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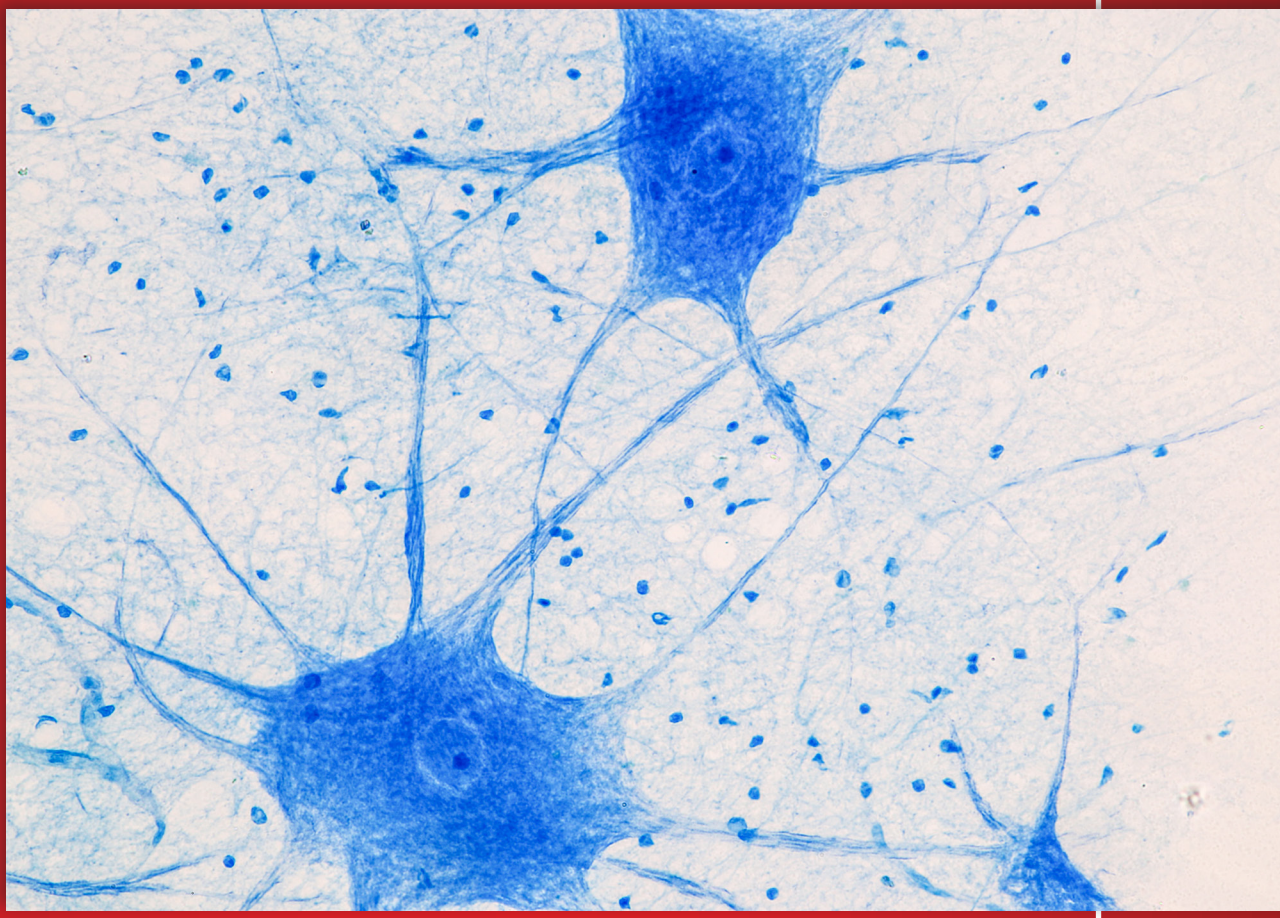

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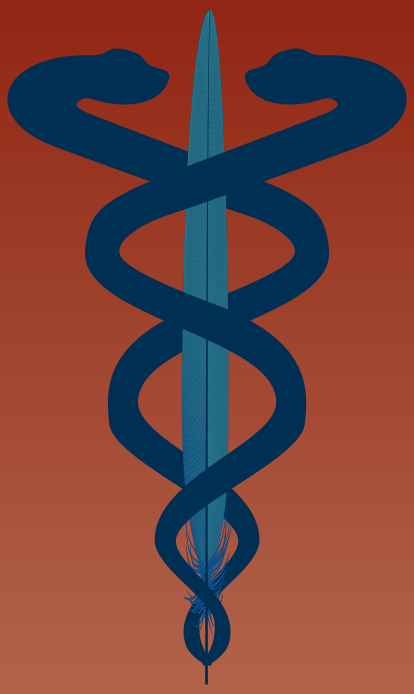

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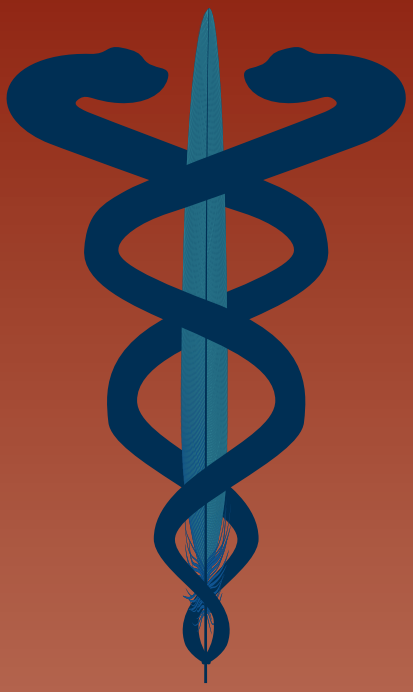

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Current Journal of Medical Research

Is it Possible to Determine Exactly When the Outbreak Started?

Salgının Ne Zaman Başladığını Tam Olarak Saptayabilmek Mümkün Mü?

Gamze GOKALP[1], Tugce NALBANT[2], Yuksel BICILIOGLU[3], Emel BERKSOY[4], Sefika BARDAK[5], Gulsah DEMIR[6], Alper CICEK[7]

ABSTRACT

Aim: The outbreak of the COVID-19 pandemic, which first appeared in late 2019, has undoubtedly affected the global health system. In this study, we tried to investigate whether this disease was seen before the first case in our country with clinical diagnoses.

Methods: This study is a cross-sectional, observational, descriptive study conducted in a pediatric emergency department. The data of the cases were accessed from the hospital automation system. The number of patients who were admitted, the number of hospitalization or intensive care unit, the number of patients who were diagnosed with respiratory tract infection, the triage codes they received in the emergency department, and the viral antigen results obtained from airway swabs are the independent variables of the study.

Results: 46 525 patients were admitted to the pediatric emergency department between 01/12/2018-28/04/2019 and 44 532 patients between 01/12/2020-29/02/2020. (T = 0.8 and P = 0.4) During the 2019 period, 1316 cases were admitted to the ward, and 130 cases to the intensive care unit. During the 2020 period, 1246 cases were admitted to the ward, and 142 cases were admitted to the intensive care unit. (P = 0.06 T = 1.8) During the 2019 period, 12 cases resulted in death, while in the 2020 period, 11 cases of exitus were observed. (P = 0.4)

Conclusion: The fact that more upper respiratory tract diseases were diagnosed compared to the same period of the previous year makes us think that the outbreak may have started in our country before the first diagnosis

Keywords: *COVID-19 outbreak, Pediatric emergency, The pinpoint of an outbreak, Triage codes, Respiratory tract infection rates*

ÖZET

Amaç: 2019'un sonlarında ilk kez ortaya çıkmış olan COVID-19 virüsü şüphesiz ki küresel sağlık sistemini çok fazla etkilemiştir. Biz de bu çalışmada resmi olarak ülkemizde ilk vakanın görüldüğü tarihten önce bu hastalığın görülüp görülmediğini klinik tanılar ile incelemeye çalıştık.

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Yöntem: Bu çalışma çocuk acil servisinde yapılmış, kesitsel, gözlemsel, tanımlayıcı bir çalışmadır. Olguların verilerine hastane otomasyon sisteminden ulaşılmıştır. Belirtilen dönemde başvuran olguların sayısı, hastaneye ya da yoğun bakıma yatış durumları, solunum yolu enfeksiyonu tanısı alanların sayısı, acil serviste aldıkları triyaj kodları ve solunum yolları sürüntüsünden elde edilen viral antijen sonuçları çalışmanın bağımsız değişkenleridir.

Bulgular: Çalışmamıza çocuk acil servisine 01/12/2018-28/04/2019 tarihleri arasında 46 525 hasta ve 01/12/2020-29/02/2020 tarihleri arasında 44 532 hasta başvurusu olmuştur. (T=0,8 ve P=0,4) Olguların acil servisteki izlemleri sonucu çocuk hastalıkları servislerine yatışları incelendiğinde 2019 döneminde 1316 olgu servislere 130 olgu yoğun bakıma yatırılmıştır. 2020 döneminde ise 1246 olgu servislere ve 142 olgu yoğun bakıma yatırılmıştır. (P=0,06 T= 1,8) 2019 döneminde 12 olgu ölüm ile sonuçlanır iken 2020 döneminde 11 eksitus vakası gözlenmiştir. (P=0,4)

Sonuç: Bir sene öncesinin aynı dönemlerine göre daha fazla sayıda üst solunum yolu hastalığı tanısı koyulmuş olması ilk tanıdan daha öncesinde ülkemizde salgının görülmeye başlanmış olabileceğini düşündürtmektedir.

Anahtar kelimeler: *COVİD-19 salgını, Çocuk acil servis, Salgının başlangıcı, Triyaj kodları, Üst solunum yolu enfeksiyonu oranları*

IS IT POSSIBLE TO DETERMINE EXACTLY WHEN THE EPIDEMIC STARTED?

INTRODUCTION

An epidemic means an increase in the number of individuals afflicted by an infectious disease in a given population over a given period. When epidemics cannot be controlled, they cause both high morbidity and mortality and overload in the health system. Therefore, it is necessary to know the frequency of the identified infectious disease in a particular region (1). For this reason, it is necessary to know the frequency of the determined infectious disease in a particular region (1). In some cases, it can be evaluated as if there was no epidemic. Some of these situations can be seen as population mobility in the designated region, referral of cases to that region, use of new diagnostic tests, and changing the case definition (1,2). In order to show the existence of an epidemic, surveillance information for notifiable diseases, hospital records, expert opinions of clinicians, and previous epidemic investigations in that region should be looked at. The event is referred to as an "outbreak" occurs when the event concerns a specific region, an "epidemic" when it concerns a wider region or country, and a "pandemic" when it concerns more than one country and/or continent (1,2).

Influenza viruses affect the population at different levels by causing epidemics every year (3). In general, influenza cases are seen in the northern hemisphere, starting in autumn and continuing until spring (4,5). As a result of changes in the antigenic structure of the virus, extremely mortal epidemics/pandemics have been observed throughout history (6,7).

Towards the end of 2019, a new subspecies of the Coronaviridae family named SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus 2) was detected in the Wuhan province of China (8). This virus quickly spread all over the world, causing a pandemic (9). The first case in our country was detected on March 10, 2020 (10). The clinical picture caused by the virus was determined as fever, respiratory distress, and cough (11). It was stated that lung imaging may be normal, but may have the appearance of consolidation, atelectasis, or ground glass. It was determined that the virus spread through droplets. The World Health Organization declared it a pandemic in February 2020. After these features were determined, attempts were made to take personal protective measures from health professionals (12-14).

An interesting and even confusing point is that many patients with one or more of the above-mentioned symptoms are encountered even before the pandemic period. Of course, since this disease was not officially seen in our country in the periods before the pandemic, no diagnostic test for COVID-19 was performed in such patients. Concerning this, we observed many patients presenting with high fever, cough, and respiratory distress from the end of December 2019 to the beginning of March, when the first patient was officially seen in our country, in our pediatric emergency department. Starting from this point, in this study, we wondered whether the situation we encountered at the end of 2019 and the first two months of 2020 was the beginning of the COVID-19 epidemic. We aimed to find an answer to the question.

METHODS

This is a cross-sectional, observational, descriptive study conducted in a university hospital's pediatric emergency department. Cases admitted to the pediatric emergency service between 01/12/2018-28/02/2019 and 01/12/2020-29/02/2020 were included in the study. The cases admitted between 01/12/2018-28/02/2019 were classified under the "2019 period", and the cases admitted between 01/12/2020-29/04/2020 were classified under the "2020 period". The data of the cases were obtained from the hospital automation system. Number of cases admitted in the specified period, hospitalizations or intensive care unit admissions, number of people diagnosed with respiratory tract infection, triage code received in the emergency room (Red triage code is very urgent, for patients who need immediate intervention, yellow triage code is the first after admission, which is less urgent, for patients requir-

ing intervention within 30 minutes, the green triage code is used for non-urgent patients who need to be evaluated within 1-2 hours after admission and viral antigen results obtained from respiratory tract swabs are the independent variables of the study (15,16). The permission required for our study has been obtained by the Izmir Katip Celebi University Ethics Committee and the Ministry of Health. (Protocol No: 715, 12.05.2020)

The main setup of our study was to determine whether the results obtained in the 2020 period were different from the results obtained in the 2019 period. Therefore, all values were compared with values corresponding to the same period of the previous year. The distribution of the number of patients admitted to the emergency department, hospitalizations, intensive care admissions, triage codes, and deaths in the emergency department by months were determined and compared with the data of the other year.

The data were analyzed in the SPSS 22.0 package program, the continuous variables were presented in the form of averages, the relationships between them were analyzed with the T-Test, and the cases where the alpha value was determined below 0.05 were considered "significant".

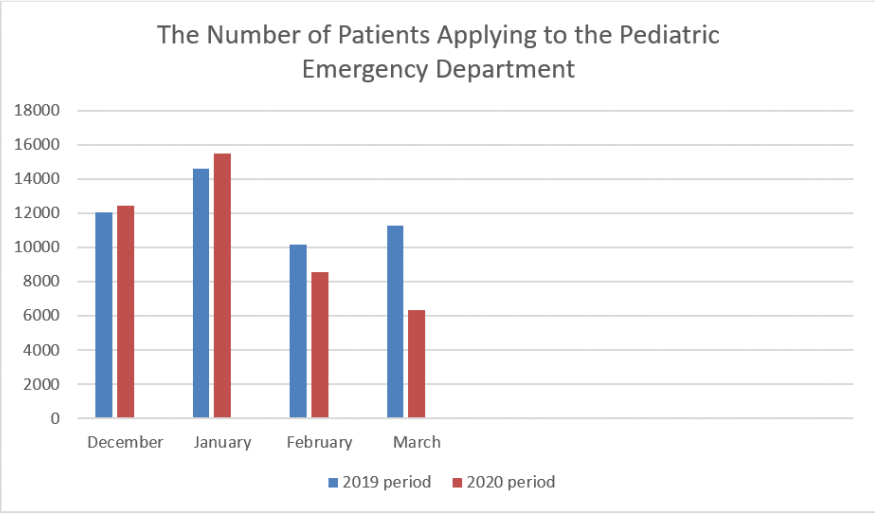
RESULTS

In this current study, 46 525 patients were admitted to the pediatric emergency service between 01/12/2018-28/04/2019, and 44 532 patients between 01/12/2020-29/02/2020. (T=0.8 and P=0.4) In December 2018, an average of 535.96 patients were admitted per day, while in December 2019, there were an average of 551.77 patient admissions per day. (353 patients in total increased by 2.9%, P=0.5, and T=0.67) While an average of 617.19 patient admissions per day in January 2019, there was an average of 651.45 patient admissions per day in January 2020. (In total, 904 people increased by 6%, P=0.3, and T=0.87) While an average of 506.70 patients were admitted per day in February 2019, there were an average of 383.87 patient admissions per day in February 2020. (A total of 1643 people decreased by 16%, P<0.01 and T=8.7)

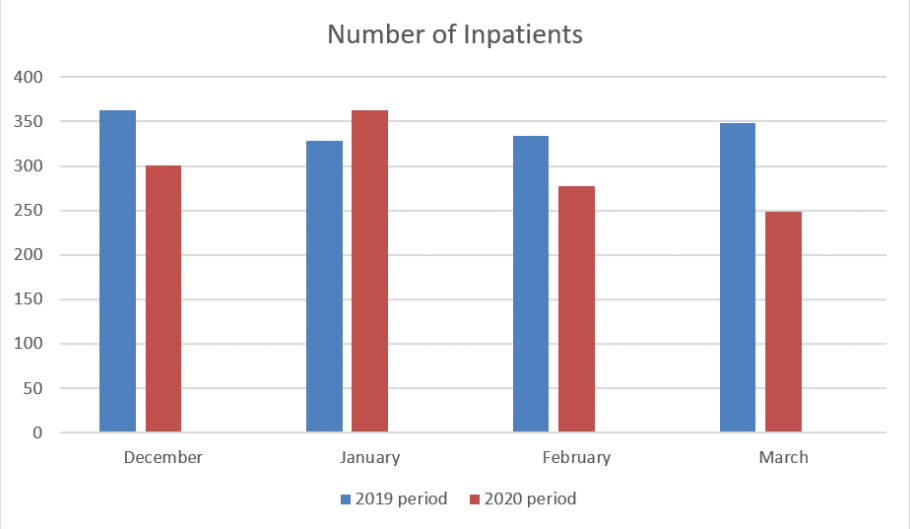
When the patients admitted to the emergency department were evaluated according to their respiratory tract infection status, it was found that an average of 117.58 cases per day in December 2018 were diagnosed with respiratory tract infection, and in December 2019, an average of 150.29 patients per day were diagnosed with this diagnosis. (639 people in total and increased by 13%, P<0.01 and T=6.5) In January 2019, an average of 157,41 cases per day were diagnosed with respiratory tract infection, while in January 2020, an average of 202.45 cases per day were diagnosed with respiratory tract infections. (In total, 1053 persons increased by 16.8% and 6%, P<0.01 and T=5.2) In February 2019, an average of 96.44 cases per day were diagnosed with respiratory tract infection, while in February 2020, an average of 106.75 patients per day were diagnosed with this. (392 people in total and increased by 12%, P=0.03, and T=2.1) (Table 1) The number of admissions by month and the cases diagnosed with respiratory tract infection are shown in graphs 1 and 4 While 11 942 (25.7%) of the cases who applied to the pediatric emergency department in 2019 received the green triage code, 34 583 (59.3%) cases received yellow and red triage codes. In 2020, the number of patients with green triage codes increased by 365 (2.9%) to 12 307, while the number of patients with yellow and red triage codes decreased by 1358 (3.9%) and reached 33 225. (P=0.1 and T=0.3 and P=0.3 and T=0.9 respectively) When the distribution of the cases with green triage code according to months was analyzed, no significant difference was observed between the 2019 and 2020 periods. (P=0.2; P=0.8; P=0.1, respectively) When the cases with yellow and red triage codes were evaluated, it was found that there were a significantly higher number of patient admissions in December, January, and February 2020 compared to the same months in 2019. (P<0.01; P=0.01; P=0.02 respectively) (Table 2)(Graphic 5)

Table 1: The number of all cases admitted to the pediatric emergency department in 2019 and 2020 and the distribution of the number of cases with respiratory tract infections by months

	2019 Period		2020 Period		P		T	
	All applications	Respiratory system diseases	All applications	Respiratory system diseases	All applications	Respiratory system diseases	All applications	Respiratory system diseases
December	535,96	117,58	551,77	150,29	0,5	**<0,01**	0,67	6,5
January	617,19	157,41	651,45	202,45	0,3	**<0,01**	0,87	5,2
February	506,70	96,44	383,87	106,75	**<0,01**	**0,03**	8,7	2,1
March	512,52	100,36	250,15	78,90	**<0,01**	**<0,01**	9,4	5,07



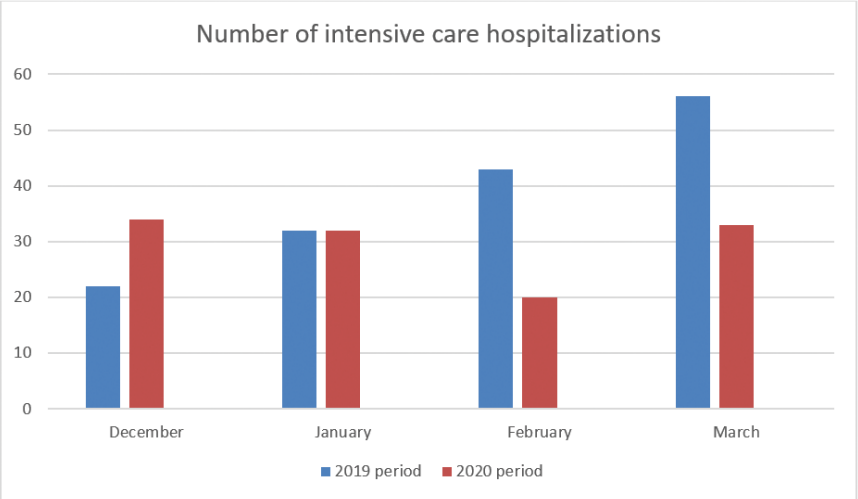
Graph 1: Number of Patients Applying to the Pediatric Emergency Department (P<0,01 ve T=4,20)



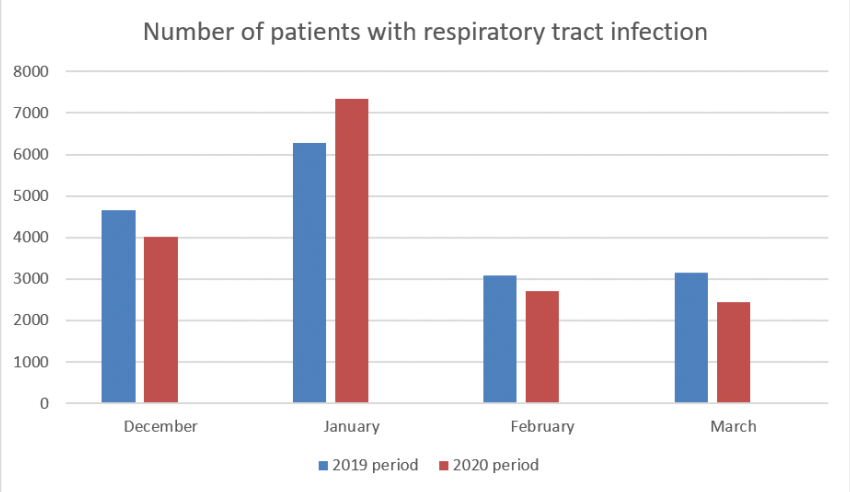
Graph 2: Number of Inpatients (Pediatric ward) (P=0,06 ve T=1,8)

Table 2: Distribution of cases with green, yellow and red triage codes in the pediatric emergency department in 2019 and 2020 according to months

	2019 Period		2020 Period		P		T	
	Green	Yellow and red	Green	Yellow and red	Green	Yellow and red	Green	Yellow and red
December	94,48	69,80	111,29	323,90	0,2	**<0,01**	1,2	8,9
January	151,41	314,22	171,09	349,67	0,8	**0,01**	0,2	0,3
February	88,37	211,62	60,65	230,96	0,1	0,2	2,4	2,3
March	78,03	287,27	42,7	165,28	**0,03**	**<0,01**	3,1	7,4



Graph 3: Number of intensive care hospitalizations (P<0,01 ve T=4,3)

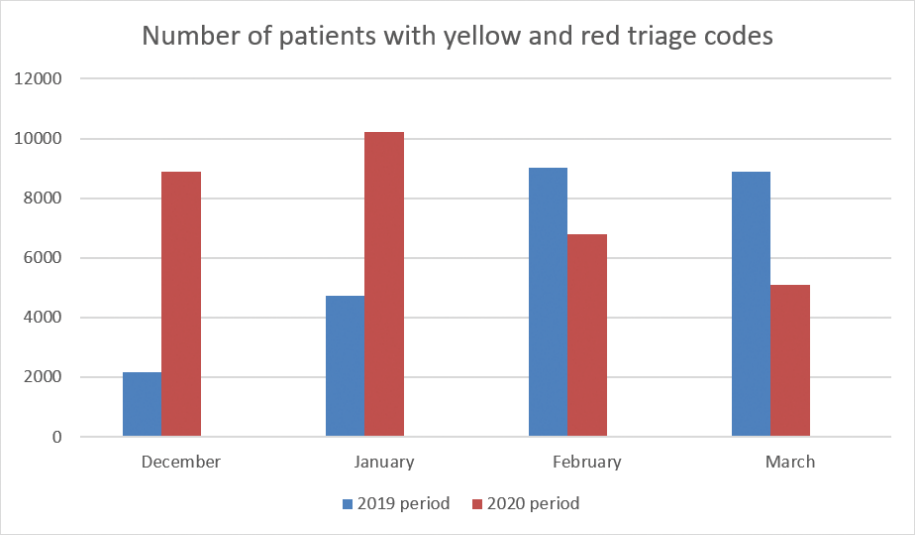


Graph 4: Number of patients with respiratory tract infection (P=0,9 ve T=0,08)

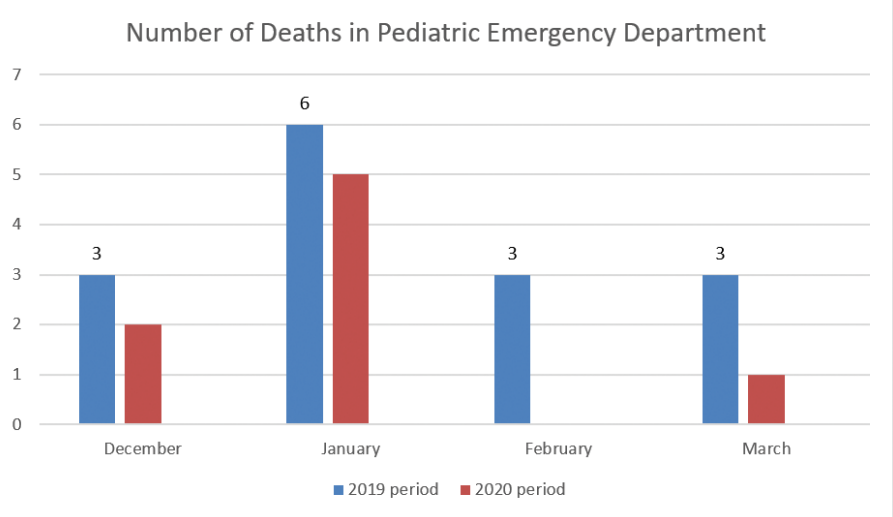
Considering the hospitalizations of the cases in the pediatric wards as a result of their follow-up in the emergency room, 1316 cases were admitted to the wards and 130 cases were hospitalized in the intensive care unit in 2019. In the period of 2020, 1246 cases were hospitalized in the wards and 142 cases in the intensive care unit. (P=0,06 T= 1,8) While there was no difference in the number of hospitalizations in the ward for December in the 2019 and 2020 periods, the number of hospitalizations in the ward was significantly higher in January and February 2020 periods (P=0.2; P=0.04; P=0.02 respectively) When examined in terms of intensive care admissions in the 2020 period, there were more hospitalizations in both December, January, and February. (P=0.03, P=0.01, and P<0.01) (Table 3)(Graphs 2 and 3)

Table 3: Distribution of cases admitted to the pediatric intensive care unit and pediatric services from the pediatric emergency department in 2019 and 2020, according to months (*PICU: Pediatric intensive care unit)

	2019 Period		2020 Period		P		T	
	PICU*	Ward	PICU	Ward	PICU	Ward	PICU	Ward
December	0,74	11,83	1,06	12,7	**0,03**	0,2	3,1	1,1
January	1,06	10,58	2,03	13,70	0,02	0,04	0,4	0,6
February	0,72	10,00	1,59	12,55	**<0,001**	0,02	5,0	1,2
March	1,61	12,7	1,09	8,06	**<0,01**	**0,02**	5,2	2,2



Graph 5: Number of patients given yellow and red codes in the Emergency Triage (P=0,3 ve T=0,9)



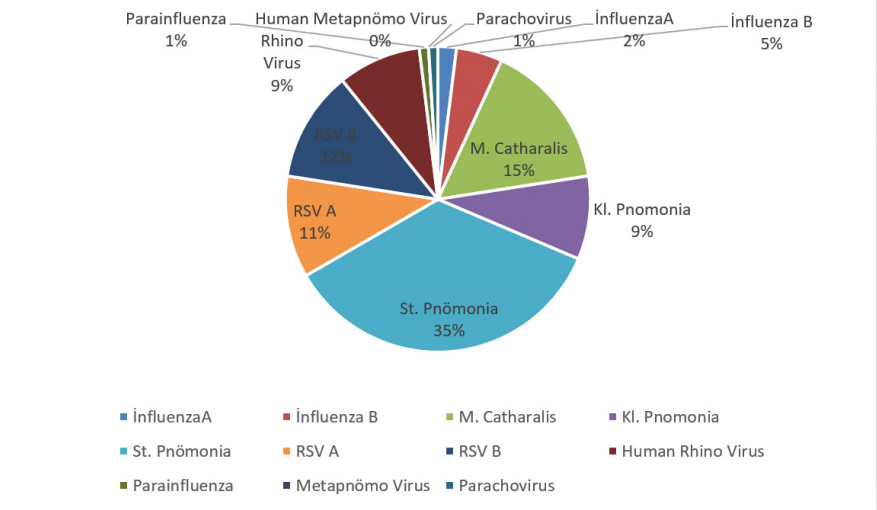
Graph 6: Number of Deaths in Pediatric Emergency Department

While 12 cases resulted in death in 2019, 11 deaths were observed in 2020. (P=0.4) (Graph 6)

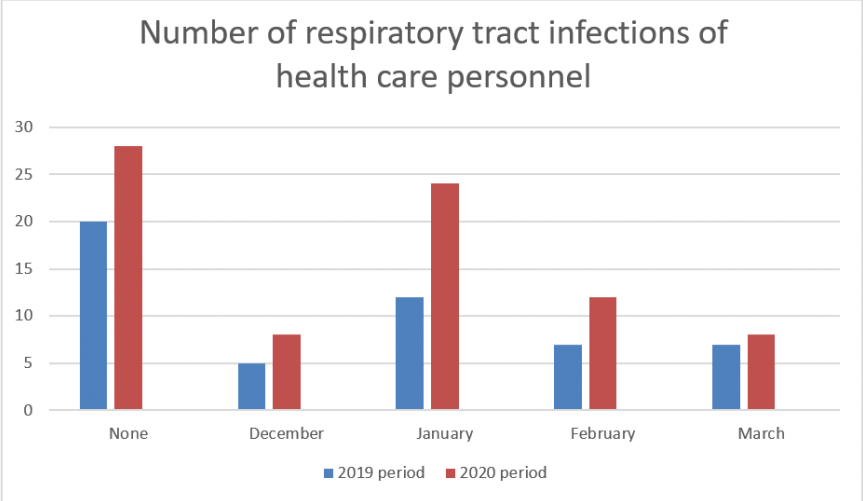
When we examined the viral and bacterial antigens in the swabs taken from the respiratory tract, 35% *S. Pneumonia*, 15% *M. Catarralis*, 9% *K. pneumonia*, 11% *RSV A*, 9% *Rhinovirus*, 7% *Influenza A* and *B* virus were detected (Graph 7).

DISCUSSION

The purpose of our study was to determine whether there were any cases of COVID-19 before the 10th of March 2020 when, according to the health authorities, the first case in our country emerged. Before the official announcement of the pandemic, COVID-19 diagnostic kits were not available in laboratories in our country, as in the rest of the world, so we investigated whether there were any abnormal patient admissions to the pediatric emergency services. While conducting this research, we thought that the most objective data was to compare the patients who applied in the same period the previous year. There was no data on any epidemic situation in the literature during 2019, but, in our study, we saw that there were more patient admissions in total in 2019 than in 2020. However, the number of patients diagnosed with respiratory tract infections was higher in 2020. Although there were more patients with respiratory diseases in the period of December 2019 and January 2020 than a year ago, fewer patients were detected in February 2020 compared to the previous year. We think that the reason for this is the increased awareness and concern among citizens about COVID-19 since February, reducing the number of visits to the hospital due to the risk of transmission. In particular, the data for December and January 2020 makes us think that the first cases seen in our country may have occurred before the officially announced date.



Graph 7: Viral Antigens Detected in Respiratory Tracts in 2020



Graph 8: 2019 and 2020 Number of respiratory tract infections of health care personnel (P=0,02)

Although some speculative comments have been made regarding the first time the COVID-19 virus was seen in the world, this issue has been clarified in general. Timing estimates made with available sequence data of the most recent common ancestor of SARS-CoV-2 point to the emergence of the virus in a time frame from late November 2019 to December 2019, which is consistent with the earliest retrospectively confirmed cases (17-19). However, regionally, there are reports in various media about the existence of the disease long before the first diagnosis in some places.

According to one of these news, some Italian scientists state that many patients with COVID-19-like symptoms, especially in the northern regions of Italy, applied to hospitals in the last quarter of 2019. There is no study showing that it was seen earlier than the dates.

We analyzed the results of swab samples taken from the respiratory tract of patients to determine whether the increase in cases at the beginning of 2020 was due to an epidemic caused by any pathogen other than COVID-19. Markers of the normal throat flora and common cold agents were detected in a large proportion (20,21). The absence of significant clustering in other agents showed us that there was no epidemic, such as a seasonal influenza epidemic.

Since our study is a retrospective study, there are surely some limitations. For example, if we had computerized thorax tomography data, which has been shown to be diagnostically reliable many times today, despite the lack of COVID-19 diagnostic kits, we could have made a much clearer inference. On the other hand, since the diagnosis of upper respiratory tract diseases includes a wide spectrum, the reliability of the diagnoses also raises questions.

As a result, even though COVID-19 patients were seen in our country simultaneously with the Republic of China, which is the source of the virus, as far as we can see, it did not

have an impact on the health system, especially on pediatric clinics. However, if the disease occurred before the officially stated date in both children and adults, this may have caused the disease to spread much faster. However, it does not seem possible to claim that the epidemic may have occurred before the first appearance of the epidemic in our country, as it is in the whole world, only with clinical data.

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Current Journal of Medical Research

A Hepatic Encepholopathy Case By Abusing Synthetic Cannabinoid and Ecstasy

Sentetik Kannabinoid ve Ekstazinin Kötüye Kullanıldığı Bir Hepatik Ensefalopati Olgusu

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ABSTRACT

The increasing prevalence of illicit drugs abuse is a significant social and medical problem. This situation can cause various results, ranging from simple intoxication to fatal organ failure. The most common illicit is ecstasy (MDMA) and marijuana (cannabis). In this case report we tried to present a hepatic encephalopathy case due to using these drugs.

Keywords: *Ecstasy, a synthetic cannabinoid, hepatic encephalopathy*

ÖZET

Önemli bir sosyal ve tıbbi sorun olan, yasadışı uyuşturucu maddelerin istismarın prevalansı artmaktadır. Bu durum basit zehirlenmeden ölümcül organ yetmezliğine kadar çeşitli sonuçlara neden olabilir. En yaygın yasadışı maddeler ekstazi (MDMA) ve esrardır (cannabis). Bu olgu sunumunda bu maddeleri kullanmaktan kaynaklanan hepatik ensefalopati olgusunu sunmaya çalıştık.

Anahtar kelimeler: *Ekstazi, Sentetik kannabinoid, hepatik ensefalopati*

INTRODUCTION

The use of drugs without the doctor's prescription, except for treatment, is named drug abuse or misuse of drugs. These drugs are; caffeine, tobacco, alcohol, morphine and its derivatives, benzodiazepines, barbiturates, amphetamines, hashish, heroin, cocaine, volatile solvents, and bonsai (1). These agents with various toxic effects can lead to many problems, from simple deprivation symptoms to death (1). In this article, we have tried to present a case that developed hepatic encephalopathy based on toxic hepatitis following the use of an intensive amount of ecstasy and bonsai.

CASE

A seventeen-year-old male patient was brought to the emergency with the ambulance due to complaints of yellowing in skin color, nausea, vomiting, meaningless speech, difficulty in walking, and uncontrolled movements.

According to the anamnesis; sudden nausea and vomiting started one day before the application, his skin color changed to dark yellow-green, and on that day, these symptoms were accompanied by meaningless speeches. He had uncontrolled movements with a big amplitude on all extremities, especially in the arms. It was reported that the patient took five MDMA pills and one bonsai tablet, and no other medicine or herbal substances. At his admission to the emergency service, he had a poor and degraded general appearance, and he also had poor self-care with an anxious mood. He was conscious of the disoriented speeches and movements. His maximum heart rate was 110/min, respiratory rate was 26/min, blood pressure was 112/67 mm Hg, and oxygen saturation was 99%. He had dark yellow-green skin. There was horizontal nystagmus. There were uncontrolled choreiform movements with high amplitude in four extremities, especially the upper extremity. Also, there were asterisk-like movements and essential tremors in the hands. The other systemic examination (and also the neurological examination) was normal.

In the serum biochemical examinations; white blood cell was 24.300/mm3, aspartate transferase was 1182 U/l, alanine aminotransferase was 1921 U/l, lactate dehydrogenase was 576 U/l, creatinine kinase was 478 U/l, total bilirubin was 18.8 mg/dl, direct bilirubin was 9.72 mg/dl, C-reactive protein was 9 mg/dl, procalcitonin was 1.82 mg/dl, active partial thromboplastin time was 36 seconds, prothrombin time was 21,6 seconds, and INR was 1.89. In urine toxicological analyses, amphetamine was positive. The other laboratory findings were normal.

With the present findings in consideration, the patient was preliminarily assessed with acute hepatitis, hepatic failure, and hepatic encephalopathy. To make the definitive diagnosis of acute hepatitis etiologically, viral hepatitis, Ebstein Barr Virus, and cytomegalovirus serologies were detected normally. To rule out autoimmune hepatitis, autoimmune antibodies were studied, and it was assessed as being normal. The serum ammonia level, which was checked to rule out metabolic diseases, was normal. Blood ceruloplasmin level was determined as normal for Wilson's disease. The abdominal and Doppler ultrasound imaging showed no abnormalities. The current liver disease of the subject was assessed as toxic hepatic related to the agents he took. As it was likely that his encephalopathy could be due to cerebral edema, a fundus examination was conducted and determined as normal. Magnetic resonance images of the brain were determined to be normal. The electroencephalographic waves showed us an encephalopathic pattern. The findings were evaluated as hepatic encephalopathy. The subject was examined together with the hepatology department, and as a general supplementary treatment, Vitamin K, Ursodeoxycholic acid, and N-Acetylcysteine treatments were started. A diet rich in carbohydrates and poor in protein was initiated for the subject, and he was put under observation. He was transferred to the liver transplantation center with the diagnosis of acute liver failure.

DISCUSSION

From the 1990s onwards, the use of ecstasy, a sort of stimulant and hallucination, has become widespread in Europe and the USA. Likewise, it has started to be used at an increasing rate in our country, as well (2,3). The use of ecstasy is so common in some regions that Andreu et al. reported that ecstasy is the second most common reason in subjects diagnosed with toxic hepatitis under the age of 25 (4). Hepatotoxicity due to ecstasy appears to be independent of dosage and frequency of use. In alignment with the literature, our subject developed a clinical picture of liver failure after the intake of just five pills. The issues with hepatotoxicity due to ecstasy can both recover spontaneously and follow a very poor process, even to death. Liver transplantation was done to some subjects with a fulminant process (4,5). The most extensive series revealing the results of liver transplantation in fulminant hepatitis due to ecstasy belongs to Brauer et al., who compared the subject to whom they applied liver transplantation for fulminant hepatitis due to ecstasy with the other nine similar subjects in literature (5). In our issue, the developing hepatotoxicity progressed fulminant and brought about the need for liver transplantation.

In Turkey, bonsai use is on the increase, like ecstasy (6). However, as pharmacology laboratories study the drug levels usually with the CEDIA method, bonsai is not determined in urine and blood samples though there is a story of bonsai use, which hides the real abuse rates of these agents (7). One of the primary problems with analyzing and recognizing such new-generation drugs is that. There are a lot of kinds of isomers and their derivatives, and their biochemical structures are often changed for them to escape the screening tests (8). This leads to difficulty in the detection of new-generation drugs. Their negative effects are convulsions, anxiety, aggressiveness, muscle rigidity, and confusion (8). The cause of profound agitations, anxiety, epileptic fits, and convulsion observed in these agents is the agonist activity and GABA enzyme inhibition (8). Neurological symptoms in our subject were nystagmus and choreiform movements, which we think are due to GABA inhibition. Some other cases have been reported for acute kidney failure, acute visual loss, Wernicke syndrome, and liver failure due to synthetic cannabinoids (9). According to the UN report of 2010, as the components of synthetic cannabinoids are many and various, the determination of its specific effect is difficult. Therefore, there is no known specific antibody or treatment for it, except for symptomatic treatments (9).

As a result, the increased use of both ecstasy and bonsai will become more and more critical for public health in the near future. Serious problems are caused by the high-distribution volume feature of synthetic cannabinoids. They can cause prolonged and exaggerated effects due to showing accumulation caused by their lipophilic component, the presence of increasing isomers and their derivatives, and the inability to determine the agents in scanning tests. Although the subject who applied to our emergency service showed indications of intoxication, the use of synthetic cannabinoids should first be thought of for the topics that prove to have a negative drug panel. Then symptomatic treatment should be started immediately. Considering that symptoms may appear in the late period, the follow-up/observation periods should be kept as long. To prevent probable deaths, pharmacology laboratories should be updated quickly. In the subjects who apply to the emergency services due to acute liver failure table, the use of these agents should be questioned and considered as an etiologic agent, especially in the adolescent group.

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A Patient With Rheumatoid Arthritis Who Developed Pasteurella Multocida Arthritis Without Animal Contact; Case Report

Romatoid Artrit'li Hastada Hayvan Teması Olmaksızın Gelişen Pasteurella Multocida Artriti; Olgu Sunumu

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ABSTRACT

Pasteurella species are immobile, non-sporeless, gram-negative coccobacilli that can be found in the respiratory tract and gastrointestinal tract flora of pets and can cause various infections with cat-dog bites. While it usually causes cellulitis and abscesses, clinical pictures such as septic arthritis, osteomyelitis, pneumonia, endocarditis, sepsis and meningitis can also be seen in immunosuppressed patients. Here, a case of septic arthritis due to Pasteurella multocida, which developed in the left shoulder joint of a 70-year-old female patient with a history of rheumatoid arthritis, diabetes mellitus, and hypertension, without animal contact or trauma, is presented in the light of the literature.

Keywords: *Pasteurella multocida, Arthritis, Rheumatoid Arthritis*

ÖZET

Pasteurella türleri, evcil hayvanların solunum yolları ve gastrointestinal sistem floralarında bulunabilen hareketsiz, sporsuz, gram negatif kokobasiller olup kedi-köpek ısırıklarıyla çeşitli enfeksiyonlara neden olabilirler. Genellikle sellülit ve apselere neden olurken, immünsuprese hastalarda septik artrit, osteomyelit, pnömoni, endokardit, sepsis ve menenjit gibi klinik tablolar da görülebilmektedir. Burada yetmiş yaşında; özgeçmişinde romatoid artrit, diabetes mellitus ve hipertansiyon tanısı olan kadın hastanın, sol omuz ekleminde hayvan teması veya travma öyküsü olmaksızın gelişen *Pasteurella multocida*'ya bağlı septik artrit olgusu literatür eşliğinde sunulmuştur.

Anahtar Kelimeler: *Pasteurella multocida, Artrit, Romatoid Artrit*

GİRİŞ

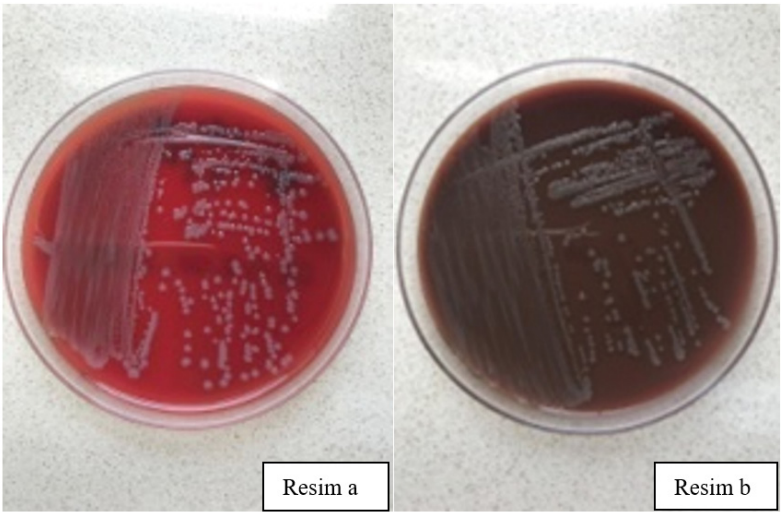
Pasteurella türleri, kedi ve köpek gibi evcil hayvanların üst solunum yolları ve gastrointestinal sistem floralarında bulunabilen hareketsiz, sporsuz, gram negatif bir kokobasil olup kedi ve köpek ısırıkları sonra-

sında çeşitli enfeksiyonlara neden olabilen başlıca zoonozlar arasında yer almaktadır(1). Genellikle insanlarda hayvan temasını takiben yumuşak dokudan başlayan sellülit ve subkutan apselere neden olurken, immünsuprese hastalarda septik artrit, osteomyelit, pnömoni, endokardit, sepsis ve menenjit gibi ciddi klinik tablolar da görülebilmektedir(2,3).

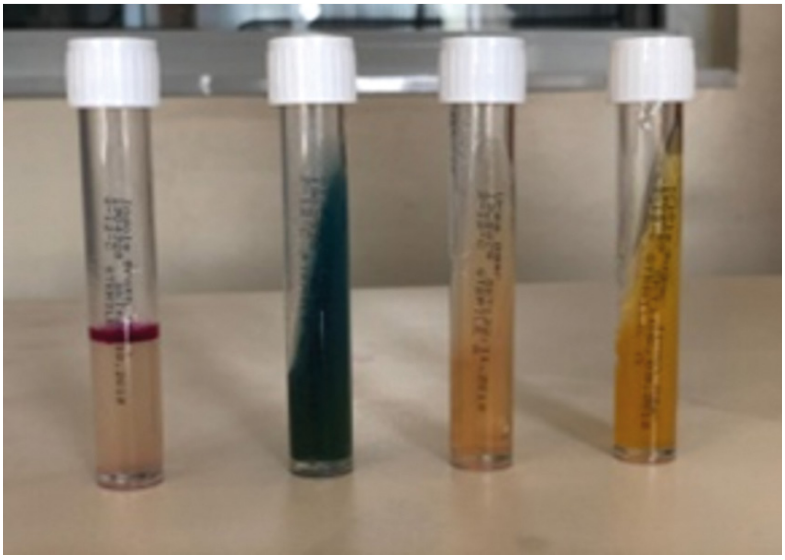
Bu makalede, hayvan teması veya travma öyküsü olmayan bir hastanın omuz ekleminde yerleşim gösteren ve *Pasteurella multocida*'nın etken olarak izole edildiği septik artrit olgusu sunulmaktadır.

OLGU

70 yaşında kadın hasta; halsizlik, iştahsızlık, sol omuzda ağrı ve hareket kısıtlılığı şikayetleriyle hastanemize başvurdu. Batın ve akciğer muayenesi normaldi. Lenfadenopati ve deri döküntüleri yoktu. Hayvan teması veya travma öyküsü yoktu. Özgeçmişinde romatoid artrit(RA), interstisyel akciğer hastalığı, diabetes mellitus, hipertansiyon ve ciddi aort darlığı tanıları mevcut olan hasta RA nedeni ile metilprednizolon, metotreksat ve rituksimab tedavilerini almaktaydı. Laboratuvar tetkiklerinde, beyaz küre sayısı 8200/mm3 (%71 PNL hakimiyeti) idi. C reaktif protein ve sedimentasyon düzeyindeki yükseklik dışında (CRP: 14.7 mg/dL, sedim: 70 mm/sa) diğer rutin hematolojik ve biyokimyasal parametreleri normal sınırlarda idi. Hastanın sol omuzunda artrit bulguları olması üzerine eklem ponksiyonu yapıldı. Mikrobiyoloji laboratuvarına gönderilen materyalin direk mikroskobik incelemesinde >50.000 lökosit/mm³ görüldü. Rutin olarak %5 koyun kanlı, eosin methylen-blue (EMB) ve çikolatamsı agarlara ekim yapıldı; plaklar 16-24 saat süreyle 35-37ºC'lik etüvde inkübe edildi ve değerlendirildi. Makroskobik görünümü kanlı ve çikolata agarlarda non-hemolitik, yuvarlak, gri koloniler şeklinde üreme olurken, EMB agarda üreme olmadı(Resim a ve b). Kolonilerin boyalı preparatında gram negatif kokobasiller görüldü. Kolonilerden yapılan katalaz ve oksidaz testleri pozitif olarak bulundu. Biyokimyasal olarak Triple sugar iron(TSI) agarda sarı-sarı H_2S negatif, üreaz testi negatif, nitrat ve indol testleri ise pozitifti(Resim c). İzolat daha sonra Phoenix(BD, USA) otomatize sistemi ile *Pasteurella spp.* olarak tanımlandı. Doğrulama ve tür düzeyinde tanımlama amacıyla MALDI-TOF MS(Bruker Microflex LT, Germany) ile identifikasyonu yapıldı ve *Pasteurella multicoda* olarak teyit edildi. 2 gün sonra septik artrit nedeniyle hastanın sol omzuna yapılan debridman materyalinde aynı üreme saptandı. Antibiyotik duyarlılık testi Kirby-Bauer disk difüzyon yöntemi ile yapıldı. Zon çapları EUCAST klinik sınır değer tablosu sürüm 8.1(2018) kullanılarak değerlendirildi. Penisilin, tetrasiklin, siprofloksasin, levofloksasin, sefotaksim ve trimethoprim-sulfamethoksazola duyarlı olarak saptandı(4). Hastaya piperasilin tazobaktam+teikoplanin(8 gün) ve sonrasında meropenem+siprofloksasin(13 gün) tedavisi başlandı. Takibinde karaciğer fonksiyon testlerindeki yükselme nedeniyle tedaviye sadece siprofloksasin ile devam edildi. Gönderilen kontrol kültürlerinde üreme olmayan hasta, 1 ay hastanede yatarak şifayla taburcu edildi.



Resim a ve b: Hastanın eklem ponksiyon materyalinden üreyen *Pasteurella multicoda*'nın %5 koyun kanlı agar(a) ve çikolatamsı agardaki(b) makroskobik görünümü.



Resim c: Hastanın eklem ponksiyon materyalinden üreyen Pasteurella multicoda'dan yapılan biyokimyasal testleri soldan itibaren sıra ile indol (+), nitrat testi (+), TSI'de sarı-sarı H_2S (-), üre testi (-).

TARTIŞMA

Septik artritin tüm olgular arasında en sık etkeni Gram pozitif koklardır. Bunun yanı sıra özel gruplar olarak 10-40 yaş arasında *Neisseria gonorrhoeae*; yenidoğan döneminde *Staphylococcus aureus*, β-streptokoklar ve Gram negatif basiller; 6 ay-5 yaş arası *Haemophilus influenzae*; immün yetmezlikli hastalarda Gram negatif basiller; alkolizm ve HIV enfeksiyonu gibi faktörlerin varlığında *Streptococcus pneumoniae*(pnömoni, menenjit gibi primer bir enfeksiyon ile birlikte) en sık etken olarak karşımıza çıkmaktadır(5,6).

Pasteurella multocida ise nadir bir etkendir; özellikle kedi ve köpek ısırması durumunda ve daha çok metakarpal eklemlerde olmak üzere artrit etkeni olabilmektedir(7). Balcı ve ark.(8), Vurucu ve ark.(9), Alpay ve ark.(10), Ceyhan ve ark.(11) yaptığı olgu sunumlarında kedi tırmalaması öyküsü olan hastalarda *Pasteurella multocida*'nın etken olduğu osteomyelit ve yumuşak doku enfeksiyonları bildirilmiştir.

Ancak *Pasteurella multocida*'nın artrit etkeni olduğu vakaların %5-10'unda görünür bir hayvan teması olmaksızın da etken olarak ortaya çıkabilmektedir(12). 34 olguluk yapılan bir vaka taramasında *Pasteurella multocida* enfeksiyonlarını üç gruba ayırmışlar: hayvan ısırığı kaynaklı enfeksiyonlar (lokal yara yeri enfeksiyonu, apse, artrit), hayvan solunum yolu ve sekresyonu ile temas(pnömoni, ampiyem), sistemik enfeksiyonlar(bakteriyemi, menenjit, beyin apsesi). Ayrıca Romatoid artritli veya protez eklemli hastalar gibi daha önceden hasar görmüş eklemlerin bulunması *Pasteurella multocida* septik artriti için bir predispozan faktör olduğunu gösterilmiştir(13). Nitoslawski ve ark. olgusunda(14) osteoartriti olan bir hastada septik artrit gelişirken, Baer Mears ve ark olgusunda(15) ise RA'lı hastada bakteriyemi gelişmiştir. Ancak her iki olguda da hastaların kedi temas öyküsü bulunurken ısırma, tırmalama veya travma kanıtı bulunmamaktadır. Bir başka olgu da kedi salyası ile temas olmasına rağmen tırmalama öyküsü olmayan *Pasteurella multocida* etkeni Zarlasht ve ark. tarafından gösterilmiştir(16). Ancak bu olguda hasta immünsuprese olmamasına rağmen bakteriyemi gelişmiştir. Bizim olgumuzda ise herhangi bir kedi-köpek teması olmamasına rağmen hasta RA'ya bağlı hem immünsuprese hem de hasar görmüş eklemi bulunmaktadır.

Sonuç olarak, *Pasteurella* türleri genellikle evcil hayvan ısırığı veya salgısı ile temas yoluyla bulaşsa da literatürde nadiren görülen hayvan teması veya travma öyküsü olmayan immünsuprese(özellikle romatoid artritli ve immünsuprese ilaç kullanım öyküsü olan) hastalarda da görülebilmektedir(15,16). Bu nedenle septik artritli immünsuprese hastalarda etken olarak *Pasteurella* türlerini de akla getirmek gerekmektedir.

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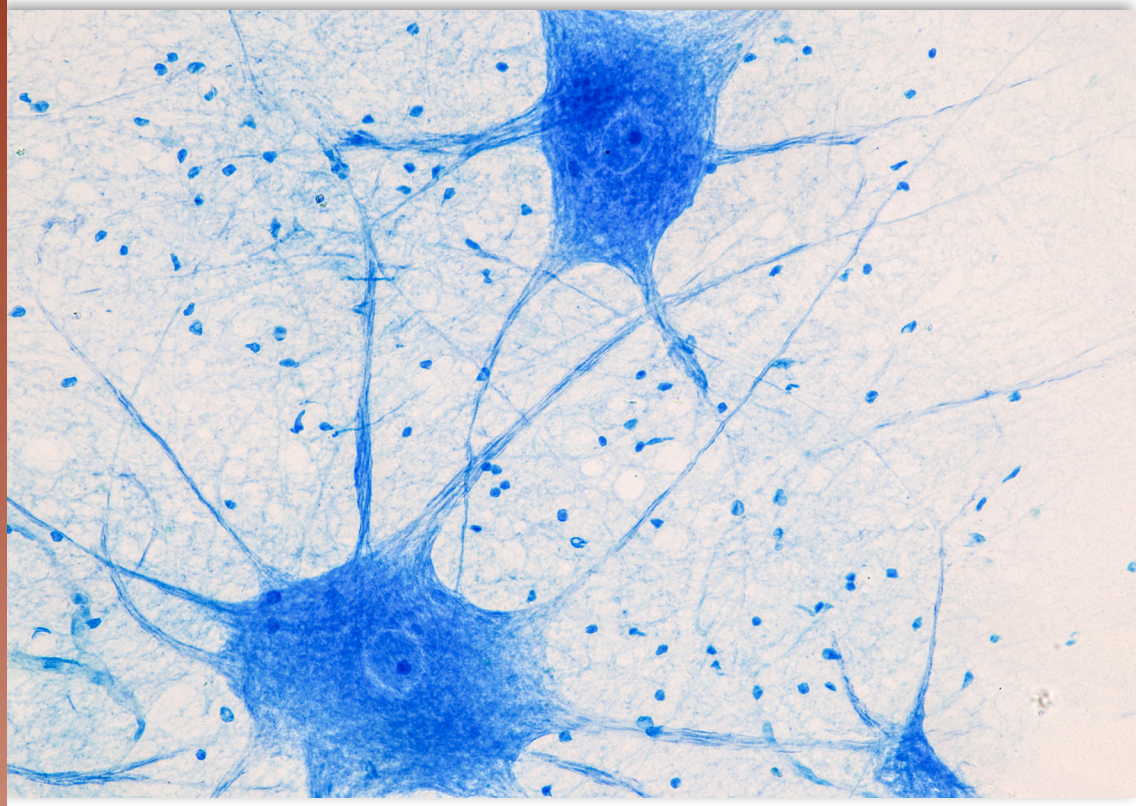

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