up to 8 mL/kg. TV and breathing frequency adjustment can also be made depending on gas exchange. LTVV can trigger respiratory acidosis. However, although there is no consensus on the upper or lower limit, the pH value should be kept above 7.2. TV can be increased when the pH reduces below 7.15-7.20[20].

While adjusting PEEP, it should be aimed to provide the highest compliance and lowest alveolar dead space, thus increasing the gas volume of the lung. The purpose of PEEP in patients with ARDS is to maintain and maximize alveolar ventilation. Thus, oxygenation is improved and oxygen toxicity is prevented. However, the response to PEEP may differ according to the origin of ARDS (pulmonary vs. extra-pulmonary), the timing (early vs. late) and the localization of infiltrates (diffuse vs. lobar)[21]. Thus, a personalized approach is best, adjusting PEEP for each patient to optimize his/her alveolar recruitment. Indeed, whwn increasing PEEP reduces the driving pressure it indicates recruitment and is associated with improved survival[16]. Optimal PEEP was found to be between 11-16 cmH_2O in moderate to severe ARDS[22]. In typical ARDS developing due to COVID-19 pneumonia, it may be beneficial to increase PEEP gradually up to 14-15 cmH_2O pressure. However, at this stage, a decrease in mixed venous oxygen saturation (SvO_2) is a sign that cardiac output is decreasing, indicating that higher PEEP levels will no longer be beneficial[13].

Efficacy and Side Effects

Many studies have shown that early administration of LTVV improves mortality and other clinical outcomes in patients with ARDS[1,23]. LTVV is generally well tolerated; however, there are potential side effects. Hypercapnic respiratory acidosis is an expected and generally well tolerated side effect of LTVV. LTVV can cause permissive hypercapnia as a ventilation strategy that allows alveolar hypoventilation to minimize complications from alveolar overstress and provide a low alveolar pressure. The degree of hypercapnia can be minimized by setting the highest respiratory rate that will not cause auto-PEEP. The LTVV strategy itself can also cause auto-PEEP. Increased breathing frequency to maintain minute ventilation during LTVV can create auto-PEEP by reducing the respiratory cycle time and therefore the time required for expiratory. When auto-PEEP is suspected, the clinician should estimate the contribution of auto-PEEP to all PEEP and manage the strategy accordingly.

LTVV may also cause an increase in the need for sedation and use of neuromuscular blocker agents and related side effects associated with sedation. When the TV falls below 7 mL/kg according to the ideal weight, the patient's effort to breathe increases and can create patient-ventilator dyssynchronies. With double triggering, higher TVs are created that can negatively affect the benefits of LTVV. If the patient's severe inspiratory effort is not brought under control, it may worsen the existing lung injury by raising the transpulmonary pressure, which is called the patient's self-induced lung injury (P-SILI)[24]. The use of sedation and neuromuscular blocking agent increases the patient's mechanical ventilation tolerance. It allows the respiratory muscles to rest, thereby reducing oxygen consumption by these muscles. As a result, oxygenation is improved, lung and systemic inflammation are reduced and survival is improved[25]. Although LTVV may require an increase in the need for sedation, the need for increased sedation is not continuous. Double examination is a form of dyssynchronization that can occur despite deep sedation. Double triggering can be corrected by providing a slightly higher TV (7-8 mL/kg, predicted body weight) or additional sedation as long as Pplat <30 cmH_2O remains.

Patients with Recovery Findings

The majority of patients with ARDS show improvement with LTVV. In these patients, FiO2 and PEEP should be

gradually decreased and partial assist or spontaneous modes should be attempted according to tolerance. Because the immobility of the diaphragm in controlled modes can quickly lead to marked muscle atrophy and reduced contraction force[26]. Airway pressure release ventilation (APRV) is a ventilation mode that combines invers ratio ventilation with pressure control ventilation that allows spontaneous breaths. Since the two valves of the ventilator are continuous, it is possible to maintain spontaneous breaths at any stage of the breathing cycle. Sustaining spontaneous breaths in APRV mode has been shown to improve respiratory functions and reduce time to stay in mechanical ventilation by reducing sedation requirements[27]. Pressure-support ventilation (PSV) is a spontaneous mode often used during the weaning period. The best time to switch from assist-controlled modes to PSV is unknown, but switching to PSV should be considered when most respiratory cycles are triggered by the patient and the underlying disease is under control. Another support mode for spontaneous breathing is a neurally adjusted ventilator-assisted (NAVA) mode that triggers assisted breaths through a diaphragmatic EMG inserted into a special naso-gastric catheter and reduces patient-ventilator dyssynchrony[28].

Treatment for COVID-19 or secondary developing disease should be optimized, and sedation and vasopressor support should be reduced as much as possible. The time of weaning from the ventilator is completely patient-based; it does not seem possible to give an exact time. This period can extend from 24-48 hours to days or even weeks.

Patients Without Recovery Signs

Patient-ventilator dyssynchrony, high alveolar pressure (Pplat ≥30 cmH_2O) hypoxemia progression ocur in patients with LTVV intolerance. It does not matter if intolerance or deterioration occurs immediately after ventilation or after a short recovery period. In both cases, the management strategy is similar. Unexpected airway pressure changes in patients with volume-limited ventilation or unexpected TV changes in patients with pressure-controlled ventilation require investigation of causes that may lead to acute changes in compliance (eg. pneumothorax, endotracheal tube obstruction).

Choosing an Option

In case of failure of the LTVV response, the underlying causes should be determined and corrected. Supportive moves such as treatment of the current disease, management of fluid therapy, consideration of alternative diagnoses, and complications of ARDS or mechanical ventilation should be made. If dissynchronization is present, it should be corrected. It can also be planned to continue LTVV by making alternative adjustments such as switching to pressure-controlled or vice versa while volume-controlled or increasing the inspiratory-expiration rate. These regulations depend on factors such as the severity of ARDS, its complications, and the patient's comorbidity. All these options should be individualized for each patient. Switching from volume-limited to pressure-limited mode or increasing inspiratory flow rates is an appropriate approach in patients with air hunger. In patients with subsegmental atelectasis causing oxygenation disruption, it is beneficial to prolong the inspiration time by decreasing flow rates in volume-limited modes and increasing the inspiratory time in pressure-limited modes.

Supportive Measures

Pulmonary edema may occur in patients with ARDS due to increased vascular permeability. This problem may require discontinuation or reduction of fluid therapy or diuresis. In cases where the fluid status is unclear, measurement techniques that reflect the fluid status may need to be used. There may be complications with conditions such as pneumothorax, ventilator-associated pneumonia, and pulmonary tromboembolism in ARDS. It is a useful approach to exclude these situations before terminating LTVV and before resorting to other ventilation strategies.

Patient-ventilator dyssynchronies occurs in about 25% of patients who undergo mechanical ventilation[29,30]. Patient-ventilator dyssynchrony may cause increased breathing effort, and in some cases, auto-PEEP and decreased gas exchange may lead to prolonged stay in mechanical ventilation, increased sedation / neuromuscular blockage requirement, and barotrauma[29,30]. Patient-related factors (eg. respiratory drive, timing, compliance, resistance to airflow) and ventilator-related factors (respiratory rate, inspiratory flow rate / shape, trigger sensitivity) are affect synchronization. Ineffective triggering or double triggering are the most common examples of dissynchronization[29,31]. It becomes evident in cases where minute ventilation requirement increases, such as metabolic acidosis or high dead space breathing in ARDS. The approach to patient-ventilator dyssynchrony is done by evaluating flow-time, pressure-time and pressure-volume curves. In the management of dyssynchronization, firstly, sedation should be increased as much as possible, and trigger changes and small changes should be made in the inspiratory flow. Double triggering is a second exhalation of the ventilator by the patient before completing the first exhalation. This causes the formation of harmful high TVs[27]. It is often caused by the adjustment of a tidal volume that is too low to meet the needs of the patient during LTVV or by keeping the inspiratory time short. In this case, the inspiratory time can be kept longer by selecting the decreas-

ing flow form, reducing the flow rate or adding an inspiratory pause[31]. Ineffective triggering occurs when the patient's respiratory effort fails to trigger the ventilator. Ineffective triggering can also contribute to auto-PEEP formation. Ineffective triggering can be corrected by reducing the trigger sensitivity. Flow dissenronization is the failure of the ventilator flow to meet patient needs and can be corrected by increasing the flow or by changing the ventilator mode.

Alternative Settings and Modes in LTVV

Alternative modes may sometimes be required for patients who are unable to tolerate volume-limited LTVV (eg. Pplat ≤30 cmH_2O failure, ventilator synchronization disorder). Pressure limited modes (pressure regulated-volume controlled ventilation and pressure support modes, APRV, volume targeted pressure controlled ventilation) or NAVA are alternative modes. Generally, it is preferred to apply alternative modes for a short time. Close monitoring of ventilator waveforms, airway pressures, tidal volumes, and gas exchange assessment is important in evaluating the response. If success can be achieved, it is an appropriate approach to continue with the same mode.

In some patients, increasing the inspiratory-expiration rate (I:E) by prolonging the inspiratory time may increase oxygenation by creating more time for gas exchange in the lung. When the inspiratory time exceeds the expiratory time, this is known as inverse rate ventilation (IRV). Despite the improvement in oxygenation, prolongation of inspiratory time or IRV has not been shown to clinically improve outcomes in ARDS[32].

REFRACTORY PATIENTS

A small number of patients with ARDS pose a special challenge due to the lack of adequate gas exchange without exposure to refractory hypoxemia (PaO_2/FiO_2<150) and/or high alveolar pressure (Pplat >30 cmH_2O) despite LTVV and other supportive measures specific to ARDS. These patients have a high risk of mortality.

Additional applications in these patients include prone ventilation, ventilator strategies that maximize alveolar flexibility (eg. high PEEP administration, open lung ventilation strategies, and recruitment maneuvers), pharmacotherapies (eg. neuromuscular blockers, pulmonary vasodilators) and exorcoral membrane oxygenation (ECMO). These applications do not have a clear advantage over each other; however, a meta-analysis showed that only prone position and ECMO were associated with a decrease in mortality rates[33]. In practice, the vast majority of clinicians prefer prone position application firstly, and ECMO is applied if there is no success.

Prone Ventilation

The prone position is to place the patients face down and maintain mechanical ventilation treatment in this position for a long period of time. Indications of prone position are resistant hypoxemia despite positive end-expiratory pressure (PEEP) >10 cmH_2O and FiO_2 >60% with protective MV application and/or difficulty to maintain MV (When VT 4-6 mL/kg is given according to ideal body weight, plateau pressure (Pplato) >30 cmH2O and pH <7.15 (respiratory acidosis)); and/or are moderate or severe ARDS patients with right ventricular dysfunction on echocardiography due to hypoxia and hypercapnia[34]. In severe ARDS, it is recommended to start the prone position in the early period (within 36 hours) following ventilation in the supine position for 12-24 hours[35]. Contraindications and complications of the prone position are shown in Table 4.

Due to prone position, the reduction of the pleural pressure gradient from the dependent lung areas to the non-dependent lung areas and the appropriate displacement of the lungs in the thoracic cavity are provided and as a result, the aeration and tension of the lungs becomes more homogeneous. In the light of all these factors, better oxygenation is achieved in ARDS cases due to prone position. Prone position may provide an increase in carbon dioxide clearance as a result of the regulation of oxygenation in ARDS along with opening of atelectatic alveoli and increased number of ventilated alveoli despite the minute ventilation does not increase[34,36]. Mechanism to improve oxygenation of the prone position:

- Opening of the atelectatic dorsal lung areas
- Improvement of ventilation perfusion rate
- Homogeneous distribution of lung elastance to all lung areas
- Increased chest wall elastance
- Decrease in the amount of alveolar shunt
- Functional residual capacity increase
- Mobilization of secretions

In addition, a homogeneous lung ventilation is provided and ventilator-associated lung damage is reduced as a result of ventilation of dependent lung areas, recruitment of alveoli and reduction of hyperinflation in non-dependent lung areas in ARDS cases due to prone position[34,36].

Improvement of oxygenation with the prone position may also improve V/Q mismatch by reversing inadequate hypoxic pulmonary vasoconstriction. Finally, while the improvement of oxygenation prevents the progression of dyspnea, reconstruction of lung tissue with prone position

Table 4. Prone position: Contraindications and Complications[34]

Contraindications	Relative Contraindications
• Shock (e.g. permanent mean arterial pressure <65 mmHg)	• Current Deep Vein Thrombosis <2 days
• Acute bleeding (e.g. hemorrhagic shock, massive hemoptysis)	• Chest tube with air leak
• Multiple fractures or trauma (e.g. femur, pelvis, facial bone fractures)	• Major abdominal surgery
• Spine instability	• Clinical conditions that reduce life expectancy
• Pregnancy	• Severe burns
• Increased intracranial pressure> 30 mmHg or Cerebral perfusion pressure <60 mmHg	• Lung transplant recipient
• Tracheal surgery or sternotomy within 2 weeks	• Having a pacemaker

Complications

- Nerve compression (e.g. Brachial plexus injury)
- Venous stasis (e.g. facial edema)
- Dislocation of the endotracheal tube
- Pressure sores
- Removal of vascular catheters or drainage tubes
- Retinal damage
- Vomiting
- Temporary arrhythmias

changes lung stress-strain relationship and intra-thoracic forces, slows the formation of lung edema and slows the progression of the disease from the L-phenotype to the H-phenotype[13]. It can be used to prevent the high rate of hospitalization of COVID-19 patients to ICUs and to improve the oxygenation and prevent their transfer to ICUs in awake patients[37].

The optimal duration of the prone position is unknown. In a randomized study (PROSEVA) demonstrating the benefit of prone position on mortality in severe ARDS, the average time in the prone position was 17 hours per day with an average of four sessions per patient[35]. Usually, a response is noted in the first hour of the first attempt, but longer times (e.g. 12 to 18 hours) are required to provide a meaningful response.

If prone ventilation fails (e.g., if the patient has no change in gas exchange, or in case of deterioration in lung mechanics, gas exchange, or cardiovascular system), the patient should be turned into the supine position and alternative strategies (e.g. extracorporeal membran oxygenation) should be focused on to improve oxygenation.

Extracorporeal membran oxygenation (ECMO)

ECMO is the life support system that directs the venous blood of the patient to the artificial gas exchanger (oxygenator), thereby ensuring oxygenation and removal of CO_2 and return of blood to the venous or arterial system of the patient again. Veno-arterial ECMO (VA ECMO) performs both heart and lung functions, while venous-venous ECMO (VV ECMO) performs lung functions only and can be used in respiratory failure[38]. The use of ECMO support has increased in recent years, the patient should have a specified indication and no contraindications to consider this treatment option. Patients who do not respond to optimum conventional MV may be candidates for ECMO in institutions with appropriate resources (equipment and staff). The ECMO mode used in COVID-19 patients is usually VV ECMO. In this section we will focus more on VV ECMO.

Indications for VV ECMO can be listed as follows[38]:

1. For any reason (primary or secondary) in hypoxemic respiratory failure, ECMO should be considered when the mortality risk is 50% or more, and it should be started when the mortality risk is 80% or more.
   - Mortality risk ≥ %50: When FiO_2: 0.9, PaO_2/FiO_2 <150 and/or Murray score = 2-3 or age adjusted oxy-

genation index (AOI) >60 or Plateau Pressure Score (APPS) = 5-7
- Mortality risk ≥ %80: If FiO_2: 0.9, PaO_2/FiO_2 <100 and/or Murray score = 3-4 or AOI >80 or APPS = 8-9 despite optimal treatment for at least 6 hours

2. CO_2 retention despite high plateau pressures (>35 cm-H_2O)
3. Serious air leak syndromes
4. A patient who is in the lung transplant list, requiring intubation
5. Sudden cardiac or respiratory collapse (e.g. pulmonary embolism)
6. Hypercapnic respiratory failure with arterial pH <7.20

There is no strict contraindication for ECMO support, as each patient should be evaluated individually for gain and loss. However, despite ECMO, there are situations that are associated with a poor result and can be considered as a relative contraindication[38]:

1. MV requirement for 7 days or more (FiO_2 >0.9, p plateau >30 cmH_2O). Many centers think that the duration of ventilation is not a contraindication.
2. Major pharmacological immunosuppression (absolute neutrophil count < 400/mm^3)
3. Recent or progressive central nervous system (CNS) bleeding
4. Irreversible major CNS damage or terminal malignancy
5. Although advanced age is not a contraindication; increasing risks with increasing age should not be ignored

ECMO components (Cannulas, Pumps, Oxygenators)

Cannulas: Although the use of a negative pressure chamber is ideal for any invasive procedure in COVID-19 patients, this may not be possible most of the time. The Centers for Disease Control and Prevention (CDC) and other organizations state that surgeons, anesthesiologists and other clinicians who participate in the cannulation and initiation of ECMO should wear ideal personal protective equipment (PPE). The main differences between the VA and VV ECMO circuits are the cannula types and the location of the vessels in which they are located. Drainage cannulas are larger in diameter (22-31 Fr), multi-holed and long; while it is sufficient to select the return cannula with a small diameter (15-22 Fr). By using two separate cannulas for VV ECMO, neck-femoral region or right-left femoral region can be selected, while right internal jugular vein cannulation with a double lumen cannula can also be performed. Recently, double lumen cannula is preferred. In this type of cannulation, drainage is provided from the superior and inferior vena cava, while the return is towards the tricuspid valve in the atrium. Therefore, this system appears to be more advantageous because it provides more oxygen to the pulmonary arteries, reduces recirculation, requires only a single cannula to be inserted and facilitates rehabilitation and individual mobilization in patients requiring long-term ECMO[39].

Pumps: For ECMO units, there are two types of pumps: roles and centrifugal. Today, centrifugal pumps for ECMO systems have almost become a standard. The smaller centrifugal pumps deliver blood from the center of the vortex to the periphery with a magnetically driven impeller rotating up to 10,000 rpm in a conical cavity. When using a centrifugal pump, venous blood is taken independently of gravity and the patient's height relative to the pump does not affect the rotation. The blood flow depends on the pump's rotation rate per minute (rpm), front and afterload. Since high pressure gradient is not possible in centrifugal pumps, they do not cause significant embolism or tube rupture. Excessive negative pressure at the pump inlet can cause cavitation and hemolysis, but the degree of hemolysis is much lower compared to roller pumps[40].

Oxygenators (Membrane Lung, ML): The blood exiting the pump enters the oxygenator, the most important part of the ECMO system. ECMO oxygenators serve as artificial lungs to replace both oxygen (to blood) and carbon dioxide (from blood) instead of the patient's natural lungs. The basic principle in ECMO is the transport of oxygen from a semipermeable membrane to the blood. The membrane placed distal to the pump should have a high permeability for the passage of gases and have a resistant structure that prevents the passage of liquid from the blood to the gas phase. Membranes of different shapes consisting of hollow fiber tubes are used. As the sweep gas passes through the fiber cavity, effective gas exchange is achieved by passing from outside of fiber as opposite current to the blood. Modern membrane oxygenators are coated with "biocompatible-thrombus resistant polymers" that limit inflammation and thrombus formation. In the long-term use of membranes, when there is fluid accumulation in the fiber lumen and coagulation on the faces of the fibers in contact with blood; short-term sweep gas flow may need to be increased to ensure pore opening[41].

Anticoagulation during ECMO

Inflammation that develops as a result of blood contact with the non-biological ECMO circuit triggers coagulation. Immune-dysregulation, endothelial dysfunction and depletion of coagulation factors occur. Also, hypercoagulability is common in COVID-19 patients. Even though ECMO circuit and membranes are coated with heparin, systemic anticoagulation is required to prevent thromboembolic complications in ECMO treatment. One of the biggest problems during ECMO treatment is to reach and maintain therapeutic anticoagulation levels. Hemorrhagic and thromboembolic complications are major complications of ECMO therapy and are the most common causes of death. In ELSO study, it was reported that %20 of patients receiving ECMO support

had thrombotic complications[42]. In thrombotic complications, the most common cause is the lack of proper anticoagulation. The optimum hemostatic values and anticoagulant drugs used during ECMO are shown in Table 5 and Table 6.

Weaning from ECMO

Weaning from ECMO is a complex process, requires organized approach and a good ventilator management with comprehensive knowledge of ECMO physiology. Weaning is initiated when the underlying disease in the lungs is successfully treated and lung functions are recovered, improvements begin on the chest X-ray, FiO_2 < 0.45, PEEP < 10 cmH_2O or peak inspiratory pressure (PIP) <27 cmH_2O. If the ventilator settings still allow applying lung-protective ventilation strategies and CO_2 excretion is initiated by the natural lung then the ECMO blood flow is changed to adjust the pH value. According to blood gas controls, ECMO blood flow is gradually decreased to 1.5 L/min. The effectiveness of natural lung in removing CO2 is evaluated by taking blood gas before and after ML. When PCO_2 difference (pre and post ML) is less than 0.2-0.4 kPa (1.5-3.0 mmHg) the patient is considered as "balanced". This means that ML neither adds CO_2 to the patient's blood nor removes CO_2 from blood. CO_2 produced by the patient is completely cleared by the patient's own lungs. If arterial SaO_2 is sufficient, weaning from ECMO may be considered. FiO_2 is set to 0.35-0.50, the sweep gas is turned off. If turning off process is well-tolerated, sweep gas can be kept turned off for hours or all night long. If the ECMO weaning attempt fails, the sweep gas is switched on and the next day a weaning attempt is planned again. If blood gas maintains stabile and patient develops no tachypnea or dyspnea, the decision to wean from ECMO can be made. In patients receiving VV ECMO for respiratory support, the duration of support usually does not exceed 10 days[43].

Table 5. Optimum homeostatic values in ECMO patients

Parameters	**Recommended values**
Activated clotting time (ACT) (seconds)	180-220
International normalized ratio (INR)	1.3-1.5
R time in thromboelastography (seconds)	16-25
Maximum clot frequency in FibTEM (mm)	>10
Fibrinogen (mg/dL)	>100
Anti-thrombin activity (%)	70-80
Platelet count (mm3)	>80.000 (bleeding patient/high risk)
	>45.000 (no bleeding/low risk)
D-dimers **(µg/L)**	<300

Table 6. Anticoagulant agents used in ECMO treatment

Drug	**Advantages**	**Disadvantages**
Unfractionated Heparin (UFH)	Its mechanism and the drug itself are well known. Easy to antagonize (Protamine). Easy to monitor (aPTT/ACT).	Its effect is variable, it is not linear. It may cause HIT.
Low Molecular Weight Heparin (LMWH)	Easy to administer. Low risk for HIT induction.	It can accumulate in renal failure. Partially antagonizable. Not easy to monitor (anti-Xa levels).
Direct Thrombin Inhibitor (DTI)	Independent of AT levels. Good dose response. Doesn't induce HIT.	Has no antagonist. Coagulation inhibition is less in stasis areas. May have a ceiling effect on aPTT. May interact with INR measurement.
Antiplatelet agents	Inhibits coagulation at the initiation point. May reduce platelet consumption	Anticoagulant effect is not enough. Not enough evidence.

ACT: *Activated coagulation time*, aPTT: *Activated partial thromboplastin time*, AT: *Antithrombin*, HIT: *Heparin-induced thrombocytopenia*, INR: *International standardized ratio*

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Review Article
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An Insight Into The Neurological Manifestations Of Covid-19 In The Emergency Department

Sohil POTHİAWALA
Senior Consultant, Department of Emergency Medicine, Woodlands Health Campus, Singapore

Abstract

As the COVID-19 pandemic continues to evolve, there is an increasing recognition that patients with COVID-19 infection may present with neurological symptoms as the primary manifestation. These symptoms can be related to Central Nervous System like headache, altered mental status, acute encephalitis, acute stroke, cerebral hemorrhage, seizures; or the peripheral nervous system like anosmia, hypogeusia, muscle pain and weakness, movement disorders, acute myelitis and Guillain–Barré syndrome, etc. In the absence of the classic presentation with fever or respiratory symptoms, an initial neurological presentation serves as a diagnostic dilemma. This review will aid acute care physicians to have a high index of clinical suspicion to consider COVID-19 infection as a differential diagnosis for any patient presenting with primary neurologic manifestations. This will help avoid delayed diagnosis, as well as reduce exposure to health care providers.

Keywords: COVID-19; SARS-CoV-2; neurological manifestations; emergency department

Introduction

Coronavirus disease 2019 (COVID-19) has been declared a global pandemic by the World Health Organization. Majority of COVID-19 cases present with an acute respiratory infection, the commonest symptoms being fever, sore throat, cough, shortness of breath, myalgia and pneumonia. Severe cases can progress to complications like acute respiratory distress syndrome and multiorgan failure. In addition to respiratory symptoms, some patients present with gastrointestinal symptoms like diarrhea, abdominal pain, nausea or neurological symptoms like headache, altered level of consciousness paresthesia, anosmia or hypoguesia. Patients with severe COVID-19 are more prone to suffer from neurological symptoms compared to those with mild or moderate disease.[1] As COVID-19 cases continue to rise, there is an increasing recognition of neurological signs as the only initial clinical manifestation of COVID-19 infection. This review on these neurological manifestations will aid acute care physicians to have a high index of clinical suspicion and also to adopt necessary precautions when managing these patients in the Emergency Department (ED).

Discussion

SARS-CoV-2 primarily affects the respiratory system, but it is also known to invade the nervous system, similar to other coronaviruses like SARS-CoV-1 and MERS-CoV. The exact mechanism of neurological involvement is not yet known, but studies have proposed hematogenous spread or spread through the retrograde axonal route. [2, 3] Infection of endothelial cells of the blood vessels, which also have ACE-2 receptors, allows the hematogenous spread of the virus, which then crosses the blood-brain barrier, leading to various neurological disorders. [4]

Another possible route of entry for the virus from the nose to the brain, especially in patients presenting with anosmia, hypoguesia, is through infection of the olfactory neurons via the cribriform plate.[5] Direct viral invasion of the brain cells leading to encephalitis is also proposed. Neurological manifestations may also occur in COVID-19 secondary to the inflammatory cytokine storm and suppressed immunologic response of infection; or due to hypoxia from severe respiratory involvement of the virus.[6] SARS-CoV-2 virus enters the cells of the nervous system and skeletal muscles by binding to the angiotensin-converting enzyme-2 (ACE-2) receptor on their surface, thus presenting with symptoms suggestive of acute myelitis and Guillain-Barre Syndrome.[7]

Neurological complications of COVID-19 may co-relate with the disease severity, but the primary goal in the ED is to identify those patients who present only with neurological symptoms as the primary manifestation of COVID-19. In the absence of fever and respiratory symptoms, this can be very challenging and serves as a diagnostic dilemma. Since these patients may be contagious even in the absence of any

Corresponding Author: Sohil POTHİAWALA **e-mail:** drsohilpothiawala@yahoo.com
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respiratory symptoms, such atypical presentations can lead to missed diagnosis. It can also increase the risk of exposure to other patients and healthcare workers caring for the patient. Hence measures should be taken to isolate these patients if there is any suspicion in the ED.

Certain vague neurological symptoms like headache, giddiness and altered level of consciousness may be due to underlying sepsis in COVID-19 patients. They may not represent a true neurological disorder. Some patients with COVID-19 show more specific neurological signs and symptoms. These can be divided into Central Nervous System (CNS) and peripheral nervous system (PNS) symptoms. The CNS symptoms include headache, altered mental status, acute encephalitis, acute stroke, cerebral hemorrhage and seizures. PNS manifestations include symptoms of peripheral nerve or skeletal muscle involvement, like anosmia, hypogeusia, muscle pain and weakness, movement disorders, acute myelitis and Guillain–Barré syndrome.

Headache can be a non-specific symptom of any viral illness, but it can also be a manifestation of viral encephalitis or meningitis. Similarly, the differential diagnosis of altered mental status in a COVID-19 patient includes viral encephalitis or meningitis, encephalopathy, seizures and ischemic or hemorrhagic stroke.[6]

Thus, any patient who presents to the ED with headache, which is out of proportion to the fever and is associated with altered mental status and/or vomiting, should warrant further evaluation for encephalitis. RNA of SARS-CoV-2 has been detected in the cerebrospinal fluid of a patient diagnosed with encephalitis.[8]

COVID-19 infection is increasingly recognized to be associated with hypercoagulable state, as noted by elevated D-dimer levels. This may lead to a resultant increase in thrombo-embolic events, especially acute ischemic stroke, pulmonary embolism and rarely cerebral venous sinus thrombosis. Although rare compared to ischemic stroke, infection of endothelial cells of the blood vessels by the virus may increase the intra-luminal pressure of cerebral blood vessels, which combined with coagulopathy in COVID-19 patients, can lead to intracerebral hemorrhage.[4] The occurrence of seizure in a COVID-19 patient can be due to of invasion of the virus in CNS leading to a primary brain infection, or it may be secondary to reduced seizure threshold in a known epileptic patient. Electrolyte disturbances as well as neuronal injury due to hypoxia in severe pneumonia, sepsis or multiorgan failure may also precipitate seizures.[6]

A patient presenting with anosmia, dysgeusia or neuralgia should alert the physician regarding COVID-19 related involvement of the peripheral nerve involvement.[9] Involvement of skeletal muscle in COVID-19 may be due to invasion of the skeletal muscles by the virus through ACE-2 receptors, causing damage to the skeletal muscle fibers, as noted by elevated creatinine kinase and lactate dehydrogenase (LDH) levels[1], and theese patients may present with complaints of myalgia and weakness. A robust immune response and associated cytokine storm, often seen in patients with severe COVID-19, may even lead to renal failure and rhabdomyolysis.[10]

Guillain–Barré syndrome (GBS) is an immune-mediated disorder of the peripheral nerves and nerve roots. There are few case reports of GBS associated with COVID-19, but further studies are needed to determine if SARS-CoV-2 causes production of antibodies against the ganglioside.[11] Moreover, GBS due to Covid-19 should be distinguished from neuro-myopathy that occurs late in the course of severe disease states.[12]

Hence, during this evolving pandemic, emergency and acute care physicians should consider COVID-19 as a differential diagnosis in any patient presenting to the ED with central or peripheral neurological symptoms.[1] A detailed neurological examination followed by appropriate investigations, and early consult with a neurologist can help differentiate between primary or secondary involvement of the CNS/PNS in COVID-19 patients.

Conclusion

The COVID-19 pandemic presents emergency physicians with a unique challenge of patients presenting with neurological symptoms as the primary manifestation of COVID-19. These neurological symptoms may even precede classical presentation of typical respiratory symptoms. Thus, emergency physicians should consider COVID-19 infection as a differential diagnosis for any patient presenting to the ED with primary neurologic manifestations. This will help avoid delayed diagnosis, as well as reduce exposure to health care providers by adopting necessary precautions when managing these patients.

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Original Article
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Inflammatory Markers And Blood Gas Analysis In Determining The Severity Of Chronic Obstructive Pulmonary Disease

İbrahim Çaltekin[1], Emre Gökçen[1], Levent Albayrak[1], Dilek Atik[1], Atakan Savrun[2], Mikail Kuşdoğan[1], Hasan Burak Kaya[1], Sevilay Vural[1], Şeyda Tuba Savrun[2]

[1] Department of Emergency Medicine, Yozgat Bozok University Faculty of Medicine, Yozgat-Turkey

[2] Department of Emergency Medicine, Ordu University Faculty of Medicine, Ordu-Turkey

Abstract

Aim: This study aimed to evaluate the severity of the disease using inflammatory markers in patients with Chronic Obstructive Pulmonary Disease (COPD) who admitted to the emergency department.

Materials and Methods: 193 COPD patients who applied to the emergency department were included in this retrospective study. Patients were divided into two groups according to the severity of COPD. The presence of type 1 and type 2 respiratory failure was used to create Group 2 (severe, very severe, life-threatening) and in the absence, Group 1 (mild, moderate). Inflammatory markers such as Neutrophil / lymphocyte ratio (NLR), Platelet / lymphocyte ratio (PLR), Lymphocyte / monocyte ratio (LMR) and disease severity were evaluated for both groups.

Results: The high COPD severity group (Group 2) had higher NLR and PLR values ($p < 0.001$, $p < 0.001$, respectively), and LMR values were lower ($p < 0.001$). There was infection in 46.2% of Group 2, while this rate was 13.5% in Group 1 ($p < 0.001$).

Conclusion: As the severity of the disease increases, NLR, PLR values increase, and LMR value decreases. This indicates that COPD attack will be severe in the presence of infection in COPD patients.

Keywords: Blood gas analysis; emergency medicine; inflammatory markers; chronic obstructive pulmonary disease (COPD)

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is defined as a permanent restriction of airflow and respiration in the airways and alveoli as a result of exposure to harmful particles and gases[1]. COPD is one of the leading diseases that cause serious morbidity and mortality in the world[2]. Along with increased admissions of COPD patients at the emergency department day by day[3], dyspnea, decrease in exercise capacity, sputum increase are the most common admission symptoms[4].

In addition, it is a progressive disease resulting from chronic irreversible peripheral alveolar and lung parenchyma caused by increased numbers of cells involved in the inflammatory response such as alveolar macrophage, neutrophil, T lymphocyte and release of proinflammatory cytokines[5]. Changes in hematological inflammatory markers of acute exacerbation COPD (AECOPD) cases have been shown to develop[6].

Neutrophil / lymphocyte ratio (NLR) was associated with lung functions, COPD acute attack and poor outcome[7], while Platelet / lymphocyte ratio (PLR) was found to be determinant for COPD acute exacerbation. Lymphocyte / monocyte ratio (LMR), on the other hand, is a new hematological inflammatory marker that has recently been detected in patients with pulmonary embolism, lung cancer, and coronary artery disease[8-10]. In addition, blood gas analysis is a valuable test used to evaluate COPD attack severity[11]. However, complete blood count (CBC) is an easily accessible, cheaper, and more widely used test[12].

Inflammatory processes in COPD are associated with severity of COPD attack. Also, the CBC test, which can be used just like blood gas in COPD attack but is more practical, provides a separate benefit in predicting the severity of COPD. In this study, it was aimed to evaluate the severity of disease using both known inflammatory markers such as NLR and PLR and new inflammatory markers such as LMR in COPD patients admitted to the emergency department.

Material and Methods

This retrospective study included 193 COPD patients over the age of 18 who applied to the emergency department between September 1, 2018 and August 31, 2019. Ethical approval was obtained from the local ethics committee of the University (Protocol: 2017-KAEK-189_2019.10.30_17). The authors adhered to the principles of the Helsinki Declaration during the study.

Corresponding Author: Hasan Burak KAYA **e-mail:** hasanburakkaya@hotmail.com
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Records of the patients (age, gender, clinical status, clinical course, blood samples, files and electronic records) who admitted to the emergency department and followed up with COPD according to ICD-10 codes (J44.0, J44.1, J44.8, J44.9) were evaluated. All data were used in analyzing of inflammatory hematological parameters (neutrophil/lymphocyte, platelet/lymphocyte, lymphocyte/monocyte ratio), C-reactive protein (CRP), attack severity and arterial blood gas values, if any.

COPD severity assessment even if there is no blood gas analysis in mild attack cases was evaluated as recommended by Burge et al.[13]. The patients were divided into two groups according to the severity of COPD. The presence of type 1 and type 2 respiratory failure was used to create Group 2 (severe, very severe, life-threatening) and in the absence, Group 1 (mild, moderate). For both groups, blood gas analysis, inflammatory markers and disease severity were evaluated according to the determined criteria. Furthermore, with or without any chest CT or Xray findings, with an increase in purulence of sputum, fever, increased white blood cell counts, with bacterial growth in sputum, secretions or BAL sample were taken, were accepted as the presence of infection.

Patients under 18 years of age who had congestive heart failure, chronic liver disease, diabetes mellitus, metabolic syndrome, deep vein thrombosis, rheumatic disease, inflammatory disease that may affect hematological inflammatory parameters were excluded from our study. In addition, patients who had deficiencies in electronic file records, detected laboratory errors, and inaccessible blood samples were not included in the study. However, patients who did not have blood gas parameters and who met the inclusion criteria were classified in group 1, but these 22 patients were not included in the analyzes performed according to blood gas.

Evaluation tools

Acute Exacerbation of COPD

Worsening of the patients' condition beyond normal day-to-day activity that required additional treatment with oral or intravenous corticosteroids or antibiotics; admission to an emergency for worsening of symptoms; a hospital admission with a new diagnosis of COPD.

Severity of COPD

In 2003, Burge et al. suggested that the severity of the disease can be assessed in 5 categories, regardless of whether patients with COPD had gas in the blood[13].

Mild: An exacerbation with antibiotics in the treatment but without systemic corticosteroids (assuming no respiratory failure if there is no blood gas).

Moderate: An exacerbation using systemic corticosteroids with or without antibiotics in treatment (assuming no respiratory failure if there is no blood gas).

Severe: Exacerbation (pO2 <60 mmHg, pCO2 <45 mmHg) with type 1 respiratory failure and hypoxemia, but without acidosis and carbondioxide retention.

Very Severe: Exacerbation with type 2 respiratory failure that can be compensated by hypoxia but with retention of carbondioxide without acidosis (pH>7.35, pO2 <60 mmHg, pCO2>45 mmHg, H + <44 nM).

Life-Threatening: The disease was classified according to criteria specified as exacerbation (pH <7.35, pCO2>45 mmHg, H + > 44 nM) with Type 2 respiratory failure accompanied by decompensated acidosis and carbon dioxide retention.

Laboratory Analyses

Hematological parameters were studied in tubes containing ethyleneditritrile-tetraacetic acid (EDTA) using the XN-1000 hematology analyzer (Sysmex Corporation, Kobe, Japan) within the first hour to prevent errors in the parameters. CRP was studied with serum gel tubes and Cobas 6000 analyzer (Roche Diagnostics, Mannheim, Germany). Blood gas samples were studied with Siemens Rapidlab 1265 blood gas analyzer (Siemens Healthcare Diagnostics, Medfield, MA, USA) within the first 10 minutes, protecting the cold chain with heparin injectors.

Statistical Analyses

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS Inc; Chicago, IL, USA) version 20.0 software. The variables were determined using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to evaluate whether or not they are normally distributed. The independent sample t-test was used to compare continuous variables with normal distributions and the Mann-Whitney U test was used to compare variables with non-normal distributions. Analysis results of different variables were given as mean ± standard deviation, median (minimum-maximum), n (%) by investigating the test results. The Chi-square test or the Fischer's exact test (when the Chi-square test assumptions do not hold due to low expected cell counts), where appropriate, was used to compare the proportions in different groups. The relationship of inflammatory markers with COPD severity was evaluated with ROC analysis, and sensitivity and specificity of the values were calculated. A value of $p<0.05$ was accepted as statistically significant.

Table 1. Demographic data and clinical parameters of patients

Variables		group 1 (n=74)	group 2 (n=119)	p value
Age		69.01±10.66	73.20±12.44	0.017*
Gender, n (%)	male	36 (48.6)	74 (62.2)	0.647µ
	female	38 (51.4)	45 (37.8)	
Fever, n (%)	yes	6 (8.1)	34 (29.4)	<0.001µ
	no	68 (91.9)	85 (70.6)	
Infection, n (%)	yes	10 (13.5)	55 (46.2)	<0.001µ
	no	64 (86.5)	64 (53.8)	
Hospitalization, n (%)	yes	64 (86.5)	35 (29.4)	<0.001µ
	no	10 (13.5)	84 (70.6)	
Hospitalization time, median (min-max)		0 (0-9)	5 (0-30)	<0.001α

*: Student T test, α: Mann Whitney U test, µ: Chi-Square test
Data not normally distributed was shown as median (min-max.),
Normally distributed data was shown as mean ± standard deviation.

Results

Table 1 shows the comparison of demographic data and clinical parameters of patients with low attack severity (Group 1) and high attack severity (Group 2). The mean age of the patients with low attack severity (n = 74) was found to be 69.01 ± 10.66 years, and the mean age of the patients with severe attack (n = 119) was 73.20 ± 12.44 years. While 46.2% of the group with higher attack severity had infection, this rate was 13.5% in the group with lower attack severity (p <0.001).

Table 2 shows the evaluation of hematological and inflammatory markers of both groups. The group with higher COPD severity had higher NLR and PLR values (p <0.001, p <0.001, respectively), and LMR values were lower (p <0.001).

Blood gas analysis in both groups is shown in Table 3. While the pH, pO2 values of Group 2 were lower (p <0.001, p <0.001, respectively), PCO2, HCO3, H values were higher (p <0.001, p = 0.004, p = 0.002, respectively).

ROC analysis of inflammatory markers according to the severity of COPD disease is shown in Figure 1. In determining the severity of the disease, 4.33 cut off value had a sensitivity of 65% and a specificity of 66% for NLR.

While 94 (48.7%) COPD patients were hospitalized from the emergency department for clinical and intensive care, 99 (51.3%) COPD patients were discharged.

Discussion

According to the main findings of this retrospective study, the group with high COPD severity was found to have higher NLR, PLR values, and lower LMR values. At the same time, while 46.2% of the group with higher attack severity had infection, this rate was found to be 13.5% in the group with lower attack severity.

Table 2. Evaluation of hematological and inflammatory markers with the severity of COPD

Variables	Group 1 (n=74)	Group 2 (n=119)	p value
Wbc (103uL)	9.19 (2.85-20.89)	11.50 (4.62-31.48)	0.045α
Neutrophil (103uL)	5.94 (1.23-16.26)	7.76 (2.43-29.03)	0.001α
Lymphocyte (103uL)	1.80 (0.49-3.91)	1.42 (0.17-6.47)	<0.001α
Monocyte (103uL)	0.73 (0.11-2.14)	0.79 (0.05-1.80)	0.396α
PLT (103uL)	242.42±68.84	247.08±68.43	0.647µ
CRP (mg/dl)	7.55 (1-155.5)	26.10 (1-357)	<0.001α
NLR	3.60 (0.89-23.78)	5.36 (1.08-24.47)	<0.001α
PLR	132.73 (51.74-465.31)	169.40 (41.89-1638.89)	<0.001α
LMR	2.53 (0.61-9.78)	1.77 (0.32-7.27)	<0.001α

*: **Student T test**, α: **Mann Whitney U test**, µ: **Chi-Square test**
Wbc: White blood cell, PLT: platelet, CRP: C-reactive protein; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; LMR: lymphocyte to monocyte ratio
Data not normally distributed was shown as median (min-max.),
Normally distributed data was shown as mean ± standard deviation.

Table 3. Evaluation of the blood gas analysis with the severity of COPD

Variables	Group 1 (n=52)	group 2 (n=119)	p value
pH	7.40±0.43	7.37±0.78	<0.001*
pO2	55.50±19.54	39.82±12.30	<0.001*
pCO2	37.80 (23.00-66.50)	45.40 (24.80-105.60)	<0.001α
HCO3	24.35 (14.90-38.20)	25.80 (15.10-45.30)	0.004α
H	39.2 (29.76-47.33)	41.36 (28.91-85.51)	0.002α

*: **Student T test**, α: **Mann Whitney U test**
pH: Potential of Hydrogen, pO2: partial oxygen pressure, pCO2: partial carbon dioxide pressure, HCO3:bicarbonate, H: Hydrogen
Data not normally distributed was shown as median (min-max.),
Normally distributed data was shown as mean ± standard deviation.

Although there are various classifications for COPD, the most commonly used classification is the GOLD 2011. This classification is supported by symptoms, the severity of airflow limitation, history of exacerbation and presence of comorbidity[14]. Other known classification methods are BODE index (Body mass index, airflow Obstruction, Dyspnoea and Exercise), mBODE (BODE modified in grading of walked distance), ADO (Age, Dyspnoea, airflow Obstruction), DOSE (Dyspnoea, Obstruction, Smoking, Exacerbation)[15]. However, the classification made by Burge et al.[13] for the severity of disease of a patient who applied to the emergency department with an attack, seems to be more useful and practical because there is no blood gas requirement for COPD patients who apply with a light attack and no need for spirometry.

Potential of Hydrogen (pH), partial carbon dioxide pressure (pCO2), partial oxygen pressure (pO2) and bicarbonate (HCO3-) are parameters that show both the acid-base balance and respiratory functions of a person obtained as a result of blood gas test[16]. Arterial blood gas analysis is an indirect indicator of lung capacity and functions[17]. In various studies, it is known that venous blood gas, end-tidal carbon dioxide (ETCO2), pulse oximetry measurements were tried in COPD patients instead of using arterial blood gas. These studies show that there is an effort to use minimally invasive and non-invasive methods to determine the severity of the attack in COPD patients[18-20]. In a case with a severe AECOPD, pH and pO2 decreased, while PCO2 was expected to increase, pH significantly decreased, and PCO2 significantly increased. In the patient's intensive care follow-up, the need for non-invasive positive pressure ventilation (NIPPV), endotracheal intubation (ETI) was revealed[21].

In our study, in accordance with the literature, as the attack severity increased, blood pH, pO2 decreased and PCO2 increased. NLR is an inflammatory marker obtained by dividing the absolute neutrophil count by the absolute lymphocyte count. PLR is an inflammatory marker obtained by dividing the number of absolute platelets to the absolute number of lymphocytes[22]. It was reported that both markers, such as CRP and procalcitonin, showed an effective increase in inflammatory processes[23]. While Rovina et al.[24] determined the rate of NLR as 5.38 ± 4.6 in hospitalized patients with COPD attack, in our patients with high attack severity, this rate was found to be 5.36 (1.08-24.47). Demirtaş et al.[26] found the cut-off value for NLR was 9.39, with a sensitivity of 71.7% and a specificity of 61.1% in COPD attack patients. In our study, 4.33 cut off value had a sensitivity of 65% and a specificity of 66% for NLR according to the severity of COPD disease.

LMR is an inflammatory marker obtained by dividing the absolute lymphocyte count by the absolute monocyte count. Although it has been shown as a new prognostic biomarker that has been a precursor of the inflammatory response, like NLR and PLR, especially in cases of malignancy, unlike NLR and PLR, for example in stroke cases, its low value represents significance[9,25]. In a study, examining NLR, PLR, and LMR, although a relationship was found between NLR increase and death in COPD patients, it was reported that a similar relationship for PLR and LMR values was not found[27]. In our study, in the group with high attack severity, an increase in NLR and PLR and low LMR values were found significant. This shows that just like NLR and PLR, low LMR can be used as a predictor of severe COPD attack. In COPD patients, coexistence of infection is a very common condition[28].

In our study, the presence of infection is an indication of increased attack severity. Both the presence of infection and the cumulative effect of the attack results in an increase of inflammatory markers such as CRP, NLR and PLR, and reduction of LMR. Invasive and troublesome methods such as arterial blood gas and spirometry are used in the evaluation of COPD severity or during the diagnosis[29,30]. Furutate et al.[31] indicates that COPD severity can be predicted with some hematological inflammatory markers. In addition, although NLR and PLR are frequently used hematological markers[23], to the best of our knowledge, in the literature, LMR for COPD attack severity has not been studied.

Study Limitations

There are some limitations in our study. First, not having arterial blood gas analysis in all of our patients can be considered as a limitation, but it is also an advantage in terms of providing evaluation in patients with mild symptoms with-

out blood gas in the emergency practice. At the same time, because our study is a single-centered study, the limited number of patients is another limitation.

Conclusion

Although there are studies in the literature that previously examined the relationship between inflammatory markers and COPD disease, to the best of our knowledge, there is no two-way study that could evaluate the severity of the disease with inflammatory markers, with or without blood gas parameters. As the disease severity increases, the hospitalization rates increase and also NLR, PLR values increase. In addition, the newly used LMR value is decreasing. From another point of view, changes in inflammatory markers in COPD exacerbation cases directly affect disease severity and hospitalization rates. This shows that COPD attack will be severe in the presence of infection in COPD patients. The CBC test, which can be used just like blood gas in COPD attack but is more practical, provides a separate benefit in predicting the severity of COPD.

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Original Article
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Diagnosing Meningitis at the Emergency Department – How Accurate are we?

Jen Heng PEK[1], Dennis Clement FORSYTHE[2], Ling TİAH[2]

[1]Department of emergency Medicine, Sengkang, general Hospital, SingHealth, Singapore
[2]Department of accident and emergency Changi general Hospital, SingHealth, Singapore

Abstract

Objectives: Meningitis is associated with a high mortality rate and neurologic sequelae are common among survivors. However, it is a diagnostic challenge and can be under-recognized at the Emergency Department (ED). We aimed to determine the accuracy of the diagnosis of meningitis made in the ED and identify features associated with diagnostic accuracy.

Methods: A retrospective review of case records was carried out. Cases presenting to the ED an urban tertiary center from 2013 to 2017 with a diagnosis of meningitis in its records were selected. Information about patient demographics, clinical features and course were collected for analysis. Accuracy was determined by comparing the ED diagnosis with discharge diagnosis on inpatient record.

Results: There were 83 cases of meningitis diagnosed in the ED during the study period. The median age was 36 (range 15 to 96) years old and 54 (65.1%) of the patients were male. Fever (n=76, 91.6%), headache (n=50, 60.2%) and altered mental status (n=24, 28.9%) were the most common symptoms and neck stiffness (n=28. 33.7%), Glasgow Coma Score less than 15 (n=16, 19.3%) and Kernig's sign (n=11, 13.3%) were the most common signs. The accuracy of ED diagnosis of meningitis was 28.9%. Among the cases which were not meningitis, the most common diagnoses were other infections followed by conditions involving the musculoskeletal and central venous systems. Vomiting (OR 3.33, 1.24-9.09, p=0.021) was the only feature associated with diagnostic accuracy.

Conclusion: Meningitis is a great mimicker and can be difficult to diagnose in the ED. Given the lack of clinical features which can be used to differentiate meningitis from other conditions, a high index of suspicion is required so that interventions can be promptly initiated to reduce mortality and morbidity.

Keywords: Diagnosis, Emergency Department, Meningitis

Introduction

Meningitis is defined as the inflammation of the meninges which consist of the pia, arachnoid and dura mater. It is typically characterised by an elevated number of white blood cells in the cerebrospinal fluid. Causes include infection due to bacteria, viruses, fungi and parasites, as well as medications such as non-steroidal anti-inflammatory drugs. Streptococcus pneumoniae and Neisseria meningitidis are the main causative organisms responsible for community-acquired bacterial meningitis in adults.

There are approximately 1.2 million cases of meningitis per annum worldwide[1]. Meningitis is associated with high mortality rates in the world and is among the 10 most common infectious disease contributors. It is responsible for approximately 135,000 deaths throughout the world each year[2]. Mortality is higher in the elderly and healthcare associated bacterial meningitis[3]. Neurologic sequelae are common among survivors.

The diagnosis of meningitis is crucial but may prove to be challenging at the Emergency Department (ED) as patients may present with non-specific signs and symptoms. A study of 650 patients showed mimics were common and included right-sided pneumonia, gastroenteritis, otitis, tonsillitis, exanthema subitum, and urinary tract infections[4]. Therefore, the aims of this observational study are to determine the diagnostic accuracy of meningitis in the ED and to identify features associated with diagnostic accuracy. We hypothesize that the accuracy was low as diagnosis of meningitis can be difficult in the ED.

Materials and Methods

Setting

This study was conducted in the ED of an urban tertiary hospital which had an annual attendance of about 150,000 patients.

Design

This was a retrospective study based on the review of case records. All cases that presented to the ED from 1 January 2013 to 31 December 2017 with the ICD-10 diagnosis codes containing meningitis were included. The patients' medical

Corresponding Author: Jen Heng PEK **e-mail:** pek.jen.heng@singhealth.com.sg
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records were accessed for data collection and tabulated in a standardized form. Information including demographics, clinical features, investigations performed, clinical progress in the ED and hospital, length of the patient's stay in the hospital, as well as the diagnosis in ED and at discharge were collected for analysis. Any information which was not documented was analysed as not present. The discharge diagnosis on inpatient record was used as the standard to determine the accuracy of the diagnosis at the ED.

This study was approved by Institutional Review Board (CIRB 2018/2241). Waiver of patient consent was granted.

Statistical Methods

Statistical analysis was performed using SPSS version 22 (SPSS, Chicago, L). Categorical and continuous data were presented as frequency with percentage and median with range respectively. Association between categorical variable was assessed using chi-square test.

RESULTS

Patient Characteristics

There were 83 cases of meningitis diagnosed in the ED during the study period, average to about 17 cases per year. (Table 1).

Clinical Features

At presentation to the ED, fever, headache and altered mental status were the most common symptoms, whereas neck stiffness, Glasgow Coma Score less than 15 and Kernig's sign were the most common signs (Table 2). The classic triad of fever, headache and neck stiffness was only present in 16 (19.3%) patients.

Table 1. Patient Characteristics

Median age, in years (range)	36 (15 to 96)
Gender	n (%)
Male	54 (65.1)
Female	29 (34.9)
Race	n (%)
Chinese	37 (44.6)
Malay	25 (30.1)
Indian	13 (15.7)
Others	8 (9.6)

Investigations Performed

Computed Tomography of the head (CT head) was performed at the ED for 79 (95.2%) patients. Only 2 scans showed features suggestive of meningitis – one was reported as mild diffuse brain parenchymal edema as evidenced by crowding of sulci and relative narrowing of the basal cisterns, the other was reported as suggestion of diffuse leptomeningeal enhancement, which may be due to meningitis in the context of sepsis.

Blood culture was taken for 77 (92.7%) patients, with Streptococcus agalactiae (n=3, 3.6%) being the most common organism detected. Lumbar puncture was performed in 29 (34.9%) patients. Among these, cerebrospinal fluid culture grew Streptococcus agalactiae, Streptococcus intermedius and Eikenella corrodens. (Table 3)

Clinical Management at the ED

All patients were admitted to the hospital for further care. Empirical antibiotic coverage was initiated at the ED according to institutional guidelines in 73 (88.0%) patients. Acyclovir was given in 28 (33.7%) patients and dexamethasone in 3 (3.6%) patients. One (1.2%) patient required emergent right frontal extra ventricular drain insertion for relief and monitoring of raised intracranial pressure.

Clinical Outcome

The mortality in this case series was 3.6%. Two (2.4%) patients had residual neurological deficits at discharge from

Table 2. Clinical features

Clinical symptoms	n (%)
Fever	76 (91.6)
Headache	50 (60.2)
Altered Mental Status	24 (28.9)
Vomit	22 (26.5)
Neckache	18 (21.7)
Lethargy	9 (10.8)
Photophobia	8 (9.6)
Seizure	7 (8.4)
Giddy	5 (6.0)
Clinical signs	n (%)
Neck stiffness	28 (33.7)
Glasgow Coma Score less than 15	16 (19.3)
Kernig's sign	11 (13.3)
Abnormal pupils	3 (3.6)
Neurological deficit	3 (3.6)
Brudzinski's sign	2 (2.4)

Table 3. Patient Characteristics

Blood Culture	n (%)
No bacterial growth	67 (80.7)
Streptococcus agalactiae	3 (3.6)
Klebsiella pneumonia	2 (2.4)
Streptococcus pneumonia	1 (1.2)
Mixed bacterial growth	1 (1.2)
Skin contaminant	3 (3.6)
Cerebrospinal Fluid Culture	n (%)
No bacterial growth	27 (32.5)
Streptococcus agalactiae	1 (1.2)
Mixed bacterial growth	1 (1.2)

Table 4. Diagnosis at Hospital Discharge

Diagnosis	n (%)
Meningitis	24 (28.9
Other infections	33 (39.8)
Upper respiratory tract infection	11
Viral fever	7
Sepsis, source unspecified	4
Pneumonia	4
Sinusitis	2
Cellulitis	2
Urinary tract infection	1
Otomastoiditis	1
Dengue	1
Musculoskeletal conditions	12 (14.5)
Headache	11
Neck pain	1
Neurological conditions	9 (10.8)
Seizure	3
Cerebral abscess	1
Intracranial hypertension	1
Transient ischemic attack	1
Encephalopathy	1
Syncope	1
Central cord stenosis	1
Psychiatric conditions	3 (3.6)
Drug withdrawal	1
Schizophrenia	1
Bipolar disorder	1
Metabolic conditions	2 (2.4)
Diabetes mellitus	1
Gout	1

the hospital. The median length of hospital stay was 4 (range 1 to 42 days), including time spent in the rehabilitation ward.

Accuracy of ED Diagnosis

Among these 83 cases with meningitis diagnosed at the ED, 24 were diagnosed with meningitis based on the discharge diagnosis on inpatient record, giving an accuracy of 28.9%. The most common diagnoses at discharge for those without meningitis included other infections followed by conditions involving the musculoskeletal and central venous systems (Table 4).

Vomiting was the only significant predictor for an accurate ED diagnosis of meningitis among all cases of meningitis suspected in ED, OR 0.30 (95% CI 0.11-0.83, p=0.021).

Reattendance

Thirteen (15.7%) cases were diagnosed by ED as meningitis at a second attendance. The median number of days between the first and second attendances was 2 (Range 0 to 5). The misdiagnoses at the first attendance included upper respiratory tract infection (n=6, 46.2%), viral fever (n=5, 38.6%), benign paroxysmal position vertigo (n=1, 7.6%) and seizure (n=1, 7.6%). Among these, 6 (46.2%) patients were diagnosed with meningitis based on the discharge diagnosis on inpatient record. The accuracy of ED diagnosis of meningitis was not significantly different for this group of patients (p=0.135).

Discussion

In our study, the accuracy of meningitis diagnosed at the ED was low. Although meningitis was diagnosed in the ED, the inpatient team had decided otherwise following hospital admission. We postulated that the low accuracy could be due to 4 main reasons. Firstly, ED physicians might have erred on the side of caution by assuming the worst and treating the patients as for meningitis. This lower threshold for diagnosis and treatment was likely due to the significant morbidity and mortality associated with this condition. Next, ED physicians could not rely on pertinent features of history or physical examination to make the diagnosis as these patients had non-specific signs and symptoms. For instance, the classic triad of fever, headache and neck stiffness was present in less than 20% of the patients. Similarly, meningeal signs such as neck stiffness was present in about a third of patients while Brudzinski's sign and Kernig's sign were present less commonly. Furthermore, even when present, no isolated feature had been reported to be diagnostic of meningitis[5-7].

Lastly, the length of stay at the ED was shorter than at the inpatient unit. Additional time may be necessary for further clinical evaluation, performing additional investigations and observing the patient's clinical progress in order to improve the diagnostic accuracy of meningitis.

We also found that patients who had experienced vomiting were more likely to have an accurate diagnosis of meningitis at the ED. This could be explained by the following mechanism in meningitis, the intracranial pressure may be elevated as a result of the infectious and/or inflammatory processes, thus stimulating area postrema which is the vomiting centre of the brain, leading to vomiting. However, further research involving different patient populations in the ED setting would be necessary to evaluate this finding before any recommendation can be made for its utility in the ED. For now, we emphasize that ED physicians would need to take into consideration the entire clinical context of the patient and use relevant investigations to confirm or refute the diagnosis.

CT head may be performed when evaluating a patient for meningitis. Potential findings include acute cerebral swelling; moderate widening of basal cisterns, interhemispheric fissure, and subarachnoid convexity space; ventricular widening; subdural collection; focal cortical necrosis; cerebral infarcts; contrast enhancing basal meninges, ependymitis, or generalized cerebral atrophy[8]. CT head could also be used to exclude other intracranial pathology such as a mass lesion which may account for the patient's presentation. In our study, CT head was performed in more than 95% of patients but the incidence of positive finding for meningitis was very low. As with previous reports, CT scan findings may be normal in more than 50% of patients, hence the diagnosis of meningitis could not made on the basis of imaging studies alone[9,10].

Another important diagnostic study to perform in a patient with meningitis would be lumbar puncture. However, caution must be taken in selecting appropriate patients as lumbar puncture was responsible for up to 30% of deaths in the acute stages of meningitis as a result of coning from raised intracranial pressure[11]. Thus, CT head should be done in patients showing signs of raised intracranial pressure before performing lumbar puncture to avoid this fatal complication. In our setting, lumbar puncture was not routinely performed in our ED but was carried out by the inpatient team upon admission. As a result, not all patients had lumbar puncture performed. Lumbar puncture was performed in 29 patients after evaluation by the inpatient team. Of these, 24 patients were eventually diagnosed with meningitis. Cerebrospinal fluid culture was only positive in 2 patients and this was likely due to our institutional practice as antibiotics were administered early at the ED before lumbar puncture was performed at the inpatient unit.

In our study, 88% of patients who were admitted by the ED with presumed meningitis were commenced on guideline-appropriate antibiotics for meningitis. In comparison to this, a study conducted in Netherlands showed that only 33% of patients received appropriate antibiotics in compliance with the Dutch guidelines[12]. The need to administer antibiotics quickly in meningitis must be highlighted as delay between presentation and antibiotic administration was associated with worse patient outcomes[13,14]. Therefore, ED physicians must be aware of institutional guidelines for coverage. An accessible reference guide or use of an electronic prompt are viable options which can serve as a useful reminder as meningitis was uncommonly encountered in the ED. On the other hand, there was no well-designed studies available to assist the ED physician in deciding when to withhold antibiotics when viral meningitis is suspected. In our institution, all cases of meningitis would be admitted for inpatient evaluation. It may be possible to discharge a patient with viral meningitis to an early outpatient follow-up, with advice to return to the ED immediately if unwell[15]. However, risk assessment must be performed and discussed with the patient and/or family.

Adjunctive therapies of meningitis included acyclovir and dexamethasone. Acyclovir was indicated when there was concern for concomitant encephalitis due to herpes simplex virus. Dexamethasone should be given for meningitis due to Streptococcus pneumonia as it would reduce inflammation in the brain and subsequently the incidence of permanent neurologic sequelae such as hearing loss or focal neurological deficit[16-20]. However, dexamethasone was not shown to reduce mortality[21]. Interestingly, the use of adjunctive dexamethasone did not show significant benefit in developing regions. This was attributable to poor nutrition, delayed presentation, presence of chronic diseases such as HIV, or the inadvertent inclusion of cases of tuberculous meningitis[22,23]. The administration of dexamethasone in our study was only done for 3.6% of admissions suspected of meningitis. We postulated that this could be a reflection of the uncertainty surrounding the diagnosis of meningitis. Further efforts at quality improvement in care delivery would be necessary to ensure that dexamethasone was given along with antibiotics when meningitis was suspected in the ED.

Neurosurgical intervention was rare and may be indicated for monitoring or relieving raised intracranial pressure in patients with meningitis[24]. In our study, only 1 patient required an emergent right frontal extra-ventricular drain insertion for relieving and monitoring of raised intracranial pressure. Although uncommon, ED physicians should be aware of the indications for neurosurgical referral. Raised intracranial pressure and hydrocephalus should be promptly detected so that timely neurosurgical referral could be made for placement of an extra-ventricular drain or ventriculo-peritoneal shunt to improve clinical outcomes for patient[25,26].

Study Limitations

Our study was based on a single centre's experience and therefore would not be able to give a full perspective of meningitis in ED with a different setting and beyond the ED. Furthermore, aspects of clinical management were guided by institutional practices which may not be applicable in other centres, thus affecting generalizability of our results. A major

variation should be highlighted – lumbar puncture was not performed at the ED but at the inpatient unit. Therefore, all patients with an ED diagnosis of meningitis would be admitted to the hospital. Consequently, it was not necessary to differentiate between the various causes of meningitis at the ED as this would be further evaluated at the inpatient unit. Nonetheless, we believed that the results of our study had provided a glimpse into challenges of diagnosing meningitis in the ED. This knowledge would be useful for ED physicians in their assessment of patients with suspected meningitis.

Next, a retrospective study was carried out as meningitis was not a common condition with only about 17 cases a year in our context. Therefore, we could only identify patients at the ED who were diagnosed with meningitis and not patients who were assessed not to have meningitis. This thus precluded us from reviewing case records, performing phone follow up, sending out letters or checking the registry of deaths to ascertain the outcome for this group of unidentified patients. We have hence limited the definition of accuracy to the number of patients who had meningitis among all who were diagnosed with meningitis at the ED. We attempted to address this limitation by identifying 13 patients who had a second attendance to the ED which prompted a diagnosis of meningitis.

Also, due to the retrospective nature of this study, data was collected based on the documentation of various medical personnel in the ED record instead of forms with predefined data fields. The robustness of the data would be affected by inconsistency in documentation as well as missing and incomplete information. For instance, details about comorbidities and other risk factors such as diabetes mellitus, alcoholism, human immunodeficiency virus and other immunocompromised states could not be obtained for an accurate presentation and meaningful discussion.

Conclusion

Meningitis was difficult to diagnose accurately in the ED setting. Given the lack of clinical features which could be used to differentiate meningitis from other conditions, a high index of suspicion would be required so that interventions may be promptly initiated to reduce mortality and morbidity.

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Case Report
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Post partum mortality; WHY? Sheehan's Syndrome

Ahmet Burak ERDEM[1], Hakan UZUNKAYA[1], Muhittin Serkan YILMAZ[1], Bahattin IŞIK[1], Umut ÇAVUŞ[2]

[1] Emergency Department Ministry of Health University Ankara City Hospital

[2] Emergency Department Ministry of Health University Dışkapı Yildirim Beyazit Education and Research Hospital

Introduction

Sheehan's syndrome, defined in 1937, develops partial or complete ischemia in the pituitary gland due to postpartum hemorrhage. It is seen as a hypopituacism that extends to the deficiency of all hormones from a single hormone deficiency [1]. It is usually seen in women who develop severe hypotension or shock due to bleeding or hypovolemia during or after delivery. According to the severity of necrosis in the pituitary gland, the clinical extends asymptomatic state to a symptom that manifests in the acute period [2]. SS is considered to be the most common cause of pituitary insufficiency in developing and underdeveloped countries. The disease may occur for many years without symtomps as well as lack of lactation, menstrual changes, decline in secondary sex characteristics, weakness and hypotension suggest this disease in postpartum period. However, adrenal insufficiency and myxedema coma have been triggered by an intervening trauma, after infection or surgery may result shock and death[3,4].

Case Presentation

A 30-year-old female patient was admitted to the emergency department with weakness, swelling in the body and bruising of the legs. It was learned that the patient had a difficult birth at home about 10 days ago, that she had a third birth, and that 3 of her children were born healthy. There was no problem in her previous births, but there was no improvement in her postpartum weakness and fatigue. Due to this condition, the patient could not breastfeed her child and her milk was very low. She presented to different health institutions several times because of increased fatigue, frequent urination, fever, swelling of the body and bruising. In fact, no pathology was found in the hemogram, biochemical parameters and urine analysis performed one night before. When the patient came to our emergency department, her general condition was bad and his consciousness was pure and his breathing was superficial. Physical examination revealed hypotensive, tachycardic, pretibial 3 positive bilateral edema, venous ulcers in the legs and ecchymotic linear lines in the left leg (Figure1-2). The patient was observed to be in shock and cardiopulmonary arrest occurred during this period. The patient was started on cardiopulmonary resuscitation (CPR). Fingertip blood glucose 30 was measured, and 25 g dextrose was loaded simultaneously. During resuscitation, transthoracic echocardiography was performed by cardiology. There was no evidence of pericardial tamponade, massive pulmonary embolism and aortic dissection. In e-FAST imaging, no intraabdominal free fluid was observed and liver, spleen and renal parenchymal tissue were normal. WBC 4,6 $10^{3}/\mu L$, Hgb 10,6 g/dL, PLT ise 52 $10^{3}/\mu L$ were measured before the patient's arrest. Glucose was 28 mg / dl, Sodium 122 mmol / L, Potassium 7.09 mmol / L, Calcium 6.6 mmol / L (Table 1). The lactate level was 8.8 mmol / L and metabolic acidosis in venous blood gas. The patient did not respond to fluid-electrolyte (10% calcium gluconate 2 ampoule i.v. infusion) and did not respond to CPR and was considered as exitus.

We didn't get permission because our patient died. However, there is no ethical violation in the materials we use.

Discussion

The necrosis of the anterior lobe of the pituitary gland develops slowly. It is expected to develop necrosis within about 2 weeks after postpartum hemorrhage. However, sudden death due to this emerging necrosis is not expected[5]. Most of the time the disease occurs over the years and the acute picture is rarely seen. Adrenal and thyroid insufficiency due to hypopituarism causes cardiac abnormalities. If hypoglycemia and electrolyte disturbances are added to the table, fatal

Corresponding Author: Ahmet Burak Erdem **e-mail:** drabe0182@gmail.com
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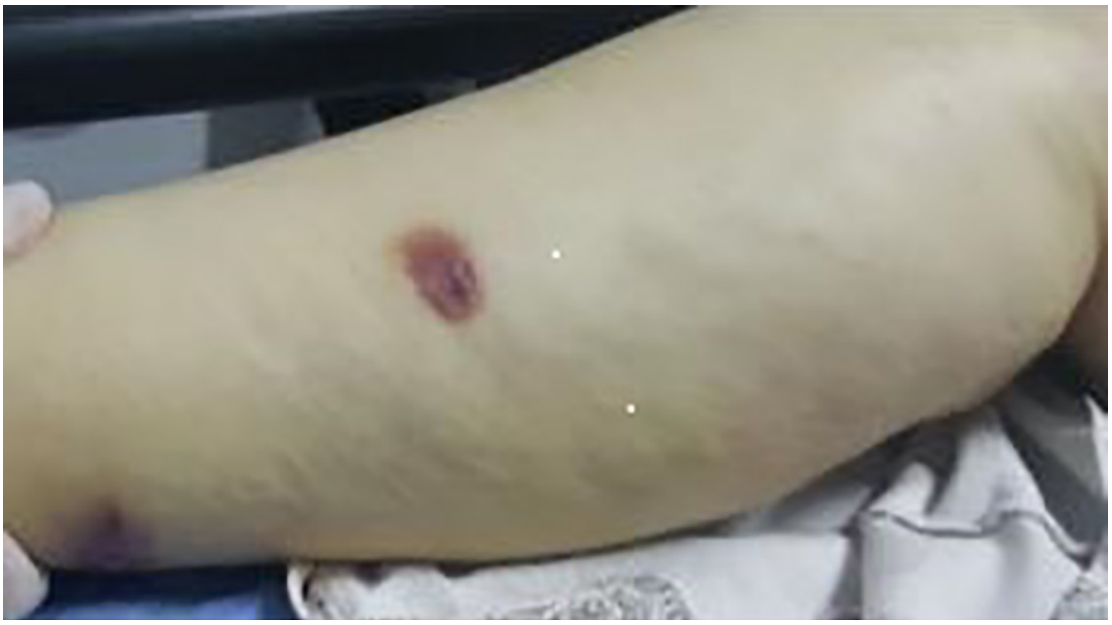

Figure -1. Ecchymos

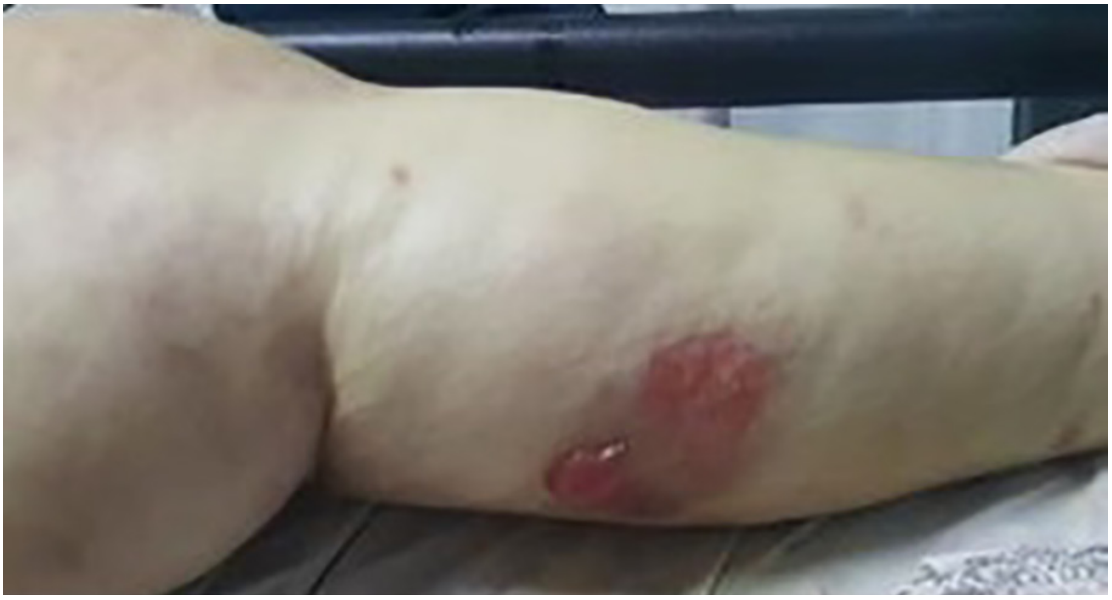

Figure -2. Venous ulcer

dysrhythmias such as ventricular tachycardia [6] or long QT [7] may develop. Peripheral effusion, mitral valve prolapse, septal hypertrophy, congestive heart failure, left ventricular hypertrophy and sinus bradycardia [8], dilated cardiomyopathy [1] due to hypothyroidism can be seen.

The pituitary gland begins to give symptoms after losing 75% of its tissue. This period was between 1-33 years. In a series of 20 cases, Dökmetaş et al. found this period between 2-40 years. The most common postpartum period is the absence of lactation and changes in the menstrual cycle. Two clinical tables are the most important clinical manifestations of adrenal insufficiency and hypothyroidism. When adrenal insufficiency develops, hypoglycemic episodes, electrolyte disturbances, hypotension, weakness and hypopigmentation can be seen. Facial edema and periorbital swelling due to hypothyroidism is not expected [4]. What is interesting in our case is that the condition associated with these two clinics is very fast and even the day before the biochemical parameters are normal. In the postpartum period, the patient did not receive pituitary insufficiency treatment and caused the

Tablo 1. Biochemical and venous blood gas values of the patient

Biochemistry	*The value of the patient*	*Blood Gas and INR*	*The value of the patient*
Glucose	28 mg/dL	INR	1.39
Urea	111 mg/dL	PH	7,18
Creatinine	2,62 mg/dL	PCO_2	26,8
GFR	24	HCO_3	9,6 mmol/L
ALT	74 U/L	Lactate	8,8 mmol/L
AST	295 U/L	BE	-17,1 mmol/L
CK	6679 U/L	Ionized Ca	0,95 mmol/L
LDH	631 U/L	Potassium	6,8 mmol/L
Sodium	122 mmol/L	Sodium	118 mmol/L
Potassium	7,09 mmol/l		
Calcium	6,6 mg/dL		
Osmolality	264 mosml/kg		
Direct Bilirubin	3,12 mg/dL		

clinic to rapidly aggravate and go into shock due to cardiac collapse. Acute SS is not a common condition in the literature. Matsuzaki et al. described the case of acute SS in a postpartum 8th day seizure [9]. A similar picture in our case was reported in a 40-year-old patient who developed secondary adrenal insufficiency during appendectomy 19 years after postpartum in the literature [10].

In our case, there was thrombocytopenia associated with anemia. Normocytic anemia of normochrome is an expected condition in SS. However, pancytopenia was encountered in rare cases. As a result, the effect of anterior pituitary hormones on hematopoietic cells has been implicated [3]. Bisitopenia was observed in our case and the fact that the patient died in a short time may be the reason of not seeing leukopenia. But I have to say; pansitopenia and SS coexistence was a case of postpartum 13th year. HELLP syndrome is a condition that may occur in the last trimester of pregnancy characterized by hemolysis, elevated liver enzymes and thrombocytopenia [11]. In this case, we think that liver enzymes elevation, thrombocytopenia and high LDH levels may be due to HELLP syndrome and even the most important factor of the increase in the severity of SS. The fact that the blood pressure values during the pregnancy of the patient is normal and does not have a seizure strengthens this suspicion.

Hypoglycemia is a rare condition in SS. It occurs as a result of defect in Growth hormone, ACTH and contour regulatory hormones. In SS, coma may be seen due to adrenal insufficiency, hypoglycemia, hyponatremia or hypothyroidism [2,12]. The cause of hyponatremia may be caused by hypopituity and adrenal insufficiency. Fatigue, nausea and changes in consciousness are easily overlooked because of symptoms. Inadequacy of cortisol and ACTH is the cause of fluid-electrolyte impairment. In adrenal crisis, hyponatremia, hyperkalemia, hypocalcemia, hypoglycemia, fever, malaise, hypotension and shock may be seen [13,14]. In our patient, there were laboratory and clinical symptoms suggestive of an acute crisis. The hormone levels could not be studied due to time of arrival in the emergency room. Magnetic resonance imaging (MRI) could not be performed due to exitus. These are the shortcomings in this case presentation for reasons that we do not have. However, the anamnesis, laboratory findings and clinical outcome are sufficiently supported. Difficult birth at home, delayed lactation in postpartum period, fatigue, hypoglycemia, fluid electrolyte disturbance, bisitopenia and elevated liver enzyme values in the hypotensive shock of the patient to us in the case of acute SS is enough to think. In addition, we did not find any case of acute SS in the literature with postpartum 10th day.

Postpartum maternal deaths should be examined and the

underlying causes should be clarified. In this case, we wanted to discuss a patient whose clinical condition deteriorated within 10 days and lost. Based on the anamnesis information of the patient, the pituitary failure is thought to be in the first place but sudden death is not expected. In the last 24 hours, the patient's laboratory values deteriorated and he died of cardiovascular collapse.

In conclusion, if patients have such as difficult birth, hemorrhage and hypovolemia, such as the patients' complaints of fatigue, nausea and weakness should be considered in the postpartum period. Even if the patients routine parameters in emergency services is normal, pituitary, thyroid and adrenal hormone parameters should be investigated.

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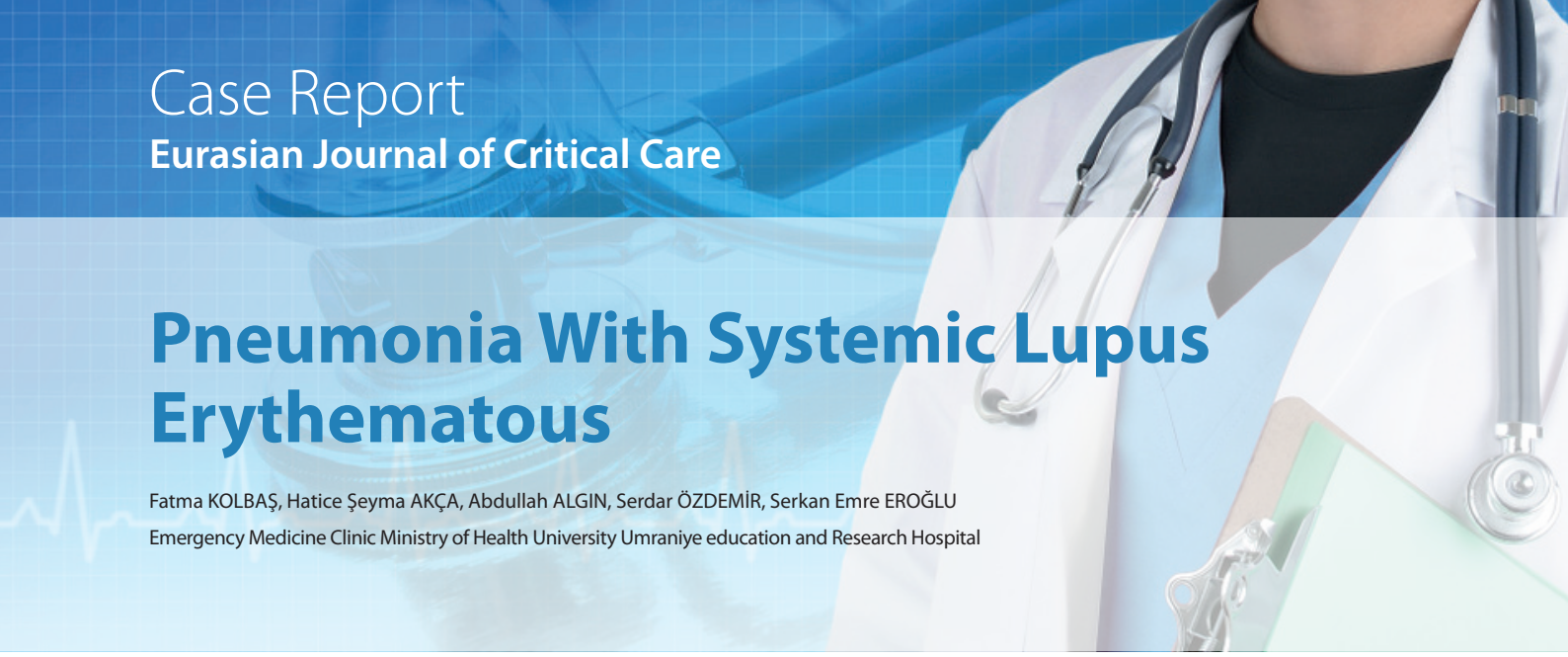

Pneumonia With Systemic Lupus Erythematous

Fatma KOLBAŞ, Hatice Şeyma AKÇA, Abdullah ALGIN, Serdar ÖZDEMİR, Serkan Emre EROĞLU
Emergency Medicine Clinic Ministry of Health University Umraniye education and Research Hospital

Özet

Acil servise sistemik lupus eritematozus (SLE) tanısı olan ancak 2 senedir tedavi almayan 19 yaşındaki kadın hasta ateş birkaç gündür artan nefes darlığı ve ateş şikayeti ile başvurdu. Fizik muayenesinde inspiratuar ralleri, ekspiryum uzaması ve wheezingleri olan hastanın çekilen kontrastsız bilgisayarlı tomografisinde her iki akciğerde yaygın dağılım gösteren parankimal infitratif dansiteler görüldü.Göğüs hastalıkları tarafından solunum yetmezliği ve akut respiratuar distress sendromu (ARDS) için yakın takip ve tedavi önerilen hastanın kliğinde kötüleşme olması üzerine yoğun bakıma sevk edildi. Enfeksiyon, SLE hastalarında morbidite ve mortalitenin en önemli nedenlerinden biridir. SLE'nin solunum sistemi tutulumlarından biri olan lupus pnömonisi özellikle genç kadınlarda görülür. Yüksek ateş, öksürük, hipoksi ve takipne en sık görülen semptomlardır ve yüksek mortalite ile ilişkilidir. Akut lupus pnömonisinde, tedaviye sistemik kortikosteroid eklenmelidir. Bu hastalarda 72 saat içinde dispne semptomlarında iyileşme olmazsa, metilprednizolon tedavisi önerilir. Acil serviste lupus pnömonisi tanısı alan ve yoğun bakıma ARDS ön tanısı ile sevk edilen 19 yaşındaki kadın hastayı sunuyoruz.

Anahtar kelimeler: SLE, lupus pnömonisi, dispne

Abstract

A 19-year-old female patient, who was diagnosed with SLE but has not received treatment for 2 years, came to the emergency service due to fever and shortness of breath that has been frequent for several days. In her physical examination, inspiratory rales, expiratory elongation and wheezing were found, and non-contrasted computed tomography of the patient showed parenchymal infiltrative densities that were widely distributed in both lungs. The patient, who was recommended close follow-up for respiratory failure and acute respiratory distress syndrome (ARDS) by the department of pulmonology, was referred to the intensive care unit because of worsening of her clique. Infection is one of the most important causes of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Lupus pneumonia, one of the respiratory system involvements of SLE, is especially seen in young women. High fever, cough, hypoxia and tachypnea are the most common symptoms and are associated with high mortality. In acute lupus pneumonia, systemic corticosteroid should be added to the treatment. If these patients do not improve dyspnea within 72 hours, methylprednisolone treatment is recommended. We present a 19-year-old female patient diagnosed with lupus pneumonia in the emergency service and referred to intensive care unit with the diagnosis of ARDS.

Anahtar kelimeler: SLE, lupus pneumonia, dyspnea

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that is 9 times more common in women. SLE is mostly seen in the hematological system, pericardium, skin, kidney and respiratory systems. The appearance of the respiratory system in lupus disease may appear as infection, pleural effusion, alveolar hemorrhage and pulmonary embolism[1]. In this case, we present a 19-year-old lupus pneumonia case who came to the emergency service.

Case

19-year-old female patient in the green area of the emergency service; She applied with the complaint of shortness of breath and fever, which lasted for about a week and became frequent especially in the last few days.It was learned that the patient was diagnosed with systemic lupus erythematosus (SLE) and has not been under any doctor's control for 2 years. She did not have any disease other than SLE in his background.The patient regularly received allopurinol 300 mg 1*1, perindopril 5mg 1*1, hydroxychloroquine sulfate 200 mg 1*1, carvedilol 6.25 mg 1*1, furosemide 40mg 1*1, acetylsalicytic acid 100 mg 1*1, prednisolone 16mg 1*1 oral.Also; It was learned that the patient had a flu infection 1 week ago and oseltamivir phosphate 75 mg 2*1 was started in an outer center primary health center.In her physical examination, the degree of Glaskow Coma Scale (GKS) was 15 orientated cooperative, and when the lung examination was examined, there were bilateral inspiratory rales, expiratory extension and wheezing, other system examinations were natural. TA: 139/81 mm/hg, SpO2:78%, Pulse:143/

Corresponding Author: Abdullah ALGIN **e-mail:** dralgin@hotmail.com
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minutes, the fever was 38.3 ◦C. ECG was sinus tachycardia.Results of the patient in laboratory examination were determined as WBC: 17.26 103 mm3, Hgb: 7.5 g /dl, Plt: 419.000/mm3, AST: 31 U/L, ALT: 12 U/L, Creatine: 0.73 mg/dl, BUN: 32.1 mg/dl Glucose: 118 mg/dl CRP: 10.2 mg/dl and procalcitonin 1.99 ng /Ml. The results in blood gas analysis were pH: 7.45, PCO2: 27mmHg, PO2: 47.5mmHg, sO2: 85% HCO3:18.6 mmol/l, SBE: -4.7mmol/l and lactate: 1.3mmol /l. On the non-contrasted computed tomography (CT) of the patient, parenchymal infiltrative densities with locally occurring air bronchograms were observed in both lungs (Figure-1). The patient was consulted for 4 l/min oxygen. Oseltamivir phosphate 75 mg 2*1, piperacillin – tazobactam 4,5 g 3*1, clarithromycin 500 mg 2*1, prednisolone 40 mg 1*1, intravenous salbutamol 2.5 mg 4*1 and budesonide 0.25 mg/ml 2*1 drugs were recommended to the patient consulted to the chest diseases clinic.Inhaler treatment was also started.Close follow-up and intensive care follow-up were recommended for the patient's respiratory failure and acute respiratory distress syndrome (ARDS). Despite the treatment recommended to the patient, his clinical condition deteriorated; the patient was referred to intensive care unit because of the need for a noninvasive ventilator.

Discussion

We encounter acute respiratory injuries due to lupus as pleural effusion, lupus pneumonia, pulmonary hemorrhage and pulmonary embolism[2]. Due to lupus findings of respiratory system, hospital stay and mortality rates increase[1]. The most common finding in respiratory system findings is pleural effusion. The frequency of pneumonia is between 15-28%[3]. There are publications reporting that hospitalization rates are higher among young women due to pneumonia in patients with SLE in the literature[3]. In these patients, pneumonia-related mortality is 10-12%[4]. Acute fever, cough, tachypnea and hypoxia are seen in pneumonia associated with SLE. The radiological sign of lupus pneumonitis is pleural effusion and infiltration, usually basal and bilateral[5].

Although the most frequently isolated factor in community-acquired pneumonia is micobacterium pneumonia; In cases with SLE, no cardia aspergillus and S.aureus are the most frequently isolated microorganisms. Therefore; In these patients, initiation of broad spectrum antibiotherapy is recommended[3]. In acute lupus pneumonia, systemic corticosteroid (prednisolone 1-1.5mg / kg day) must be added to

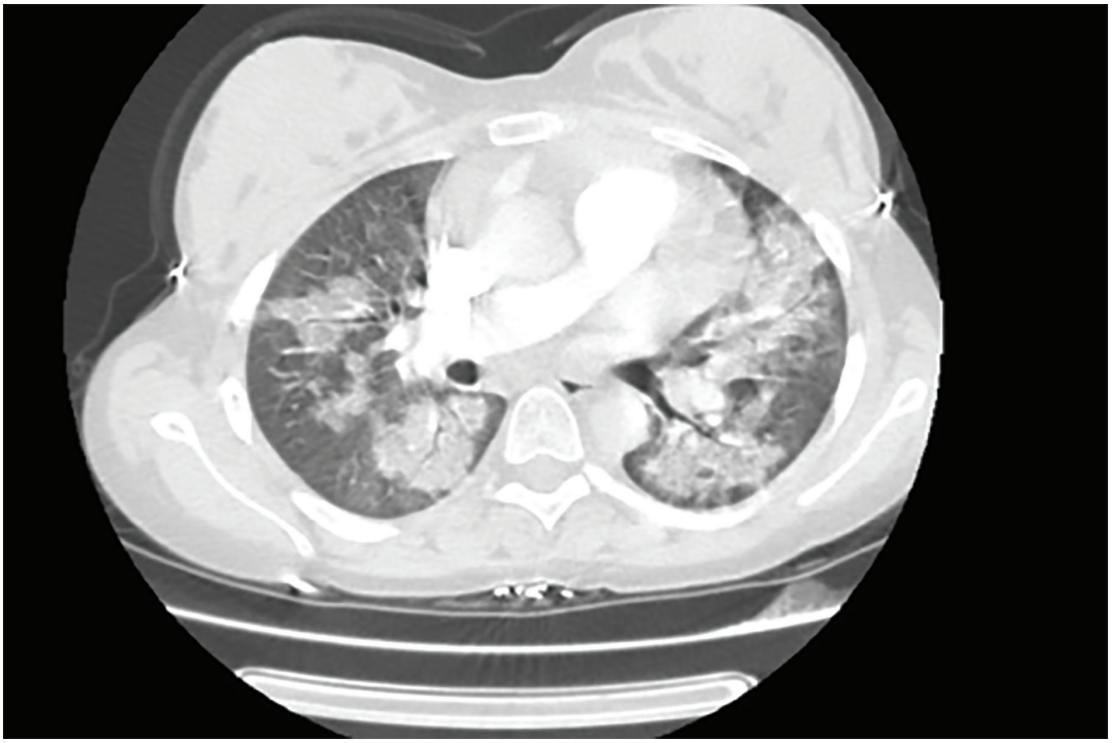

Figure -1. On the non-contrasted computed tomography (CT) of the patient, parenchymal infiltrative densities with locally occurring air bronchograms were observed in both lungs

the treatment. If there is no improvement in clink within 72 hours in these patients, 1 g of methylprednisolone treatment is recommended for 3 days[6].

Conclusion

Although pneumonia is rare in patients diagnosed with lupus, it is a clinical condition with mortality. Broad-spectrum antibiotics and immunosuppressive treatment should be started, and necessary precautions should be taken to avoid other complications and close follow-up should be done.

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Case Report
Eurasian Journal of Critical Care

Migration of Intrauterine Device and Acute Abdomen

Abdullah ERCAN, Abdullah Keyfo KAMA
Emergency Medicine Department, Ministry Of Health Elazig Fethi Sekin City Hospital

Introduction

Intrauterine device is the most commonly used contraception method in our country due to its reversible, low risk and low cost[1]. Relatively frequent complications such as ectopic pregnancy and infection may develop due to IUD, also rarely it can damage to organs through uterine perforation and migration to neighboring organs and intraabdominal region. Risk of perforation and migration is reported as 0.05-13 / 1000[2]. Especially, the insertion of IUD in the first three months postpartum increases the risk of complications. Therefore, it is recommended to be insertion from the 6th month[1]. In this study, we presented the case of intra-abdominal IUD, which caused abdominal pain in a 31-year-old female patient.

Case

A 31-year-old female patient presented to the emergency department with dysuria and pain in the lower abdomen for 3 days. It was learned that the patient who gave birth vaginally 40 days ago was inserted IUD 3 days ago. Vital signs were within normal limits. Abdominal examination revealed tenderness in the left lower quadrant and in the suprapubic region. Routine laboratory studies revealed the following ; white cell count (WBC) : 7500/ml; C-reactive protein : 1,64 mg/dl. The urinanalyse demonstrated WBC 7 / HPF, RBC 9 / HPF and leukocyte (2+). Abdominal x-ray and abdominal USG, were taken to determine the etiology of abdominal pain, revealed that IUD was not in the uterine cavity (Figure-1). A CT scan revealed that the IUD migrated into the abdomen to the left superolateral adjacent region of the uterus (Figures 2 and 3). The patient was consulted with Gynecology Service. IUD embedded in the omentum, was removed by laparoscopy. There was no any complication or organ damage as perforation. The patient received antibiotic treatment for 5 days postoperatively, was discharged without any complications.

Discussion

Intrauterine devices (IUDs) are a commonly used, effective and reversible contraception methods[3]. While the rate of use is 9.4% in developed countries, it is 16.4% in undeveloped countries[4]. Relatively frequent complications of IUD include, abdominal or pelvic pain and abnormal bleeding, especially during the first few months after its insertion. Other adverse effects are expulsion, heavy bleeding, dysmenorrhea, unplanned pregnancy, and spontaneous abortion[3]. One of the serious complications that may develop due to IUD is uterine perforation. It is rare but can be fatal. Two types of uterine perforation exist. Primary perforation may occur during insertion, which is associated with severe abdominal pain. Secondary perforation is a delayed event, proposed to be due to gradual pressure necrosis of the uterine wall. Delayed rupture can be due to uterine spasms[5]. Approximately 80% of IUDs migrate into peritoneal cavity after perforation. Omentum, rectosigmoid colon, peritoneum, bladder, appendix, small bowel, adnexa, and iliac vein are possible sites of migration[6].

These patients generally present with not finding the device string. They may be asymptomatic or have nonspecific symptoms such as abdominal pain, nausea and vomiting, constipation, fever, anorexia[6,7].

Diagnosis generally made by missing device string. As a diagnostic method, transabdominally or transvaginally ultrasonography is a safe, convenient and non-invasive method. Other radiological examinations (x-ray, tomography, magnetic resonance) are preferred diagnostic methods to evaluate complications or when there is a possibility of far-migrated intra-abdominal intrauterine device[8].

Corresponding Author: Abdullah Ercan **e-mail:** drabdullahercan422@gmail.com
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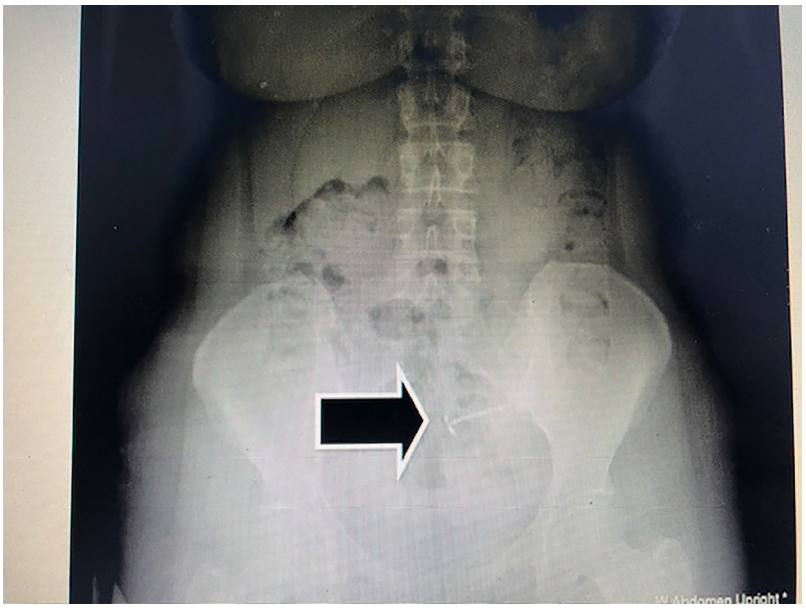
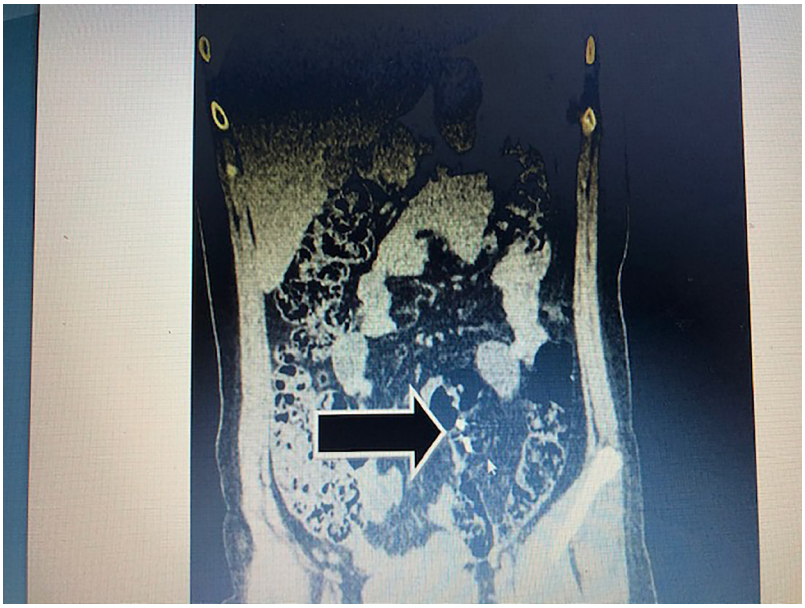


Figure -1. IUD is outside the uterine cavity.

Figure -2. IUD is outside the uterine cavity.



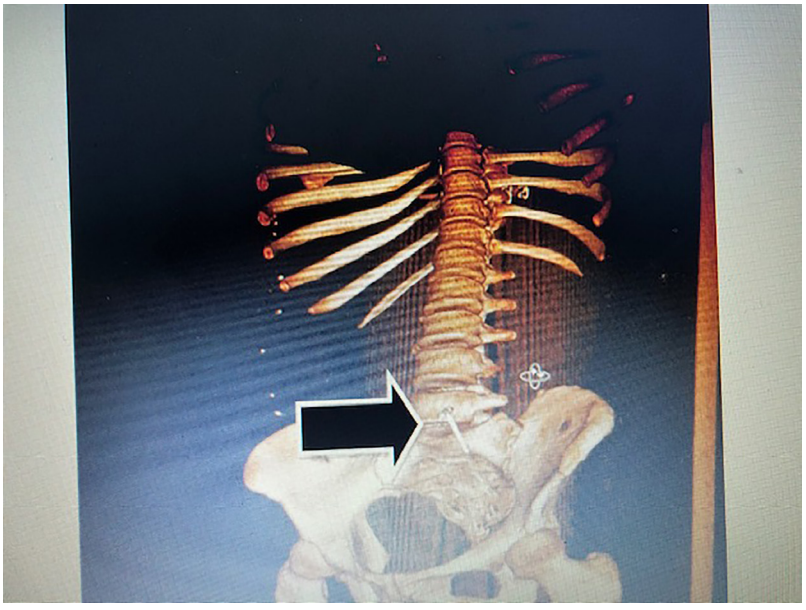


Figure -3. 3 D image of CT scan.

The World Health Organization recommends removing the migrated device as soon as possible. It is suggested that surgical removal should be considered even in asymptomatic patients[9]. It is recommended that to use minimally invasive methods if possible, including hysteroscopy, cystoscopy, colonoscopy, or laparoscopy. If the device is embedded in an organ, exploratory laparotomy should be performed, not minimally invasive methods[5].

Conclusion

Serious complications related to IUD are not common and mostly occur during IUD insertion. This procedure should be performed only by experienced healthcare professionals to prevent possible complications. Patients should be monitored closely and the device should be changed when the expiration date expires. Especially, the insertion of IUD in the first three months postpartum increases the risk of complications. Therefore, it is recommended to be insertion from the 6th month.

Case Report
Eurasian Journal of Critical Care

Young Patient Applying To Emergency Room With Complaint Of Syncope

Sinan Cem Gül[1], Celal Bitiş[2], Başar Cander[3]

[1] Department of General Surgery, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Turkey

[2] Department of Orthopedics and Traumatology, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Turkey

[3] Emergency Medicine Department, Istanbul Health Sciences University, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul,Turkey

Abstract

In this case report, the clinical course of a 30-year-old male patient who presented to the emergency department with complaints of fainting and urinary incontinence will be explained.

Our aim is: firstly, the anamnesis given by the patients in the emergency department, which leads us to central pathology with the complaint of coming to the emergency department, but whose pulmonary pathology is detected as a result of detailed and persistent anamnesis, is taken in detail even if the patients do not care. In this way, pathology will be reached more quickly. The second is; It is not to be ignored that vein thromboses from superficial veins can cause pulmonary embolism even in young patients with no additional disease and ideal body mass index.

İntroduction

An important theory describing the pathogenesis of venous thromboembolism (VTE), often referred to as the trio of Virchow[1,2], predicts that VTE occurs as a result of**:**

- Stasis in the blood flow
- Vascular endothelial injury
- Coagulopathies

Most emboli are thought to originate from the lower extremity proximal vessels (iliac, femoral, saphenous, and popliteal vein), and over 50 percent of patients with deep vein thrombosis (DVT) are present in the proximal veins simultaneously.[3,4].

In the superficial veins of the lower limbs, phlebitis and thrombosis are usually benign and self-limiting; however, deep venous thrombosis [DVT]) and even pulmonary embolism (PE) may occur in the case of larger axial vessels, such as large saphenous or small saphenous vessels.[5,6].

Case

30-year-old male patient with our emergency department with syncope, eyes darkening simultaneously was admitted with complaints of urinary incontinence. In the CV of the patient with a body mass index of 25.4, 6 months ago, he had mild head trauma, no additional disease, he did not use any drugs or cigarettes. Hemodynamics of the patient was stable upon arrival in the emergency room. Ekg in normal sinus rhythm, venous blood gas taken; ph: 7.37, So2: 61%, pco2: 37 mmhg, glucose 142, lactate 4.5. Syncope, urinary incontinence and lactate height caused the patient to suspect central pathologies. In addition, because of the Covid-19 pandemic, patients were not masked in the emergency room, and the patient had a mask. The patient stated that he had difficulty in breathing during this period and wanted to remove the mask. Considering the complaint of dyspnea due to a pandemic, we also took Thorax CT next to Brain Computed Tomography (CT). In the emergency report by the Brain CT Radiology clinic; It was interpreted as a suspect in terms of 9 mm subacute epidural hematoma in the right frontal region in the basal ganglion plane. Thorax CT was reported as normal. The patient was then consulted to neurosurgery. As a result of the neurosurgical consultation, he stated that there was no neurological finding in the patient and suggested polyclinic control.

When the patient got up at the 4th hour of his follow-up, we looked again at the hemodynamic parameters after the patient developed syncope for the second time. Blood pressure was 100/60 mmhg, heart rate was 128, fingertip blood sugar: 140, so2: 96%, and the patient stated that shortness of breath increased. On this, we studied Brain CT, cardiac panel and D-dimer from the patient again. In the emergency

Corresponding Author: Sinan Cem GÜL **e-mail:** sinancemgul@gmail.com
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report of the radiology clinic; The last drawn Brain CT reported as normal and corrected the 9 mm subacute epidural hematoma interpretation as an artifact in the right frontal region in the basal ganglion plane indicated in the previous Brain CT. Diffusion MR was performed on the patient who was contacted with simultaneous neurology. Normal reporting of diffusion MR has taken us a little further from central pathologies. The patient's D-dimer result was 8.8 µg / ml. On top of that, when the patient's anamnesis was taken again and in detail, he stated that he had a slight shortness of breath for 2 weeks. Upon this, we performed urgent pulmonary CT angiography. The pulmonary CT Angio report reported a compatible appearance with pulmonary thromboembolism starting from both main pulmonary arteries and allowing partial flow in both main pulmonary arteries to fill the lumen in the middle and lower lobar branches on the right and almost in the lower lobar branch on the left (Figure 1,2,3). As a result, we diagnosed the patient with pulmonary embolism, immediately started DMAH treatment and hospitalized the patient in the chest diseases service.

Then, in lower extremity doppler ultrasonography for etiology; Vena safena magna (VSM) was measured 11 mm proximally and 19 mm in the knee joint. In the proximal neighborhood of VSM, varicose venous structures up to the knee joint attracted attention. The appearance of slowed blood flow in VSM and varicose structures was observed. As a result, it was concluded that this is the source of pulmonary embolism.

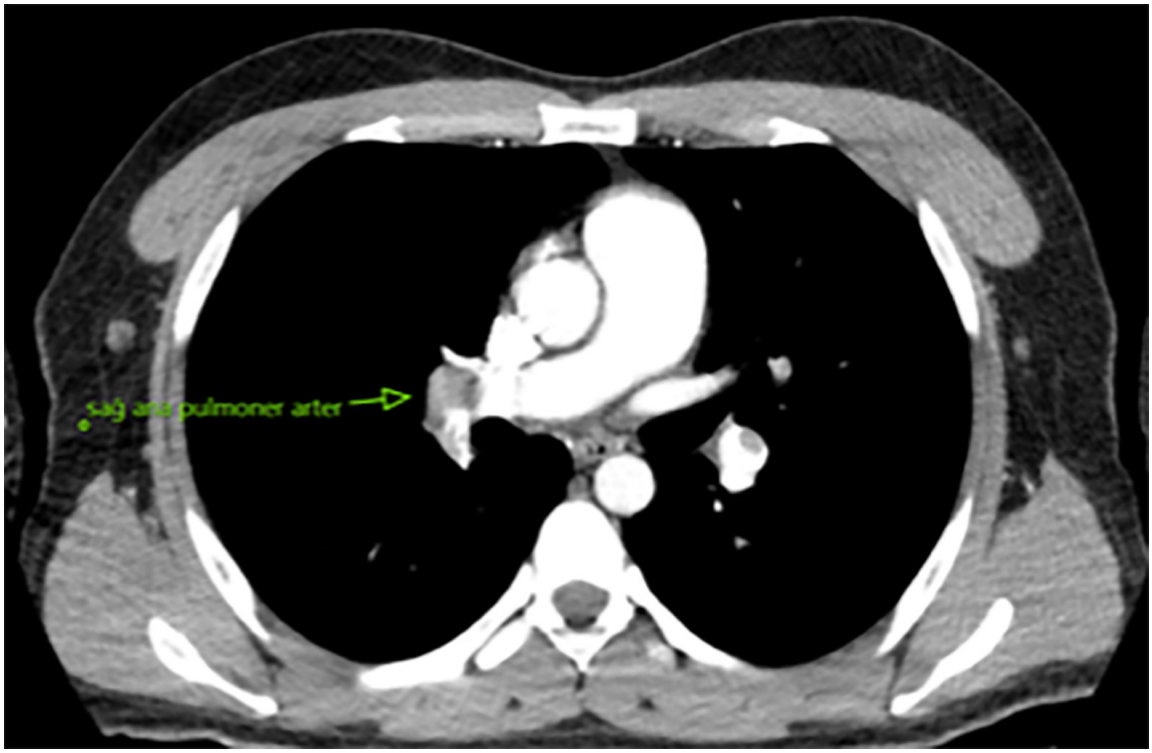

Figure -1. Nearly complete thrombus and very low flow in the right main pulmonary artery, axial pulmonary CT angio view.

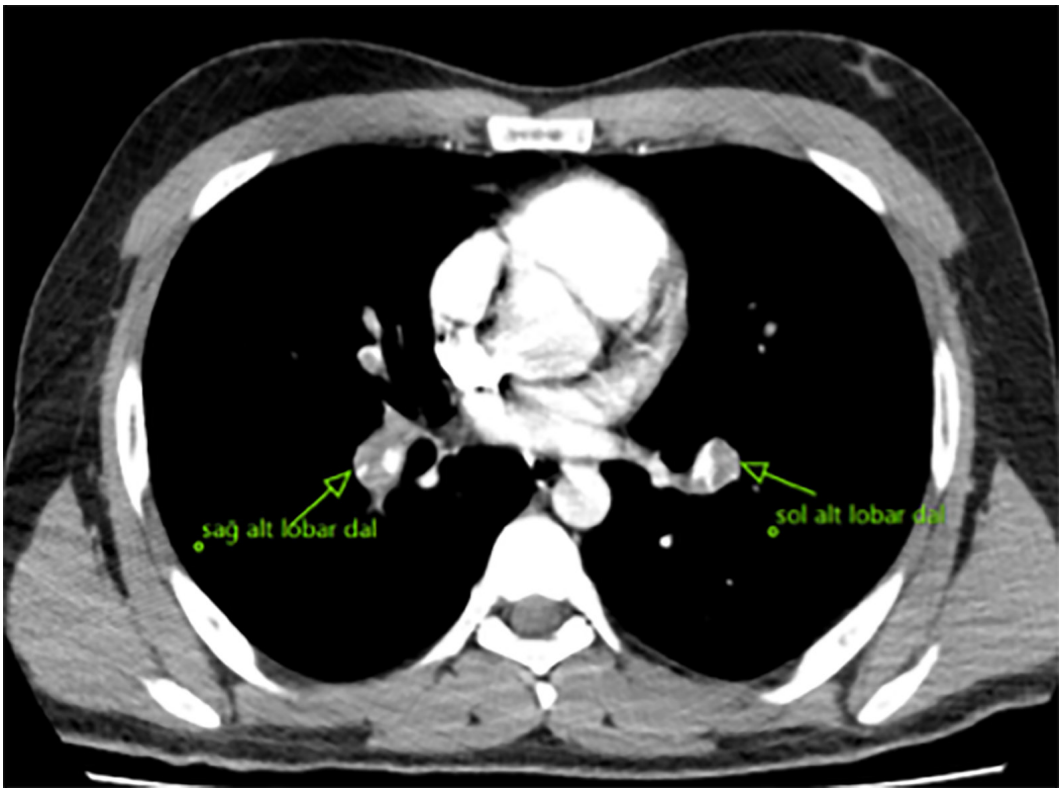

Figure -2. Nearly total thrombus in the right and left pulmonary al lobar arteries and very low flow, axial pulmonary CT angio view.

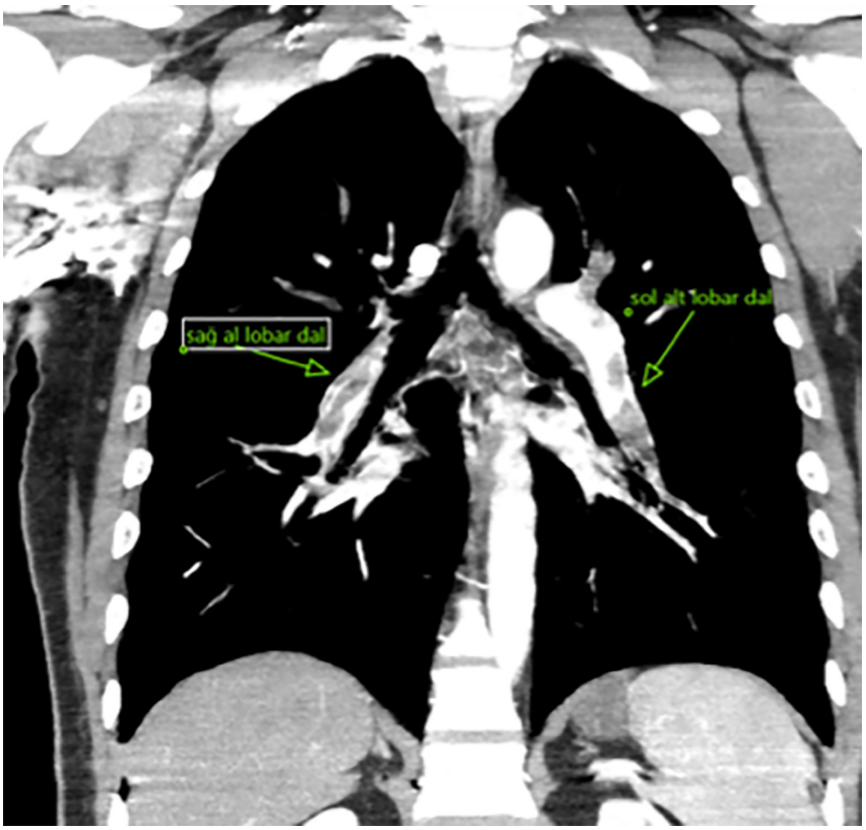

Figure -2. Nearly total thrombus in the right and left pulmonary al lobar arteries and very low flow, axial pulmonary CT angio view.

Discussion

Most deaths due to pulmonary embolism occur approximately within the first few hours after application and if no diagnosis has been made. While the mortality of the hospital increases up to 30% due to undiagnosed Pulmonary Embolism, mortality decreases to around 8% in patients diagnosed early. For this reason, patients who come to the emergency department with the complaint of shortness of breath should be vigilant even if the body mass index is normal, even a young patient with no additional disease, and care should be taken to take detailed anamnesis.

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Case Report
Eurasian Journal of Critical Care

Management of Sigmoid Volvulus Patient Diagnosed by Emergency Department

Sinan Cem Gül[1], Ahmet Erdur[2], Murat Yıldırım[3]

[1]Department of General Surgery, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Turkey
[2]Emergency Medicine Department, Istanbul Health Sciences University, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul,Turkey
[3]Tokat Zile Devlet Hastanesi Genel Cerrahi Birimi

Summary

In this case report, we aimed to present the clinical course of a 53-year-old male patient who was admitted to the emergency department with a complaint of swelling and pain in the abdomen for 3 days and who was diagnosed with sigmoid volvulus. These pathologies, which we rarely encounter in the colonic dysmotiliter and advanced age population, appeared at an earlier age due to the comorbid diseases of our patient. Surgical and endoscopic detorsion options and indications will be explained in the direct management of the patient with typical sigmoid volvulus image.

Introduction

Sigmoid volvulus (SV) constitutes 2% to 5% of colon occlusions in western countries and 20% to 50% of occlusions in Eastern countries. Africa, Asia, Middle East, South America, Eastern and Northern European countries and Turkey, are endemic to the SV[1].

SV usually affects adults with the highest incidence seen in 4 -8-decattageous. Constipation history and colonic dysmotility are well-known risk factors for sigmoid volvulus[2].

About 17 percent of patients develop symptoms of sudden onset acute severe pain, congestion, and vomiting before or with the onset of abdominal pain. Rarely, impaired blood flow to the sigmoid colon can cause necrosis, peritonitis and sepsis[3].

Successful sigmoidoscopy can detort the sigmoid volvulus when advanced along the twisted segment of the colon[4].

Emergency surgical management is required in patients with positive perforation and peritonitis findings[5].

In patients with recurrent sigmoid volvulus, surgical resection is recommended during index acceptance or after a short time due to high risk of recurrence and high mortality rates[5].

Case

A 53-year-old male patient has known diagnoses of previous cerebrovascular disease (SVH), epilepsy and diabetes. She is using levetiracetam, valproic acid, clopridogrel and metformin. No previous abdominal operation history. He applied to the emergency room with the complaint of abdominal pain and swelling that has been existing for 3 days. It was informed that the patient had not discharged gas and feces for approximately two days. When the anamnesis was deepened, it was found out that the patient had a decrease in his movements secondary to cerebrovascular disease secondary to hemiplegia and lived a sedentary life. It has been learned that the problem of constipation has been for many years.

The patient's hemodynamia was stable when she was admitted to the emergency room. The physical examination findings were abdominally distal. There was no defense and rebound, there was sensitivity. A urinary catheter was inserted for follow-up, and routine blood tests were requested. Then, the patient was taken to the patient with direct abdominal x-ray (ADBG) and chest x-ray. In the laboratory, White Blood Cell count 11.5 10^3/ml, Hemoglobin 11.6 g/dl, C-reactive protein 1mg/L, kidney function tests and liver function tests were normal. Image compatible with sigmoid volvulus reverse U image was present in ADBG (figure 1). The patient was consulted with general surgery and successful colonoscopic detorsion was performed in the emergency endoscopy unit. During colonoscopy, there was no ischemia and necrosis on the colon mucosa. Then he was interneed to the general surgery service. The patient was discharged with full recovery at the end of the 3-day service follow-up.

Corresponding Author: Sinan Cem Gül **e-mail:** sinancemgul@gmail.com
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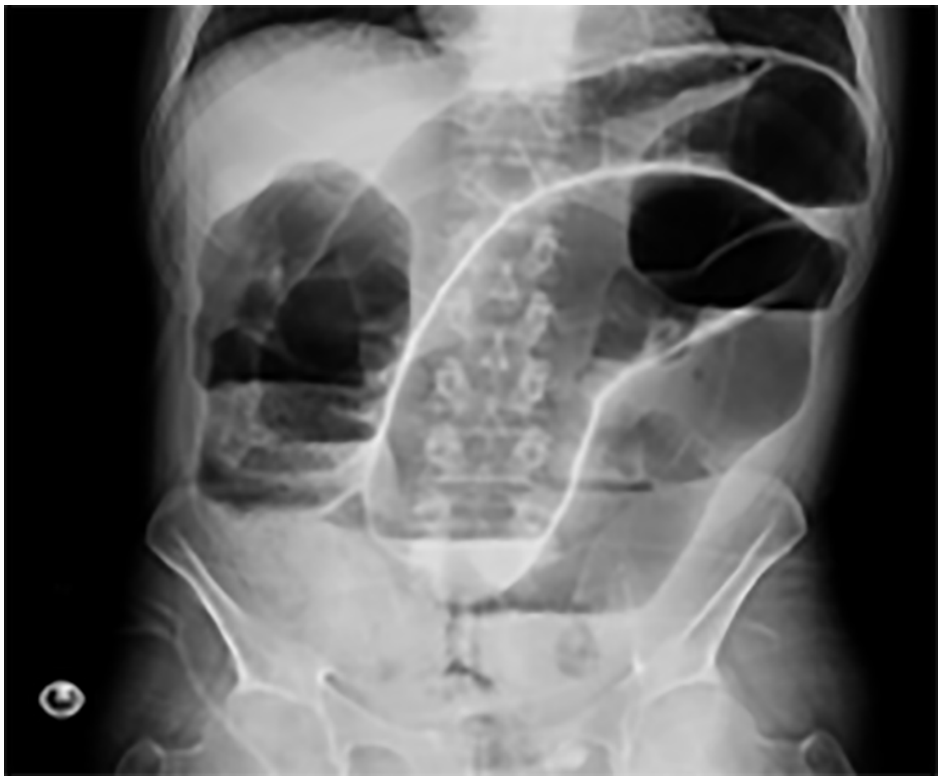

Figure -1. Direct radiograph taken in the emergency room

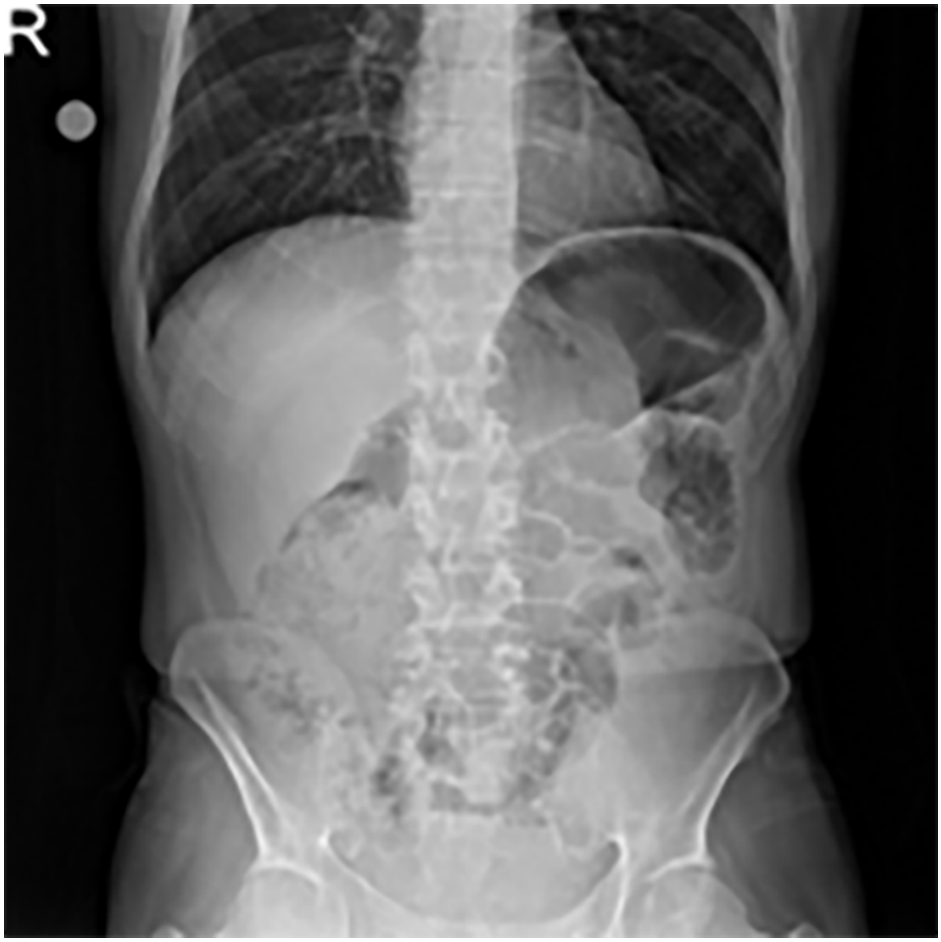

Figure -2. Control direct radiography after detortion

Discussion

Colon volvulus is the twisting of the colon along its axis. The word volvulus is derived from the Latin term volvere, which means twist. This twist will cause a complete or partial obstruction of the arterial and venous circulation in the intestine. Consequently, rapid and accurate diagnosis is required to speed up the treatment of this potentially fatal condition.

The volvulus itself is a rare cause of intestinal obstruction, which accounts for 5% of cases of gastrointestinal obstruction and 10-15% of large intestinal obstruction. The most common places for colon volvulus are sigmoid colon (75%), cecum (15%), transverse colon (3%) and spleen flexion (2%)[6].

A sigmoidoscopy can detort the sigmoid volvulus when advanced along the twisted segment of the colon, thereby ensuring enteric luminal flow. It provides protection of blood flow to the affected sigmoid colon. An additional advantage of sigmoidoscopy is that it allows evaluation of mucosal ischemia and necrosis in the colon[4,5].

Mortality associated with sigmoid volvulus is highest in patients who develop ischemia and necrosis and ranges from 11 to 60 percent in case series. In contrast, mortality is less than 10 percent in patients who do not develop gangrene[7].

The age of the patient in this case is smaller than the average age of sigmoid volvulus, but the patient's 7-year sedentary life and chronic constipation explain the reason for the current condition.

Recurrent sigmoid volvulus occurs in 84 percent of patients after a first attack that is not treated by surgery. In a retrospective study of 168 patients, the mean recurrence time was 58 days. However, the recurrence time can range from hours to weeks or months. Recurrence rates increase in later periods. Mortality rates seem to be higher in patients presenting with recurrent sigmoid volvulus, and have been reported in up to 21% in one study[8].

Result

Sigmoid volvulus is one of the causes of ileus in the elderly and is important because of its life-threatening complications. It is the first choice for early and successful detorsion treatment in patients without acute abdomen and necrosis findings.

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Case Report
Eurasian Journal of Critical Care

A Rare Cause of Pediatric Acute Abdomen: Isolated Tubal Torsion

Mehmet H. Atalar[1], Neslihan Köse[2], Cengiz Güney[3], Levent Cankorkmaz[3]

[1] Department of Radiology, Cumhuriyet University, School of Medicine, Sivas, Turkey

[2] Clinic of Radiology, Bozüyük State Hospital, Health Ministry, Bozüyük, Turkey

[3] Department of Pediatric Surgery, Cumhuriyet University, School of Medicine, Sivas, Turkey

Introduction

Isolated tubal torsion (ITT) is an extremely rare cause of acute abdomen frequently observed in women of reproductive age. Its diagnosis may become difficult due to its nonspecific clinical signs and symptoms including abdominal pain, nausea, vomiting, and fever. Its prevalence ranges between 1:500.000 and 1:1.500.000. It was first described by Bland-Sutton in 1890. The first pediatric case in the literature was described by Hansen in 1922; since then, a total of seventy-seven pediatric ITT cases have been described until 2019. Radiological imaging methods provide information supportive of the diagnosis of ITT [1-5]. In this paper, we aimed to report the clinical features and ultrasonographic (US) and magnetic resonance imaging (MRI) findings of a pediatric patient with ITT that was radiologically diagnosed and confirmed by surgery.

Case

A 10-year-old girl presented to emergency service with abdominal pain that had lasted for one week. She stated that the pain was cramp-like and particularly involved in the right lower quadrant. On abdominal examination, she had diffuse tenderness, rebound tenderness, and guarding at the lower abdomen, which was particularly prominent at the right lower quadrant. She had a stable general condition and was conscious, and she had no nausea, vomiting, loss of appetite, or fever. Her biochemical parameters, urinalysis, and coagulation parameters were within normal limits.

She underwent an abdominal US and MRI to detect the underlying pathology. On the transabdominal US, there was a regular contoured, thick-walled, cystic formation with a tubular appearance, internal echoes, and fluid-hemorrhage levels; it was located at the pelvic level at the right side and compressed the urinary bladder from its anterior aspect (Figure-1). Both ovaries were visualized clearly. A contrast-enhanced MRI was taken for lesion characterization and detection of coexisting findings. The MRI examination showed a dilated, thick-walled, tubular, cystic pelvic formation with contents suggestive of hydro-hematosalpinx. Additionally, there was the whirlpool sign representing vascular torsion at the right adnexal area (Figure-2 A, B, C). There was also fluid in Douglas pouch. Considered to have an adnexal torsion based on the available findings, the patient was taken to laparoscopic exploration, which showed that the uterus, both ovaries, and the left salpinx had a normal appearance but the ampullary region of the right salpinx was twisted around its axis. Based on the operative findings, the case was considered an ITT (Figure-2). The patient developed no complication during the postoperative period and was ultimately discharged with follow-up instructions. She had no residual sign or symptom at her follow-up appointment one month later.

Discussion

Adnexal torsion is most commonly observed with salpinxes and ovaries twisting around the broad ligament. However, twisting of a salpinx alone around the mesosalpinx creating an adnexal torsion is an extremely rare event in childhood. Its etiology may include congenital anomalies of the salpinxes, a long mesosalpinx, hydrosalpinx, hematosalpinx, and tubal mass lesions. Although ITT constitutes a rare cause of lower abdominal pain among women of reproductive age, it may also be observed in premenarchal girls and postmenopausal women. More rarely, ITT may also complicate pregnancy. Although ITT has no specific symptoms, lower abdominal pain is a common finding. There may also be nausea, vomiting, and signs of peritoneal irritation and an adnexal mass. ITT is commonly seen at the right side as a result of partially restricted motion of the left salpinx due to its close anatomical relationship with the sigmoid colon[2-5].

Three types of torsion patterns based on operative findings have been described in the literature [6].

Corresponding Author: Mehmet H. Atalar **e-mail:** mhatalar@gmail.com
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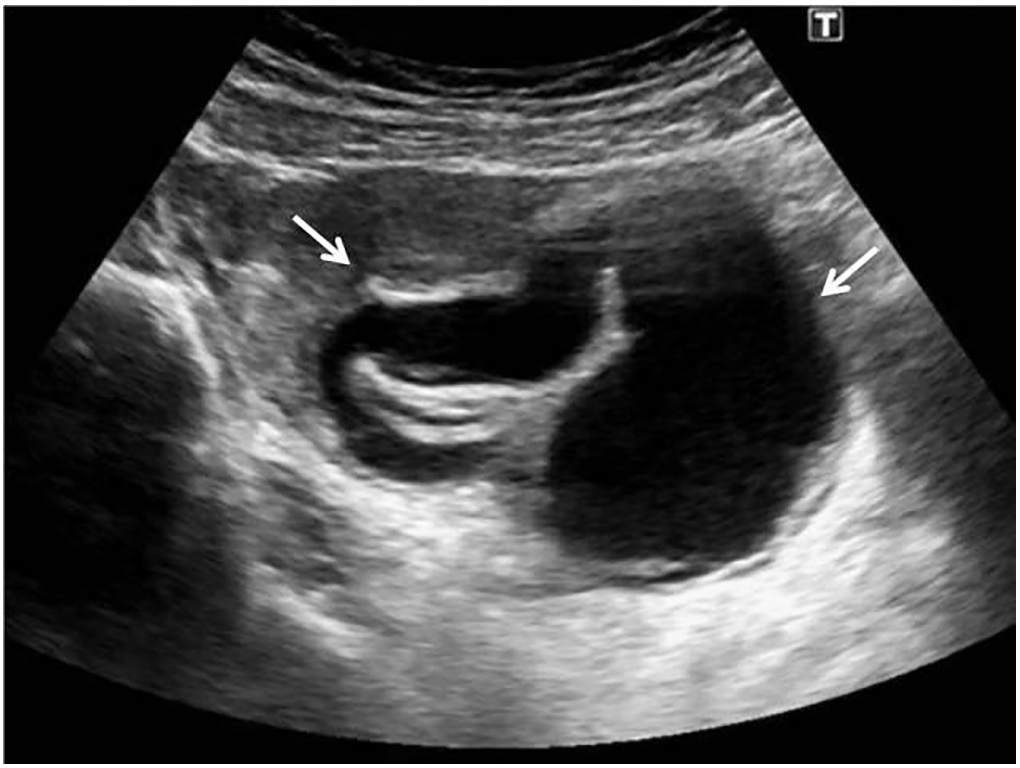

Figure -1. An ultrasonographic image depicts a thick-walled, dilated, cystic right fallopian tube (arrows).

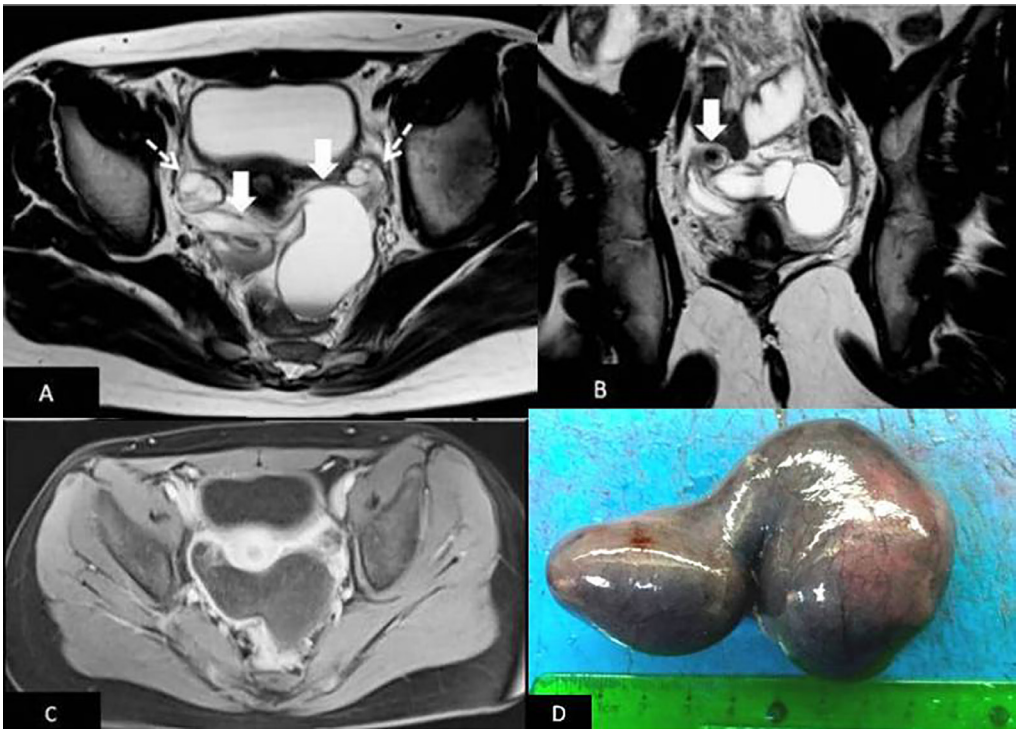

Figure -2. (A) An axial T2-weighted MR image shows a dilated, thick-walled, tubular cystic formation that contains hemorrhagic content in its lumen and takes up contrast material (white arrow). Both ovaries appear normal (dashed white arrows). (B) A coronal T2-weighted MR image shows the whirlpool sign of the right fallopian tube (white arrow). (C) An axial post-contrast fat suppression T1-weighted MR image shows diffuse contrast uptake on the walls of the fallopian tube. (D) A photograph of the surgical specimen depicts a blackish-colored, edematous, ischemic, necrotic fallopian tube with torsion.

- Type 1, Long axis torsion with full-length dilation of the fallopian tube
- Type 2, Short axis torsion with full-length dilation of the fallopian tube,
- Type 3, long-axis torsion with distal dilation of a fallopian tube or a para-tubal cyst.

Based on the above classification, our patient had a type 3 pattern.

Although the US should be the first-line imaging modality by virtue of its rapid, readily available, and noninvasive nature, it, unfortunately, has a low specificity. Among the ultrasonographic signs of tubal torsion are tubal thickening, haemato-/hydrosalpinx, and an adnexal mass. Doppler US may prove useful in suspected cases. It may demonstrate a high impedance coupled with an absent or reversed diastolic vascular flow. However, one should also keep in mind that the presence of a normal flow pattern does not necessarily exclude the possibility of torsion. MRI is a useful technique with a better tissue contrast and the ability to detect the underlying disorder. MRI allows the detection and characterization of an underlying mass and its organ of origin. The whirlpool sign of adnexal torsion is characteristic for its diagnosis. The whirlpool sign was also confirmed by MRI in our case. Other cross-sectional imaging findings of ITT include dilated tubal structures wider than 15 mm, thickened and contrast-enhanced tubal wall, free pelvic fluid, thickened broad ligament, contamination of peri-tubal fat, and localized ileus [4, 6, 7]. As there are no specific radiological, clinical, and biochemical signs despite all of the above-mentioned signs, the preoperative diagnosis of ITT may be difficult. Thus, surgical exploration is considered the gold standard for its diagnosis and treatment. Early diagnosis of ITT is important. A study showed that a time window from the onset of pain to surgical exploration longer than 10 hours increased the risk of tubal necrosis in patients with adnexal torsion [1, 5, 8, 9]. Hence, we opted for surgical exploration since the time from the onset of our patient's symptoms to her hospital admission was one week. In ITT, the risk of interrupted blood supply to the ovaries is low since they receive blood supply from both the ovarian and uterine arteries.

The differential diagnosis of ITT should include acute appendicitis, ovarian cyst rupture or torsion, ectopic pregnancy, pelvic inflammatory disease, cystitis, endometriosis, leiomyoma degeneration, intestinal obstruction or perforation, diverticulitis, and renal colic [3, 6, 7, 8, 10].

Conclusion

In conclusion, despite rare, ITT should be considered among the causes of acute abdomen in women of reproductive age and adolescents. ITT's nonspecific signs and laboratory findings may easily lead to a wrong diagnosis. Radiological imaging should be carried out to evaluate any meaningful finding of tubal torsion in suspected cases. Making a correct diagnosis of ITT and implementing its treatment early in its course is of paramount importance for the preservation of the fertility potential of affected patients.

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