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Complications of Meckel's diverticulum in children: A 10-years experience

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ABSTRACT

Meckel's diverticulum is the most common congenital anomaly of the gastrointestinal tract. We aimed to evaluate the risk factors which could be cause complications of Meckel's diverticulum. The patients who were operated in our clinic on for Meckel's diverticulum complications between 2008-2018 were evaluated retrospectively for age, gender, timing of surgery, scintigraphic detection of bleeding, histopathological evaluation, type of resection and surgical method. 62 patients (38 males, 24 females) (6 months-17.08 years), 35 underwent emergent and 27 elective surgery. Only 3 had preoperative diagnosis who underwent emergency surgery. In the emergency group, the number of invagination, internal herniation, diverticulitis and perforation were 14, 11, 6, 4 respectively. Twenty two patients were managed with laparatomy and the thirteen patients were managed with laparoscopy asisted. Ileal segment resection and wedge resection were performed in 16 and 19 patients retrospectively. In emergency surgery group 16 patients had both ectopic stomach and pancreas tissue and six patients had gastric tissue alone in histopathological evaluation. On the other hand 13 patients had no ectopic tissue. All the elective surgery group patients had rectal bleeding and scintigraphic imaging was performed to the all patients. Ectopic focal radionuclide substance accumulation was detected in the 22 patients. In this group, 21 patients were managed with laparoscopy asisted and only six patients underwent laparatomy. Ileal segment resection and wedge resection were performed in 11 and 16 patients, respectively. In the all cases, histopathological specimens had gastric mucosa in the elective surgery group. Meckel's diverticulum has serious complications in children. Existance of ectopic mucosa does not affect the development of complications rate requiring urgent surgery.

1. Introduction

Meckel's diverticulum (MD) is the most common congenital gastrointestinal system anomaly in children. The incidence is 2% in population (Sagar et al., 2006). MD develops as a result of omphalomesenteric canal not completely obliterated embriyologically. MD is a real diverticulum and it contains 45% to 80% heterotropic tissue (Sagar et al., 2006; Menezes et al., 2008). Gastric mucosa, pancreatic mucosa or colonic mucosa are the heterotrophic tissue in MD. The heterotopic mucosa is at the distal end of the diverticulum in most cases. Sometimes it extends to ileum (Menezes et al., 2008). The majority of patients with MD are clinically silent and are often identified incidentally in the operation which made for different intestinal pathologies other than MD. In the literature, it is controversial whether MD should be excised, which was encountered incidentaly in the operation.

Some authors recommend that it should be resected because of its own risk of complications, on the other hand some authors argue that it is unnecessary surgery for the patients until the complications occur (Zani et al., 2008; Gezer et al., 2016). The complications of MD which require surgery are bleeding, intestinal obstruction, diverticulitis, internal herniation due to fibrous band and perforation in childhood (Blevrakis et al., 2001). If risk factors can be determined about the development of complications, more clear decisions could be made about how the approaches should be made in cases diagnosed incidentally (Slivova et al., 2018). In current study, we aimed to determine the risk factors that affect the complication development rate by evaluating the patients who underwent excision of the MD because of complications.

2. Material and methods

We evaluated the patients who underwent operation for MD and its complications between 2008-2018 in Ondokuz Mayıs University Department of Pediatric Surgery, retrospectively. The parameters that were evaluated are age, gender, timing of surgery (elective or emergency), scintigraphic detection of ectopic tissue, ectopic tissue presence or not in histopathological examination, type of resection (wedge resection or ileal resection with anastomosis), type of surgery (laparoscopy asisted or laparatomy). The data were then entered into a database and analyzed. We used descriptive statistical methods for calculated means, medians and percentages.

3. Results

Sixty two patients had undergone surgery for MD complications in our center between 2008 and 2018. Of the patients, 38 (61.3%) were male and 24 (38.7%) were female. The male / female ratio was approximately 3/2. The mean age of the patients was 6.04 years and the median age was 4.45 years in the range from 6 months to 17.08 years. Emergency surgery was performed in 35 (56.45%) patients and elective surgery was performed in 27 (43.5%) patients.

In emergency surgery group, age ranges from 8 months to 17.08 years (median 7 years). In this group, only three (10.5%) patients were preoperatively diagnosed with ultrasound. All the other patients were diagnosed during the operation. MD was found to cause invagination in 14 patients, axial torsion fibrous band and internal herniation in 11 patients, diverticulitis in six and perforation in four of them (Table 1) (Fig. 1). Of the 14 patients who were operated for invagination, eight patients underwent an ultrasound-guided hydrostatic reduction. The first reduction was successful in two patients but the invagination recurred in seven days in these patients. A repeat hydrostatic reduction was performed but it was not successful. In these two patients, a diagnostic laparoscopy revealed that MD was the leading point. Laparoscopy-assisted surgery was performed in a total of 13 (37.2%) patients; in whom MD caused invagination in eight, diverticulitis in four and perforation in one patient. An open surgical intervention was performed in other 22 (62.8%) patients. Wedge resection was performed in 19 (54.3%) patients. Of these patients; nine had an internal herniation, six had diverticulitis, two had invaginations and two had perforation. Ileal resection was performed in 16 (45.7%) patients. Of these patients; 12 had invagination, two had perforations, and two had internal herniation. The resection strategy was determined by taking the margins of the ectopic tissue into consideration when palpable ectopic tissue was present. When no macroscopic ectopic tissue was suspected, the type of resection was selected on the basis of aiming to achieve sufficient intestinal passage. The histopathological evaluation of MDs in the patients undergoing emergency surgery revealed ectopic gastric tissue in 16 (45.7%) patients. In these patients, MD caused invagination in seven patients, perforation in two, diverticulitis in four, and axial torsion, fibrous bands, and internal herniation in three patients. Ectopic pancreatic and gastric tissue was present at the same time in six (17.1%) patients. In these patients; three had axial torsion, fibrous band, and internal herniation, two had diverticulitis, one had invagination. No heterotopic mucosa tissue was observed in 13 (37.1%) patients. Of these patients, six had invagination, five had axial torsion, fibrous band, and internal herniation, two had obstruction and two had perforation (Table 2). The youngest patient was an eight-month-old male, operated on for invagination. No heterotopic mucosa was identified in the histopathological examination made for thispatient. The oldest patient was 17.08 years old, diagnosed with axial torsion, fibrous band, and an internal herniation. The histopathological examination revealed the presence of ectopic pancreatic and gastric tissue in this patient.

Table 1. Distribution of complications in patients with Meckel's diverticulum.

Complications	Patient number (n)	Percentage (%)
Bleeding	27	43.5
Invagination	14	22.6
Axial torsion, fibrous band, and internal herniation	11	17.7
Diverticulitis	6	9.7
Perforation	4	6.5
Total	62	100

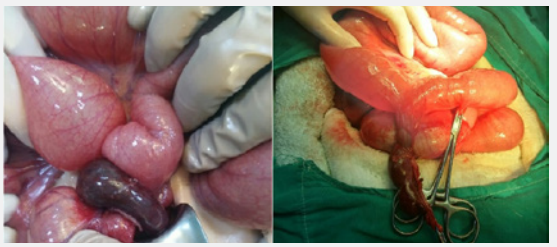

Fig. 1. Complications of Meckel.

Table 2. Distribution of complications in patients with Meckel's diverticulum.

Complications	Histopathological evaluation of ectopic tissue		
	Stomach	Stomach and pancreas	No heterotopic tissue
Bleeding	27	-	-
Invagination	7	1	6
Perforation	2	-	2
Diverticulitis	4	2	-
Internal herniation	3	3	5
Total			

Of the 27 patients, who underwent elective surgery, the age range was from six months to 14.25 years (median 4.73 years). The physical examination were completely normal in all patients, all of them had painless rectal bleeding and they were conservatively followed up with intravenous fluid therapy and ranitidine administration. The hemoglobin concentrations were in the range between 4.23 and 14.6 mg/dl and the median hemoglobin level was 10.6 mg/dl. During the follow-up period, eight patients (29.6%) required erythrocyte replacement. Hypovolemic shock was observed in one (3.7%) patient. Tc-99m pertechnetate imaging was performed in all patients who presented with rectal bleeding and had normal findings in colonoscopy. In twenty two patients (81.4%) MD was detected by scintigraphy. In five patients, there were not any finding in the scintigraphy and the diagnosis was made during the diagnostic laparoscopy. Of the patients, who underwent elective surgery, twenty one (77.7%) were operated on with laparoscopy-assisted and 6 underwent laparotomy. Resection of the ileac segment was performed in 11 patients (40.7%) and wedge resection was performed in 16 patients (59.3%). The histopathological examination of the diverticulum revealed the presence of ectopic gastric mucosa in all patients and all of those presented with rectal bleeding were subsequently diagnosed to have an MD.

Sixty two patients were operated for complications of MD; 34 (54.8%) underwent laparoscopy-assisted surgery and 28 (45.2%) underwent open surgery. Wedge resection was performed in 35 (56.4%) patients and ileal resection was performed in 27 (43.6%) patients (Table 3).

Table 3. Meckel's diverticulum complications and surgical method.

Complication	Laparoscopy-assisted		Open	
	Wedge resection	Ileal resection	Wedge resection	Ileal resection
Bleeding	11	10	1	5
Invagination	2	6	-	6
Perforation	1	-	1	2
Diverticulitis	1	3	2	-
Internal herniation	-	-	9	2

Only one patient underwent laparotomy because of postoperative intestinal obstruction after laparoscopy-assisted surgery. Long-term follow-up of all other patients was uneventful.

4. Discussion

Complications related to MD are 3-4 times more common in males than females (Celebi, 2017). Similarly in our series, MD complications were 1.5 times higher in males. The most common complication of MD is gastrointestinal bleeding due to ectopic mucosa in childhood (Lin et al., 2017a) In the study of Park et al., bleeding was reported in 38% of the patients with complicated MD in a series of 1476 patients with MD (Park et al., 2005). All of our patients had complicated MD and bleeding occurred in 43.5% of these patients. Hemorrhage may sometimes be severe enough to require transfusion and patients may even present with varying degrees of hypovolemic shock (Tseng and Yang, 2009). All of our patients received intravenous fluids and 29.6% of them required transfusion. The typical bleeding encountered in cases of MD is painless rectal bleeding (Tseng and Yang, 2009; Robinson et al., 2017). The cause of bleeding is ulcer development due to the ectopic stomach or pancreatic tissue on the diverticulum (Robinson et al., 2017). Scintigraphic imaging with Tc-99m pertechnetate is useful in the diagnosis of MD. The presence of gastric mucosa is in favor of MD with scintigraphic imaging (Irvine et al., 2017). In twenty two (81.4%) of our patients presented with rectal bleeding were diagnosed by scintigraphy. Although ectopic gastric tissue was encountered in the histopathological evaluation of all patients, it could not be demonstrated by scintigraphy.

Complications such as perforation, diverticulitis, invagination, peritoneal bands, Littre hernia, diverticular stricture, and bezoar in the diverticulum have been reported among the complications of MD (Huang et al., 2014; Chen et al., 2018). There is no specific test or visualization technique for MD diagnosis and most of the patients presenting with acute abdomen cause these patients to be diagnosed more frequently during surgery (Chen et al., 2018). We were able to diagnose MD in the preoperative period in only 3 patients out of 35 in emergency surgery group. All other patients were diagnosed intraoperatively.

MD may act as a leading point and may be cause invagination (Lin et al., 2017b). In most of the centers, ultrasound-guided hydrostatic reduction is applied primarily in the treatment of invagination (Talabi et al., 2018; Simon et al., 2019). In our patients, 14 MD excision was performed which caused invagination and hydrostatic reduction was tried in eight of these patients. The ultrasound-guided hydrostatic reduction neither did reduce the invagination nor could prevent it to be recurred. The success rate of hydrostatic reduction is very low in the presence of MD. At the same time, if reduction achievement occurred, recurrence is likely very high. Heterotopic tissue was not observed in six of 14 invagination cases related to Meckel's diverticulum. The cause of invagination of Meckel's diverticulum appears to be independent of the presence of ectopic tissue. Another complication of MD is internal herniation. Torsion of MD is a rare complication in childhood (Ahmed et al., 2016). The torsion reason is the fibrous band extending from the diverticulum to the abdominal wall or mesentery. The necrosis of the torsioned MD and internal herniation due to fibrous band are the causes of intestinal obstruction (Rattan et al., 2016). Six of 11 patients underwent surgery because of axial torsion fibrous band and internal herniation did not have ectopic tissue. Therefore we suggest that this complication was independent of ectopic tissue.

Clinically, diverticulitis and perforation of MD have similar symptoms and signs as appendicitis, laboratory results and radiological imaging even does not make difference among them. MD should be considered in the differential diagnosis in patients when the radiological evaluation of appendix be normal (Farah et al., 2015). Surgical treatment is inevitable in the treatment of MD complications. Laparoscopy or minimally invasive method laparoscopy assisted surgery can be performed. In a study comparing laparoscopic and open MD resections, outcomes were reported to be similar (Ezekian et al., 2019). We performed laparoscopy-assisted surgery in 54.8% of our series. Laparoscopy provides both diagnosis and treatment. Only one patient required laparotomy during long-term follow-up after laparoscopy among our patients. Lei et al. performed basal ligation of MD similar to appendectomy and verified that they did not have ectopic tissue with frozen biopsy (Lei et al., 2018). However, in our opinion, current method is not very accurate, because appendectomy-like basal ligation in the MD may lead to localized stenosis in the ileac segment. In MD surgery, not only the experience of the surgeon but also frozen biopsy are important in deciding wedge resection or ileac resection. Wedge resection is sufficient if all the ectopic tissue can be removed and intestinal stricture is not expected. However, when ectopic tissue cannot be excised totally or intestinal narrowing is considered, ileac resection must be performed (Glenn et al., 2018). Wedge resection was sufficient in 45% of our patients. Success rate of MD surgery was high and morbidity and mortality are very rare. Although the outcomes of the surgical treatment are successful, the lack of preoperative diagnosis cause delay in intervention and increase the mortality and morbidity. The complications of MD should be considered in pediatric patients, presenting with an acute abdomen (Choi et al., 2017).

In our study, we considered that ectopic tissue is a risk factor for MD complications. In addition, we found that the size of the diverticulum, regardless of the ectopic tissue, lead to intussusception via the mass effect. MD also may cause internal herniation in case of extension to the abdominal wall or mesentery with a fibrous band.

Surgical excision of an incidentally recognized MD should be recommended due to the risk of ectopic tissue, big enough to cause mass effect or has a narrow neck that predisposes to obstruction and diverticulitis.

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The effect of acupressure at the Sanyinjiao point on the labor pain relief and duration of labor in Turkish nulliparous women

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ABSTRACT

Aim of this study was to determine the effects of acupressure Sanyinjiao (Sp-6) point on the labour pain relief and duration of labor in Turkish nulliparous women. It was conducted at a private hospital from the Medipol Healthcare Group between April and September of 2014. Nulliparous women were randomly assigned either to the acupressure group (AG) or placebo groups (PG). In the initial session, a total of 100 of the participants were included, with 50 allocated to the AG and 50 to the PG. The Visual Analog Scale (VAS) was used to measure the intensity of the nulliparous' labor pain. Differences between groups after interventions were analysed using IBM SPSS Statistics 21.0., which were compared by t-test or Mann-Whitney U-test according to the distribution of the variables. The mean age of the participants was 28.2±4.1 years. This study showed that acupressure at the Sp-6 point could reduce the pain intensity and shorten the duration of the active phase of labour when compared to PG. The duration of the second stage of labor and the rate of caesarean section did not show a significant difference between the groups. Findings from this study suggest that if acupressure is practiced by midwives, the experience of childbirth is facilitated.

1. Introduction

Childbirth is one of the most important experiences in the mothers' lives, and this experience has been associated with severe pain (Bjelland et al., 2016). Labor pain is defined as a form of acute pain but it is a physiological part of childbirth while other acute pains develop due to certain pathologies (Whitburn et al., 2019). Labor pain causes women to experience anxiety and fatigue. Anxiety and fear are related to increased excretion of stress hormones and weakened uterin contractility during labour, which results in prolonged labour (Tzeng et al., 2017). Prolonged labour is related to increased adverse perinatal outcomes (Abalos et al., 2018). Therefore, using of the intrapartum pain relief techniques is one of the significant aspects of midwifery care.

Intrapartum pain relief techniques include many different aspects such as religious, cultural, and maternity care systems (Van der Gucht and Lewis, 2015). In the light of these critical aspects, the subject of coping with labor pain for women is a phenomenon. For example, Koyyalamudi et al. stated that labor pain is a significant action that determines how childbirth experience is for women (Koyyalamudi et

al., 2016). In addition, there are pharmacological and non-pharmacological methods in dealing with labor pain during childbirth, which effects the experiences of birth positively. The neuraxial blocade, which uses spinal, epidural or combined spinal-epidural techniques as a pharmacological method to reduce labor pain, is considered the foremost standard. Pharmacological analgesic agents used in combination with these techniques are patient controlled analgesia, nitrous oxide, opioids and non-opioids (Jones, 2012). Although the use of pharmacological agents for labor pain reduces pain, they increase the rates of instrumental vaginal delivery due to fetal distress (Jones, 2012; Hasegawa et al., 2013). In addition, pharmacological agents cause side effects such as nausea, vomiting, hypotension (Jones, 2012), itching, somnolence and pruritis (Hein, 2018). Therefore, eliminating or minimizing the known side effects of analgesic methods used in coping with labor pain may be essential to positively increase the birth experience.

On the other hand, non-pharmacological methods such as exercise during pregnancy, acupuncture, hypnosis, yoga, hydrotherapy, massage, music, subcutaneous electronic stimulation, and relaxation techniques are used to reduce pain at birth (Koyyalamudi et al., 2016; Smith et al., 2018). Acupressure is a non-pharmacological method with the same basic principle as acupuncture. Acupuncture and acupressure, the components of traditional Chinese medicine, are based on the stimulation of the energy pathways called meridian which run along the whole body (Gregson et al., 2015). Although traditional Chinese medicine uses the meridian system in treatment protocols, scientists are avoiding using these methods since they have not been scientifically proven. According to Western medicine, meridians have no anatomical basis. The effects of the meridian system on treatments were studied through several theories such as opioid peptide theory or gate control theory (Kang et al., 2016).

Acupressure as a non-invasive technique which is applied through physical pressure to specific meridian points (Smith et al., 2017). A variety of acupoints are reported in obstetric studies (Akbarzadeh et al., 2013; Asadi et al., 2015; Dong et al., 2015) to reduce labor pain. The most cited of these acupoints are SP6, LI4, BL32, and GB21 which are believed to stimulate uterine contractions through oxytocin release and to reduce labor pain by decreasing catecholamines and increasing endorphins from the pituitary gland (Yesilcicek Calik and Komurcu, 2014; Mollart et al., 2015; Hamlacı and Yazici, 2017; Gönenç and Terzioğlu, 2019; Türkmen and Çeber Turfan, 2019). The other common acupoint is Sanyinjiao (Sp-6) point or sanyinjiao that is at the junction of three meridians of liver, spleen and kidney and has a strong influence on the physiological function of the uterus (Lingling et al., 2017).

There is no enough research to show the relation of Sp-6 acupressure and the labor pain and duration of labor. The aim of this study was to investigate the effects of Sp-6 point acupressure on the labor pain and duration of labor in Turkish nulliparous women.

2. Materials and methods

Study sample

This study designed as single-blinded, prospective, placebo controlled. It was conducted at Bahcelievler Nisa Hospital in Istanbul which is a private hospital from the Medipol Healthcare Group between April and September of 2014. Nulliparous women were randomly assigned either to the acupressure on Sp-6 point (AG) or touch on Sp-6-point placebo (PG) groups. The criteria for participating in the study were: 1) 18-49 years of maternal age; 2) nulliparous women who had at least three uterin contractions lasting >30 seconds within 10 minutes; 3) literate in the Turkish language; 4) 37–42 gestational weeks; 5) singleton, cephalic presentation 6) fetus in an anterior position; 7) spontaneous onset of labour and a cervical dilation of 4–5 cm; 8) intact membrane 9) normal foetal heart rate (FHR) 10) Bishop score ≥ 6. Women were excluded from the trial if they had any systemic disease and any mental health problems, damage and injury at the Sp-6 acupoint, required any sedation or analgesic drugs during labor or if they chose to withdraw.

Following assessment and allocation 130 nulliparous women were recruited. The women with regular uterine contractions (at least three uterin contractions lasting >30 seconds within 10 minutes) were randomly assigned to the AG or PG groups.

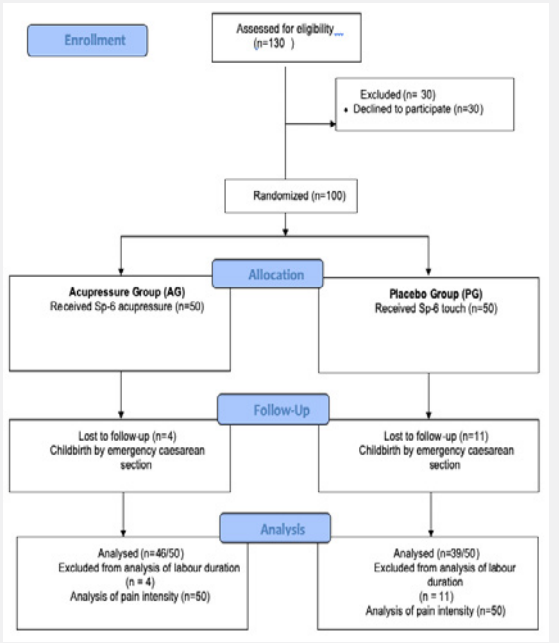

Fig. 1. Consort flow diagram.

Simple randomization was used based on their hospital admission code. Participant admission codes ending with odd or even numbers were allocated to AG and PG groups, respectively. The sample size was predetermined at the percentage differences in the pain using the Visual Analogue Scale (VAS) before and after the intervention in the study of Lee et al., Mafetoni and Shimo using power analysis based on a medium effect size, an alpha of 0.05 and power=0.92 (Lee et al., 2004; Mafetoni and Shimo, 2016). In the initial session, a total of 100 of the participants were included, with 50 allocated to the AG and 50 to the PG. In the treatment follow-up session, a total of 85 nulliparous women were included in the analysis, of whom 46 were assigned to the AG and 39 to the PG (Fig. 1).

Ethical considerations

The study protocol was approved by institutional review board of Istanbul Medipol University. Recruired participants in the two groups received a written description of the research purposes, and asked to give written consent. Moreover, they were kept informed about they could withdraw themselves from the study at any stage without giving any explanation.

Outcome measurements

VAS was used to measure the intensity of the nulliparous' labor pain. This scale consisted of a 10 cm horizontal descriptor (no pain on the left - worst possible pain on the right). Participants were asked to evaluate pain level of labor pain from 1 to 10. For each group, VAS evaluated four times: before the intervention (T0), immediately after the intervention (T1), thirty minutes after intervention (T2) and sixty minutes after intervention (T3). At every stage of the trial, the participants were requested to asses their pain level on a VAS. Some participant in both groups underwent cesarean section after pain intensity at all time points was measured.

The primary outcomes were the Sp-6 acupressure would increase the duration of the active phase, the duration of the second stage and labor pain. Secondary outcome measure included the type of birth and Apgar scores of the newborns. The two groups were compared for factors that could potentially affect the labour process such as maternal age, neonatal birth weight, the pattern of uterus contraction, cervical dilation, cervical effacement and foetal station at the start of the study. For all the subjects, vaginal exam, measurement of newborn's birth weight, Apgar score assessment and administration of research tools were performed by the researcher. The number of contractions in ten minutes was calculated to determine the contraction frequency. The duration of contraction was calculated from the beginning to the end of the contraction (as second).

The duration of the first labour stage was calculated as the period from 4 cm cervical dilation to full cervical dilation. The duration of the second stage was calculated as full dilation to the time of birth. Neonatal Apgar score was assessed at the first- and fifth-minutes afterbirth.

Interventions

Interventions were started after 4 cm vaginal dilatation. These interventions (acupressure on Sp-6 and touch on Sp-6) underwent between contractions. The Sp6 acupressure was performed by primer researcher, who was certified for acupressure. The vaginal examination, acupressure (true and placebo) and VAS were administered by the same researcher. The study was carried out the both of AG and PG were included the same conditions. The pressure was applied when the participant was laid down by the semi-fowler position with the legs straight. Sp-6 was located four finger's width, measured with the woman's own fingers, above the tip of the medial malleolus at the posterior border of the tibia. Proper location of the acupoint was approved when the participant felt heaviness, pressure, tingling, or numbness in the area or a gratifying feeling (Hjelmstedt et al., 2010). The pressure contained rotational and vibratory pressure. When the participant felt as a severe pain at the point of pressure, the pressure was ended immediately and continued after a few minutes.

In the AG, acupressure was applied with vertical pressure by the thumb of the researcher at the onset of the active phase of labour (cervical dilation of 4 cm). This process continued for 30 minutes in total. Five pressures on the Sp-6 acupoints were applied every ten minutes during the contractions. Each period included 60 seconds of pressure and 60 seconds of rest. The intensity of the pressure was determined by the researcher's thumb-nail color. The pressure was considered enough when the nail bed was partially white (Sehhatie-Shafaie et al., 2013; Torkzahrani et al., 2015). The 30-minutes intervention time was based on previous studies (Hjelmstedt et al., 2010; Shahali and Kashanian, 2010; Cui et al., 2011).

In the PG, a placebo intervention was performed by touching the Sp-6 point with the palm of the hand by the same researcher. The time and duration of applications were the same as the AG.

Data analysis

Differences between groups after interventions were analized using IBM SPSS Statistics 21.0., which were compared by t-test or Mann-Whitney U-test according to the distribution of the variables. Chi-square tests were used for categorical variables and statistically significant for the measurements means were calculated using an alpha value of 0.05. The normally distributed variables were shown as mean±standard deviation (SD), while non-normally distributed variables and

categorical variables were presented by median (min-max) and n (%), respectively.

The retrospective power analysis of the study was carried out fort he duration of labor (hours) and VAS. The power was 99.99% when alfa=0.05, n1=46, n2=39 for the effect size for the active phase of the labour of 1.338. The power of pain intensity analyses was 100%, when effect size f=0.659, alfa=0.05, total sample size=100, number of groups=2, number of measurements=4, nonsphericity correction=0.582 and correlation among repeated measures=0.755. Power analysis was performed with G Power 3.1.9.2 software.

3. Results

Baseline demographic and clinical characteristics

The baseline characteristics of 100 women who participated in this study was summarized in Table 1. The mean age of the participants was 28.2±4.1 years, and ages ranged from 20 to 37 years. There were not any statistically significant differences compared the AG and PG groups in demographic and obstetric characteristic and the groups were homogeneous (p>0.05) (Table 1).

Table 1. Baseline demographic characteristics.

	Acupressure group (n=50)	Touch group (n=50)	Total (n=100)	*p*
Age in years (Range:20-37) [Mean±SD]	28.8±4.4	27.5±3.8	28.2±4.1	0.120
Number of prenatal cares [Median (min-max)]	12 (6-17)	12 (5-18)	12 (5-18)	0.546
Education [n (%)]				0.184
Elementary school	11 (22%)	6 (12%)	17 (17%)	
Secondary school	9 (18%)	4 (8%)	13 (13%)	
High school	16 (32%)	22 (44%)	38 (38%)	
University	14 (28%)	18(36%)	32 (32%)	
Occupation [n (%)]				0.679
Employed	17 (34%)	20 (40%)	37 (37%)	
Housewife	33 (36%)	30 (60%)	63 (63%)	
Income [n (%)]				1.000
Earn more than spend	5 (10%)	5 (10%)	10 (10%)	
Earn equal to spend	40 (80%)	40 (80%)	80 (80%)	
Earn less than spend	5 (10%)	5 (10%)	10 (10%)	
History of abortion [n (%)]				0.054
Yes	21 (42%)	11 (22%)	32 (32%)	
No	29 (58%)	39 (78%)	68 (68%)	
Type of pregnancy [n (%)]				0.362
Planned	49 (98%)	46 (92%)	95 (95%)	
Unplanned	1 (2%)	4 (8%)	5 (5%)	

Before the using interventions on Sp-6, details of maternal obstetric-exam were compared amongst groups and there could not be found significant difference in respect of the pattern of contraction, cervical dilatation and effacement and foetal station at the start of the study (p>0.05) (Table 2).

Table 2. Baseline clinical characteristics.

	Acupressure group (n=50) Median (min-max)	Touch group (n=50) Median (min-max)	*p*
Frequency of contraction	3.0 (2-5)	4.0 (2-5)	0.005
Duration of contraction (sec.)	30.0 (20-40)	30.0 (20-40)	0.910
Cervical dilatation	4.0 (4.0-4.0)	4.0 (4.0-4.0)	1.000
Cervical effacement, %	60.0 (50.0-80.0)	60.0 (40.0-80.0)	0.084
Foetal station	-2 [(-3)-(-1)]	-2 [(-3)-(-1)]	0.898

Subjective labour pain

The mean baseline pain scores were 6.08±1.54 in the AG (Table 3). Immediately after the intervention, the mean pain scores were reduced to 5.36±1.24 (p<0.001 for T1 vs. T0). Half an hour after the intervention, the pain scores of the AG increased to the same level as those immediately after intervention (p=1.000 for T2 vs. T0), then the mean pain scores reached the highest level, 7.16±1.33, at 60 minutes (p<0.001 for T3 vs. T2, T1, T0). The effect size for the differences in pain score was moderate with 0.590 (95% CI:0.439-0.659).

Table 3. Distribution of VAS scores and their changes in the groups.

Stage↓ Group→	Acupressure group (n=50) Mean±SD	Touch group (n=50) Mean±SD	*p*	*dH (95% CI)*
T0 (Before)	6.08±1.54	4.96±1.23	<0.001	0.797 (0.388-1.207)
T1 (Immediately)	5.36±1.24	5.82±1.04	0.048	0.399 (0.001-0.797)
T2 (30th minute)	6.30±1.13	7.06±1.35	0.003	0.606 (0.203-1.009)
T3 (60th minute)	7.16±1.33	8.82±1.16	<0.001	1.320 (0.885-1.755)
p-value	<0.001	<0.001		
$p\eta^2$(95% CI)	0.590 (0.439-0.659)	0.749 (0.642-0.791)		

The mean baseline pain scores were 4.96±1.23 in the PG, which was considerably less than those in AG (p<0.001) (Table 3). The mean intensity of pain at T1, T2 and T3 were 5.82±1.04, 7.06±1.04 and 8.82±1.16, respectively, showing a permanent increase (p<0.001 for all pairwise comparisons of time points) with an effect size of 0.749 (95% CI:0.642-0.791).

There were significant differences between the subjective pain scores of AG and PG at all-time points with effect sizes ranging from 0.399 to 1.320 (p<0.05).

The change of pain levels across time points was significantly different between the groups (p<0.001, pη2=0.303, 95% CI:0.280-0.523) (Fig. 2).

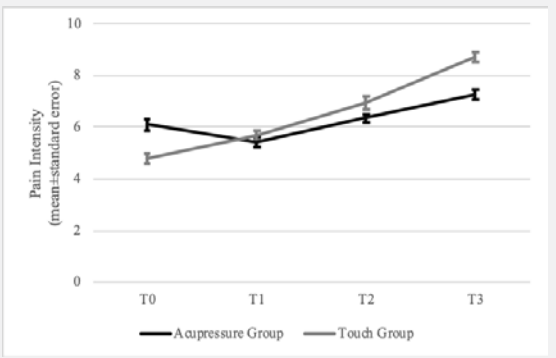

Fig. 2. Change in VAS mean scores from baseline (T0) to immediately stage (T1), after thirty min stage (T2), and after sixty min stage (T3) in the groups.

Duration of labour

Although 85 volenteer participants were completed at end of the study, 15 partcipants had to excluded from the duration of labor as a study outcome, because they became emergency caesarean section. Therefore, AG contained 46 women and PG included 39 women in this part.

The duration of active phase of labour was 3.0 (min:1-max:6) in the AG and 4.0 (min:2-max:10) hours in the PG. The duration of the labor was significantly shorter in the AG (p<0.001) (Table 4). The effect size for the differences was large with 1.292 (95% CI: 0.859-1.726). The median duration of the second stage of labor was 20.0 minutes (min:7-max:62) in the AG and 20.0 minutes (min:8-max:62) in the PG (p=0.784) (Table 4).

Table 4. Distribution of duration of labor in the groups

	Acupressure group (n=46) Median (min-max)	Touch group (n=39) Median (min-max)	*p*	*dH (95% CI)*
Duration of first labour stage, h, 4 cm-full dilatation	3.0 (1-6)	4.0 (2-10)	<0.001	1.292 (0.859-1.726)
Duration second stage of labour, min, full dilatation-fetus delivery	20.0 (7-62)	20.0 (8-62)	0.784	0.072 (-0.322-0.466)

Delivery outcomes

Table 5 was summarized the delivery outcomes for each group. In both groups, 85% of the participants had a vaginal delivery. Four women (8%) in the AG and 11 (22%) in the PG had a caesarean section (CS) (p=0.093).

One-minute Apgar score was 8 (min-max:6-10) in the PG and 9 (min-max:6-10) in the AG (p<0.001). Five-minute Apgar score was 10 (min-max:7-10) and 9 (min-max:7-10) in the AG and PG, respectively (p<0.001) (Table 5). The effect size of the difference in one-minute Apgar scores was large (1.253, 95% CI:0.821-1.684), where the effect size of five minutes Apgar was 1.011 (95% CI:0.593-1.430). There was no significant difference between the groups in terms of newborns' mean birth weight (p=0.647).

Table 5. Delivery outcomes

	Acupressure group (n=50)	Touch group (n=50)	p	dH (95% CI)
Type of delivery [n (%)]			0.093	0.644 (-0.033–1.320)
Vaginal	46 (92%)	39 (78%)		
Caesarean section	4 (8%)	11 (22%)		
Sex of new-born [n (%)]			0.648	0.136 (-0.307–0.578)
Male	28 (56%)	31 (62%)		
Female	22 (44%)	19 (38%)		
Apgar score at 1 min. [Median (min-max)]	9 (6-10)	8 (6-10)	<0.001	1.253 (0.821-1.684)
Apgar score at 5 min. [Median (min-max)]	10 (7-10)	9 (7-10)	<0.001	1.011 (0.593-1.430)
Neonatal birth weight (g) [mean±SD]	3349.2±335.7	3317.8±347.2	0.647	0.091 (-0.303–0.485)

4. Discussion

The findings of this study, which was conducted to compare the effect of AG with the effects of PG, regarding the pain intensity of the first stage of labour, the duration of labour and delivery outcomes, demonstrated a complex interaction. These findings, which included dominant parameters such as the duration of labour, intension of pain are summarized on three themes: 1) The effect of acupressure on labor pain relief, 2) The effect of acupressure on duration of labor, 3) The effect of acupressure on delivery outcomes.

This study showed that acupressure at the Sp-6 point could reduce the pain intensity and shorten the duration of the active phase of labour when compared to PG. Some other studies have reported similar findings (Shahali and Kashanian, 2010; Cui et al., 2011; Akbarzadeh et al., 2013; Asadi et al., 2015; Mafetoni and Shimo, 2015). Although previous studies showed that the rate of cesarean section reduced (Shahali and Kashanian, 2010; Akbarzadeh et al., 2013) our study did not display a reduction in the rate of CS.

This study showed that acupressure at the Sp-6 point could reduce the pain intensity and shorten the duration of the active phase of labour when compared to PG. There was not any significant differences between the

two groups concerning the patterns of contraction, cervical dilatation, effacement and foetal station which were among the variables thought to affect the labor process. The duration of the second stage of labor and the rate of caesarean section did not show a significant difference between the groups.

The effect of acupressure on labour pain relief

Although the mean VAS scores were higher in the AG in the beginning of the study compared to the PG, it was seen that the mean VAS score in the acupressure group decreased immediately after the intervention. While the VAS scores continued to increase in the acupressure group at 30 and 60 minutes after the intervention, the mean VAS score in the placebo group continued to much more increase significant statistically. Even if the present findings showed that the pain gradually increased during the active phase of the labor, the reason for this might also be attributed to a physiological condition that occurs due to the increased oxytocin hormone secretion. Some cross-cultural studies have demonstrated that the risen in the pain of scores may be connected with the increased oxytocin hormone (Gregson et al., 2015; Smith et al., 2018). On the other hand, although this physiological condition may be related to the increased the frequency and duration of contractions, the findings of the study showed that there was no difference in both groups with the frequency and duration of contractions.

The study findings demonstrated that the use of Sp-6 acupressure can be considered an effective way to reduce labour pain in nulliparous women. A potential explanation for acupressure-related pain relief may based on the endorphin-release theory (Makvandi et al., 2016). Some international cross-cultural studies have showed that the effectiveness of Sp-6 acupressure for pain reduction during the first phase of the labour (Mafetoni and Shimo, 2015; Kang et al., 2016; Smith et al., 2017).

The effect of acupressure on duration of labour

According to the findings of most studies evaluating the duration of labor from the time of a dilation of 4 cm to full dilatation, the active phase of labor experienced by the participants was shortened in the Sp-6 group (Cui et al., 2011; Smith et al., 2017). In addition, the study stated that the AG of the present study exhibited a significantly shorter duration of the active phase of first stages of labour compared to the PG. However, participants, who were given birth with CS, were excluded from the analysis of the labor duration in this study. Moreover, it was showed that acupressure shortened the active phase of labor, but was not effective at the second stage of labor in this study. Okumus's study has demostrated that the primiparous women giving birth in Turkish hospitals had higher rates of induction, instrumental birth, fundal pressure and episiotomy rates (Okumus, 2017). The duration of second stage may be related to the increased the frequency of obstetric intervention using to shorten second stage of labor.

The effect of acupressure on delivery outcomes

Four women in the AG and 11 participants in the PG were given birth with CS, but there was not a significant difference between the groups in terms of the CS rates. The meta-analysis study of Makvandi et al. revealed that the application of acupressure reduced the rate of cesarean section (Makvandi et al., 2016). Turkey is one of the countries possesing the highest rates of the cesarean delivery. In addition, these rates were 69.5% in private hospitals and 35.5% in state hospitals in Turkey (MoH Turkey, 2014).

The Apgar scores after the one-minute and five-minute marks of birth showed that first- and fifth minute Apgar scores did not differ statistically in the AG and PG. Noting the results of the present study and the other studies, no significant differences were observed between the one-minute and five-minute Apgar scores of newborns in the selection groups (Akbarzadeh et al., 2013; Lingling et al., 2017; Smith et al., 2017). The study found that the use of acupressure during labour has no adverse effects on the newborns.

In this study, applying pressure to the Sp- 6 acupoints to reduce labor pain and duration of delivery for primiparous women seems effective. In addition, acupressure is one of the non-invasive methods that midwives can learn easily and apply in midwifery care. Findings from this study suggest that if acupressure is practiced by midwives, the experience of childbirth is enhanced.

Further studies should be included in the clinical trials to establish standard acupressure practice at childbirth and future research is needed regarding the effects of process of acupressure on all pregnant women. Further research is needed to understand the practice implications of the use of the acupressure during all childbirth process both of primiparous and multiparous women. The lack of standardization for acupressure should be investigated. In particular, strategies to identify and minimize the effect of acupressure applied at different durations must be investigated. Further, more research is needed to understand that the practice acupressure aimed at improving childbirth outcomes and to enhance midwifery care delivery in clinical settings. Acknowledgements This study was accepted as a master thesis by Istanbul Medipol University Health Sciences Institute on August 1st, 2016. The authors are grateful to the women and their babies who participated in the study. They also wish to thank the midwives and gynecologist staffs of the Medipol Health Group for their support.

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The effect of intravenous N-acetyl cysteine on the incidence of postoperative atrial fibrillation in coronary artery bypass graft surgery patients

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ABSTRACT

Atrial fibrillation is the most frequent arrhythmia after open heart surgery. The aim of this study was to determine the effect of intravenous (IV) N-acetyl cysteine (NAC) administration in the early postoperative period of coronary artery bypass (CABG) surgery on the incidence of postoperative atrial fibrillation (POAF). A total of 60 patients who had undergone isolated CABG surgery between June 2014 – July 2015 in our clinic included in this retrospective study. The patients divided into two groups: Group 1 (n=30) included the patients who had been administered standard saline solution infusion and Group 2 (n=30) included the patients who had been administered IV NAC (10mg/kg) infusion while they were under mechanical ventilation support. All patients were administrated oral 600 mg NAC once a day for 5 days after weaning from mechanical ventilation support. The ECG's were evaluated for POAF by the same cardiovascular surgeon who was blinded for patient groups. POAF was seen in 12 (40%) patients in Group 1 and 4 (13%) patients in Group 2. The POAF incidence was significantly higher in Group 1 (p=0.020). We think that administration IV NAC is an effective way to prevent the POAF after CABG surgery.

1. Introduction

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia after coronary artery bypass graft (CABG) surgery and it is frequently seen in the early postoperative period (Soleimani et al., 2014). Although the incidence of postoperative atrial fibrillation (POAF) changes according to the surgical procedure, perioperative attributes of the patients, monitorization methods and the definition of AF accepted by the researchers, it is reported to be between 3 – 50% in the literature (Gholipour Baradari et al., 2016).

There is an increasing number of studies proving the role of oxidative stress and inflammatory reactions in the pathophysiology of POAF. The anti-oxidants reduce the level of intracellular oxidative stress molecules which occur after the CABG surgery. N-acetyl cysteine (NAC) is a promising molecule in the prevention of POAF with its anti-oxidant and anti-inflammatory effects in addition tothe well-known mucolytic effect of it (Kazemi et al., 2013). The aim of this study was to determine the effect of intravenous (IV) NAC administration on prevention of POAF after CABG surgery.

2. Material and methods

We have been administrating NAC intravenously as a medication protocol in the postoperative period of the CABG patients while they are under mechanical ventilation support in our intensive care unit (ICU) since 2015. We had set up two groups selected from the patients who underwent open heart surgery before and after the application of the NAC protocol. The inclusion criteria were having been undergone isolated CABG surgery, having preoperative normal sinus rhythm. The exclusion criteria were having been undergone concomitant cardiac surgery other than CABG and having any kind of preoperative arrhythmia. The incidence of POAF in the groups was evaluated in both groups in the early postoperative period.

A total of 60 patients included in this retrospective study who underwent isolated CABG surgery between June 2014 - July 2015 in Bulent Ecevit University Department of Cardiovascular Surgery. The patients divided into two groups: Group 1 (n=30) included the patients who had been administered standard saline solution infusion and Group 2 (n=30) included the patients who had IV NAC (10 mg/kg) while they were under mechanical ventilation support. All patients were administrated oral 600 mg NAC once a day for 5 days after weaning from mechanical ventilation support. Routine postoperative laboratory findings and standard 12-lead electrocardiograms (ECG) of the patients were recorded. The ECGs were evaluated for POAF by the same cardiovascular surgeon who was blinded for the patient groups. Also the demographical data, comorbidities, preoperative medications, preoperative echocardiography (ECHO) results of the patients were evaluated as well as the operative and postoperative data such as postoperative medications, intra-aortic balloon pump applications, cardiopulmonary bypass (CPB) times, aortic cross-clamp times and postoperative anti-arrhythmic medications.

If AF occurred, the following standard up-to-date treatment protocol was applied independently from the study: 150 mg IV bolus amiodarone was administered followed by an infusion at the rate of 15mg/kg for 24 hours. If the amiodarone treatment was ineffective, then electrical cardioversion was performed to regulate the heart rhythm. If the heart rhythm was successfully converted to normal sinus rhythm (NSR) then oral amiodarone therapy was administered for 30 days and if not, heart rate control was done by administration of oral beta-blockers or calcium channel blockers. The protocol of the study was summarized in Fig.1.

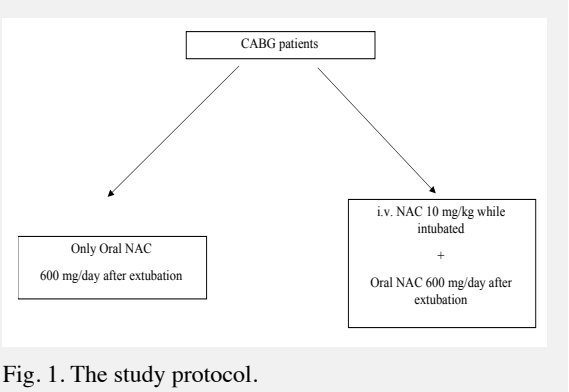

Fig. 1. The study protocol.

2. Results

The demographical data of the groups were presented in Table 1 and they were similar between the groups except the number of hypertensive patients was significantly higher in Group 1 (p=0.020) and the mean BMI was significantly higher in Group 2 (p<0.000).

Table 1. Demographical data SD: Standard deviation; BMI: Body mass index; DM: Diabetes mellitus; HT: Hypertension; HL: Hyperlipidemia; COPD: Chronic obstructive pulmonary disease.

	Group 1 (n=30)	Group 2 (n=30)	P value
Age (years) (Mean±SD)	65.73±8.18	64,87±8.35	0.686
Male (n)(%)	21 (70)	22 (73)	0.774
BMI (kg/m²) (Mean±SD)	23.10±2.65	28.09±4.48	<0.000
DM (n) (%)	14 (46.7)	11 (36.7)	0.432
HT (n)(%)	26 (86.7)	18 (60)	0.020
Smoking (n)(%)	23 (76.7)	17 (56.7)	0.100
HL (n)(%)	11 (36.7)	11 (36.7)	1.000
COPD (n)(%)	6 (16.7)	8 (26.7)	0.542
Thyroid dysfunction(n)(%)	2 (6.7)	2 (6.7)	1.000

In Group 1, mean preoperative ejection fraction (EF) was 51.50±9.04%, preoperative left atrium (LA) mean diameter was 3.99±0.45 cm, preoperative mean SPAP was 35.31±9.76 mmHg and mean preoperative interventricular septum (IVS) thickness was 1.21±0.11 cm. In Group 2, mean preoperative EF was 49.67±8.04%, preoperative LA mean diameter was 3.84±0.44 cm, preoperative mean SPAP was 28.13±5.6 mmHg, mean preoperative IVS thickness was 1.19±0.15 cm. The preoperative mean SPAP was significantly higher in Group 1 (p=0.016, Table 2).

Mean aortic cross-clamping time was 70.97±28.91 min and mean CPB time was 113.83±48.78 min in Group 1 and 64.20±19.61 min and 99.70±29.84 min respectively in Group 2. There was no significant difference of these values between the groups (p=0.566 and 0.282 respectively). Postoperative inotropic agent support was needed in 10 (33.3%) patients in Group 1 and 5 (16.7%) patients in Group 2. There was no

Table 2. Preoperative ECHO findings. SD: Standard deviation; EF: Ejection fraction; LA: Left atrium; SPAP: Systolic pulmonary artery pressure; IVS: Interventricular septum.

Preoperative data	Group 1 (30)	Group 2 (30)	P value
EF (Mean±SD)(%)	51.50±9.04	49.67±8.04	0.410
LA diameter (Mean±SD)	3.99±0.45	3.84±0.44	0.223
SPAP (Mean±SD)	35.31±9.76	28.13±5.6	0.016
IVS thickness (Mean±SD)	1.21±0.11	1.19±0.15	0.744

significant difference of this data between the groups (p=0.136). The procedural data is presented in Table 3.

Table 3. Comparison of the perioperative data. SD: Standard deviation; XCL: Aortic cross-clamp.

	Group 1 (30)	Group 2 (30)	P value
XCL time(min) (Mean±SD)	68.40±29.17	64.20±19.61	0.516
CPB time (min) (Mean±SD)	108.97±43.26	99.70±29.84	0.338
Postoperative inotropic agent support (n)(%)	10 (33.3)	5 (16.7)	0.136
Mechanical ventilation support time (hr) (Mean±SD)	14.13±9.07	13.27±5.79	0.994

Mean time of postoperative mechanical ventilation support was 14.13±9.07 hr in Group 1 and 13.27±5.79 hr in Group 2 (p=0.994). Mean time of postoperative ICU follow-up was 9.23±3.67 days in Group 1 and 8.83±2.87 days in Group 2 (p=0.799). Mean total length of stay time in hospital was 12.37±2.15 days in Group 1 and 11.93±3.47 days in Group 2 (p=0.071). There was no significant difference of these data between the groups. Postoperative atrial fibrillation was seen in 12 (40%) patients in Group 1 and 4 (13.3%) patients in Group 2. The POAF incidence was significantly higher in Group 1 (p=0.020). The data is represented in Table 4.

Table 4. Comparison of the effect of NAC on POAF incidence and hospitalization time. AF: Atrial fibrillation; ICU: Intensive care unit.

	Group 1 (n=30)	Group 2 (n=30)	P value
Postoperative AF (n)(%)	12 (40)	4 (13.3)	0.020
ICU follow-up time (days) (Mean±SD)	9.23±3.67	8.83±2.87	0.799
Total hospitalization time (days) (Mean±SD)	12.37±2.15	11.93±3.47	0.071

Statistical analysis

The PASW (Predictive Analytics Software) Statistics for Windows v18 programme was used for statistical analyses. Percent rates were calculated for qualitative data. Mean values and standard deviation were calculated for quantitative data. The normality of the distribution of the data was tested with Shapiro-Wilk test. Normally distributed data were analysed with t-test and non-normally distributes qualitative data were analysed with Pearson's Chi-square test and quantitative data were analysed with Mann-Whitney U test. P value <0.05 was accepted as statistically significant.

3. Discussion

According to the results of this study, we can say that NAC reduces the incidence of postoperative arrhythmic complications after isolated CABG surgery. Also the ICU follow-up times and the in-hospital stay times tend to be lower after NAC administration although it was not statistically significant.

Postoperative atrial fibrillation is mostly benign in nature but it sometimes causes unwanted events that prolong the hospitalization time which increases the medical expenses. Thus many treatment modalities have been applied to prevent and/or cure the POAF (Baradari et al., 2016). It is believed that the reactive oxidative metabolites that rise in blood after CBP cause oxidative stress and systemic inflammation. Thus the drugs which have anti-oxidant and anti-inflammatory effects can be used to prevent POAF in cardiothoracic surgery (Kazemi et al., 2013)

NAC is a mucolytic, anti-oxidant and anti-inflammatory agent which can reduce the cellular oxidative injury and systemic inflammation in cardiovascular surgery (Liu et al., 2014). It is a free radical scavenger which reduces the myocardial ischemic/reperfusion injury. Because of the major role of oxidative stress in POAF pathogenesis, many studies were conducted to determine the anti-arrhythmic effect of NAC (Baker et al., 2009).

In four meta-analyses including NAC, it was reported that NAC could reduce the incidence of POAF with its potential anti-arrhythmic effect but it could not reduce the time of ICU follow-up and the time of hospitalization significantly (Baker et al., 2009; Gu et al., 2012; Ali-Hassan-Sayegh et al., 2014; Liu et al., 2014). But the meta-analysis of the studies in which NAC was used for a short time and the studies in which NAC was used for a longer time is different in the literature. It may be caused by the anti-inflammatory effect of NAC. It is generally accepted that POAF has usually been seen in postoperative 2nd or 3rd days and the levels of the inflammatory cytokines are at maximum in these days (Mathew et al., 2004; Cairns et al., 2011). Soleimani et al also prolonged the IV administration of NAC until postoperative 2nd day in their study. They reported that this NAC administration protocol did not reduce the times of ICU follow-up and hospitalization but they managed to achieve a 13.2% reduction in POAF incidence (Soleimani et al., 2018).

In a randomized placebo controlled study conducted by Ozaydın et al., it was reported that NAC administration significantly reduced the incidence of POAF after CABG and/or heart valve surgery (Ozaydın et al., 2008). NAC administration was started 1 hr before the surgery and continued for 48 hrs postoperatively in this study. This could be the reason that explained the attribute of this study's being the only study which reported the high rate reduction ability of NAC on POAF incidence.

In our study, there was no significant difference of total mechanical ventilation support times between the groups and NAC was administered orally for 5 days after surgery in both groups. We think that the reduction in POAF incidence in our study could not be due to total NAC administration time but be due to administration of NAC in the early postoperative period in which the CPB stimulated inflammatory cytokine blood levels were at maximum.

Propofol is an anaesthetic agent which has a strong anti-arrhythmic effect and it may affect the incidence of POAF (Krzych et al., 2009). It was administered as IV infusion for anaesthesia maintenance in both of our groups. The total administered doze equivalence of this agent between the groups may be biased to Group 2 because the mean BMI was significantly higher in Group 2. The significant low level of POAF incidence in Group 2 in our study may be due to this propofol effect.

NAC has a good safety profile (Kazemi et al., 2013). In our study, the IV dose of NAC was very low according to other studies in the literature and we did not observe any side effects or complications caused by NAC infusion.

Limitations of the study

We did not monitor and evaluate the levels of oxidative stress related markers in blood which could affect the incidence of POAF. We did not measure and evaluate the effect of concomitant administration of NAC and other well-proven POAF preventive drugs such as beta-blockers, amiodarone, etc. on POAF incidence. Also the optimal dose and the optimal treatment time of NAC is still unknown. We suggest that more studies should be conducted on this subject. Also we think that the definition of POAF should be standardized and larger scale studies should be conducted with a primary end point of POAF incidence.

It seems that NAC is a promising drug to prevent the postoperative arrhythmic complications of open heart surgery but it is not well-proven. We think that IV NAC administration in the postoperative period of high risk CABG patients should be considered as a preventive treatment against POAF.

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Case Report

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Traditional nanny circumcision and dressing with sumac, onion and oil: A case report and review of the literature

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ABSTRACT

Roughly every one out of three men is circumcised today. Complications are very common given the fact that circumcision is the most widely conducted surgical procedure by traditional circumcisers and doctors. The aim of this article is to present the case of a three-day old male infant who was brought to the emergency department with intractable bleeding as a complication of circumcision. This case is interesting because of the traditional circumcision technique, the circumciser being women, and the dressing compound being unusual. Three days old male baby was circumcised by a traditional technique called the nanny circumcision and wound was dressed with a compound consisting of sumac, onion and grease. The patient was surgically treated and had no complications in follow-up. Circumcision may cause serious complications if not done properly by people who are not health care professionals. Hereby, we present the case of a traditional circumcision and review the literature. Our goal as health care providers should be to educate people about possible complications of circumcision, so that they would demand surgeons who are educated for circumcision of their children.

1. Introduction

Circumcision is the world's oldest and most commonly performed surgical procedure with a history of 5000 years in the world (Yegane et al., 2006; Perera et al., 2010). Roughly every one out of three men is circumcised today (Weiss et al., 2010). The procedure can be done for therapeutic or prophylactic, religious, cultural, social reasons (Perera et al., 2010).

Traditionally, almost all boys in Turkey are circumcised. With higher public education levels achieved, circumcisions are not performed in tents that are pitched in between neighborhoods anymore. Instead properly trained medical personnel perform circumcisions at hospitals. In Turkey vast majority of the circumcisers are men. Complications are very common given the fact that circumcision is the most widely conducted surgical procedure by traditional circumcisers and doctors. These complications may arise from extraordinary incision techniques or methods used for wound healing or bleeding controls that differ from routine techniques (surgical tools, dressing, aftercare materials etc.).

The purpose of this article is to present the case of an infant brought to the emergency room with circumcision bleeding and to review literature. Case is interesting in terms of the incision technique and the materials used for bleeding control and wound healing.

2. Case

Infant was brought to the emergency department with intractable bleeding six hours after circumcision. In the patient's history the parents indicated that the bleeding did not stop after nanny circumcision. The wound was covered repeatedly with the dressing material but the application was unsuccessful to stop the bleeding and that is the reason why they have decided to come to the hospital.

On physical examination the inguinoscrotal region was covered with a material, a cloth was used to wrap it around the penis and there was active bleeding (Fig. 1). In his laboratory tests complete blood count and PT, INR values were within normal limits. After taking him to the operating room, 1mg of vitamin K was administered intramuscularly. Inguinal region was cleaned from the wound dressing. Under general anesthesia penis was degloved. Bleeding point was determined and cauterized. Inner and outer foreskin was brought together with simple interrupted sutures. Dressing was applied to the wound and 50 mg/kg/day IV ceftriaxone treatment was initiated. The patient was discharged on the next day with a prescription of antibiotics and no complications were detected in early and late follow-ups.

Fig. 1. The inguinoscrotal region was covered with herbs and oil, a cloth was used to wrap it around the penis and there was active bleeding.

In the detailed history taken from the family, the parents indicated that an elderly lady conducted "nanny circumcision" on the baby. Dressing of the wound was prepared using onion (Allium cepa), sumac (Rhus coriara) and grease. Most children are circumcised with the same traditional way in that particular region. Written informed consents was obtained from the parents.

3. Discussion

This case of a 3-days-old infant who was brought to the emergency room with intractable bleeding after circumcision is presented because of the circumcision technique and the dressing material used to stop bleeding. The infant was circumcised with a local technique called "nanny circumcision" by a woman using a razor and dressing material was a mixture of onion, sumac and grease.

In Turkey, circumcisers do most of the circumcisions. Most circumcisions are done not for a medical need but either for traditional or religious reasons (Verit et al., 2002). Studies show that 85% of the circumcisions are made by circumcisers, 10% of them are done by health care personnel other than doctors and 5% are done by surgeons (Ozdemir, 1997). Circumcisers, most of whom are male, are trained by using a master-apprentice approach and this training is neither official nor medical. In this region, circumcisions are most common in the first three days after birth mainly because of tradition and also according to a belief that bleeding has a protective power over jaundice and it's beneficial for infant's health at later stages in life. Although almost most all circumcisers are male in Turkey; in this particular region circumcisers are generally female and the eldest women undertake the procedure and experience is passed along generations. The oldest lady of the family or the neighborhood usually performs the circumcision and she also teaches the procedure to younger women in the community. Historically it is known that Serefeddin Sabuncuoglu (fifteenth century), and his female students performed penile surgery (Sabuncuoglu, 1465).

Although perception about circumcision is changing especially among younger generation, it is still not conceived as a serious surgical procedure. It is performed outside operating rooms, environments that are not sterile like open spaces or at home (Ozdemir, 1997; Verit et al., 2002; Atikeler et al., 2005; Chaim et al., 2005).

While the most common early stage complications of circumcisions are; bleeding, infection, fistula, meatal stenosis, over trimming of skin and loss of penis; psychosocial problems are also common in the longer term like castration anxiety, dissatisfaction, and increased pain response. Complication rates range in between 0.2-2% in literature. Rates can go up to 8-17% in circumcisions performed under non-medical conditions. The actual complication rates might be even higher when minor appearance disturbances and related psychological problems are also taken into account (Ozdemir, 1997; Verit et al., 2002; Atikeler et al., 2005; Chaim et al., 2005; Perera et al., 2010; Weiss et al., 2010). In the region circumcision is conducted in a non-sterile environment with help of a razor.

Many plants are used for dressing wounds to facilitate healing or stop bleeding in Turkey and around the world. In Turkey *Abies cilicica, Achillea biebersteinnii, Achillea millefolium, Achillea nobilis, Ajuga sp., Allium sativum, Althaea officinalis, Amygdalus communis, Anchusa azurera, Echinophora sp., Euphorbia anacampseros, Echium italicum, Hypericum perforatum, Helichrysum plicatum, Salvia aethiopsis, Abiesbom mülleriana, Smilax sp., Olea europea, Papaver somniferum, Pinus nigra, Nicotiana glauca, Sambucus ebulus, Vitis vinifera* are used for wound healing (Sezik et al., 1991; Sezik et al., 1992; Yesilada et al., 1993; Tabata et al., 1994; Fujita et al., 1995; Honda et al., 1996; Tumen et al., 2006). Langermannia sp., P. Persica, Urticadioica, Centaurea lycopifolia and Juglans regia are used both for wound healing and to stop bleeding. Pinus nigra is first applied to stop bleeding and then an ointment prepared by mixing tail fat, honey wax, sugar and tar is applied for rapid healing. The majority of plants in Turkey are employed for treating skin problems such as cuts, wounds, abscesses, scabies, etc. and this makes 14.4-25% of overall recorded usages (Sezik et al.,1991; Honda et al.,1996).

The Eastern region of the Mediterranean has been distinguished throughout the generations with a rich inventory of natural medicinal herbs used by local herbalists (Saad et al., 2006). In Anatolia there are healers who also try to treat people with plant, animal and mineral mixtures other then circumcisers. Historically Heliodorus and Antyllus were the first to describe the partial resection of glans penis due to hypospadias. Bandaging, cauterization and the local application of vinegar were used to stop the hemorrhage (Buyukunal, 2004).

Onion and garlic have been used as medicine and food traditionally in Anatolia since ancient times (Kosar et al., 2006). Onion is a staple food with a high content of flavonoids (Javadzadeh et al., 2009). The flavonoid compound exerts several biological properties including antioxidant activity, tumor suppression, and reduction of scar formation. The mechanism of action of Allium cepa extract is thought to work by inhibiting fibroblast function in addition to reducing the formation of ground substance necessary for the formation of scar matrix. Allium cepa is also known to possess antibacterial properties (Jackson and Shelton, 1999). As well as being used for wound healing; onion is also used in Turkey's many regions for treatment of bee sting and hemorrhoids, for abscess maturation, as a painkiller in rheumatism, sprains and headache (Yesilada et al., 1995; Tumen et al., 2006; Kosar et al., 2006).

Rhus coriara comes from the berries of a wild bush that grows in all Mediterranean areas. In the medical literature it is reported that methanolic extracts of Rhus coriara L. fruits may be a source of natural antioxidants (Zargham and Zargham, 2008). Rhus coriara is used in wound healing, to treat animal bites, for edema in legs, dysentery, diarrhea, to promote maturation of abscess, to pass kidney stone, for treatment of gastric ulcer, stomachache, common cold, burns and elevated cholesterol (Sezik et al., 1991; Tabata et al., 1994; Fujita et al., 1995; Yesilada et al., 1995; Honda et al., 1996; Lev, 2006).

Reviewing the literature, we have seen that a lot of natural products are used for traditional folk medicine. There are so many reasons for these types of treatments to be popular in certain areas: In some countries some villages especially the ones on the mountains cannot be reached for months during winter because of snow covering the roads, transportation is hard or socioeconomical and sociocultural levels of the people are low. In this case nanny circumcision and unusual wound dressing is still common in the region probably also because Eastern Anatolia is still rich in folk medicine as a result of the geographical remoteness of this region from medical centers and facilities, and the difficulty of transportation in long and cold winters (Tabata et al., 1994).

Although abolition of nanny circumcision in this region is not likely to happen in near future, intervention by education of general public and circumcisers is vital to prevent short and long term complications of circumcisions that are performed in non-sterile environments and to also ensure that circumcision is only performed by healthcare personnel. Attention has to be brought to these traditional and regional practices and their complications that is a serious public health problem. Education to general public may arise awareness about the serious complications and may help to stop unhealthy practices.

Serious complications of circumcision, even mortality after circumcision may be seen especially when medically not trained people do it in a non-healthcare setting. Our goal should be to raise awareness among people so that they demand the circumcisions to be done by properly trained surgeons.

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Case Report

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A very rare complication of sublingual captopril

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ABSTRACT

Captopril inhibits angiotensin-converting enzyme and it is the most used sublingual drug in emergency departments to decrease blood pressure. Sublingual captopril is safe, effective and useful in treating hypertensive urgency. However, it is known that captopril has fewer systemic and dermatologic side effects such as headache, weakness and oral ulcers, oral pemphigus, consecutively. No data is available about captopril induced oral mucositis. Herein, we present a 50-year-old hypertensive woman who uses sublingual captopril frequently and suffers from recurrent, reversible and painful oral mucositis that thought to be caused by sublingual captopril.

1. Introduction

Captopril inhibits angiotensin-converting enzyme and it is the most useful sublingual drug in emergency departments to decrease blood pressure. Sublingual captopril is safe, effective and useful in treating hypertensive urgency (Guerrera et al., 1990). It shows a quick decrease in blood pressure with in 10 minutes and the maximum efficiency was seen after 30 minutes (Maleki et al., 2011). A gradual blood pressure drop with the absence of serious side effects makes captopril an ideal anti-hypertensive agent (Gemici et al., 1999). Headache and weakness are well known side effects of sublingual captopril. Herein, we present a 50-years-old hypertensive woman who uses sublingual captopril frequently and suffers from recurent, reversible and painful oral mucositis that thought to be caused by sublingual captopril.

2. Case

A 50-year-old female patient applied to the cardiology clinic with hypertension and headache complaints. It was learned that she used trandolapril 4 mg / verapamil 240 mg (once a day). As the patient has frequent headache and measured arterial blood pressure during this period is about 160/90 mmHg, she uses sublingual captopril often. She mentioned that after

taking sublingual captopril, she had a sense of burning under the tongue after half an hour and painful and itchy lesions emerged under the tongue after two hours (Fig. 1A). The lesion makes it difficult for the patient to eat and speak. It was learned that the lesions always emerged under the tongue and had declined during the day (Fig. 1B) and had dissappeared completely within two days (Fig. 1C). There was no other suspected sublingual drug that could cause this kind of lesion in her medication. For revealing possible allergic reactions, at the same time with sublingual captopril, a quarter, half, and full dose of captopril was mixed with the vaseline and rubbed on to the patient's forearm skin. After waiting for two days it was seen that there was no reaction against captopril. A biopsy from the lesion was taken and was sent for pathological investigation. The finding of non-specific inflammatory cells and bacterial clusters (Fig. 2) gave rise to thought that the lesions are oral mucositis secondary to the sublingual captopril.

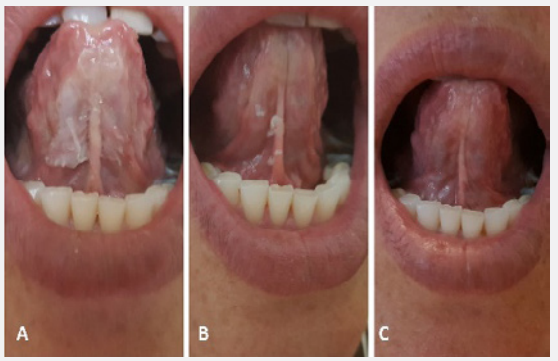

Fig. 1. A: After using sublingual captopril. B: Oral mucositis decreases as the effect of captopril decreases. C: Normal appearance of the oral mucosa with the end of the captopril effect.

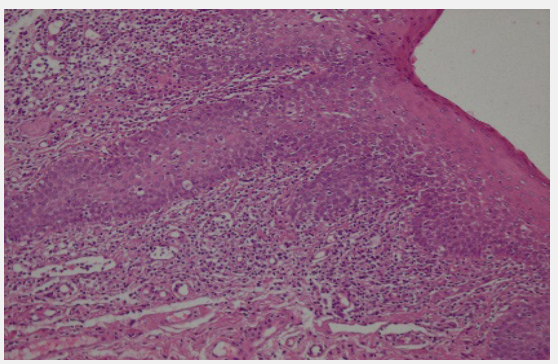

Fig. 2. A biopsy from the lesion demonstrated nonspecific inflammatory cells and bacterial clusters.

3. Discussion

Sublingual captopril is an effective and frequently used anti-hypertensive agent in the treatment of hypertensive urgency. Oral mucositis caused by sublingual captopril is a rarely seen complication making it difficult to maintain oral functions like eating as well as speaking. Oral medications can cause adverse side effects such as salivary gland disease, oral ulcers, taste sense alteration, mucosal pigmentation, and tooth decay (Shinkai et al., 2006). Angiotensin-converting enzyme inhibitors are a well known cause of cutaneous adverse reactions. It is known that captopril, an angiotensin converting enzyme inhibitor, causes pemphigus in the oral mucosa (Wolf et al., 1991). Captopril contains the thiol group, so, as a result of the interaction of thiol group with the keratocyst membrane, acantholysis occurs, resulting in pemphigus and ulceration on the oral mucosa (Lombardi et al., 1993). This mechanism may have contributed to the formation of oral mucositis in the present case. Findings suggesting that the lesions are not pemphigus 1) biopsy samples from lesion were consistent with oral mucositis, 2) spontaneous resolution of the lesion after stopping sublingual captopril, and 3) negative autoantibodies (Lombardi et al., 1993).

In the present case, appearance of lesions after using captopril sublingually but not by ingestion, suggests that captopril causes mucosal damage and inflammation due to direct contact with sublingual mucosa. Non-specific inflammatory reaction is another finding which supports that the lesions are related to the contact of captopril directly with sublingual mucosa. Lack of reaction formation after applying captopril-vaseline mixture over skin may be attributed to the fact that the sublingual mucosa differs from the other skin mucosa in that it is thinner, more sensitive and has a different blood supply (Narang and Sharma, 2011; Goswami et al., 2013).

Sublingual drug application have some advantages such as direct transition to the systemic circulation without elimination in the liver, rapid absorption of drug compared to other oral cavity mucosa and good patient compliance. In addition to the advantages of sublingual mucosal delivery, there are some disadvantages such as short duration of action (Goswami et al., 2008) and development of oral mucositis as in the present case. Clinicians always should be alert to this rare adverse side effect.

The clinician should keep in mind that a very rare cause of oral mucositis may be sublingual captopril.

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Wunderlich Syndrome: A case report

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ABSTRACT

Wunderlich syndrome is a rare cause of abdominal pain. This is spontaneous, nontraumatic kidney bleeding confined to the subcapsular and perirenal space. Various terms have been used including spontaneous perirenal haematoma, spontaneous subcapsular renal haemorrhage, nontraumatic perirenal haematoma and spontaneous perinephric haematoma. The etiology of spontaneous renal rupture has not been described yet. Possible causes include benign [e.g., angiomyolipomas (AML), tuberous sclerosis, renal cyst, adenoma, lipoma, and hamartoma] and malignant (e.g., oncocytoma, renal clear cell carcinoma, and Wilms' tumor) tumors or it can occur secondary to vasculitis (polyarteritis nodosa), nephritis, blood dyscrasias (anticoagulant agents, polycythaemia), renal stone disease, arteriovenous malformations and fistulas, venous thrombosis or rupture of renal artery/intraparenchymal aneurysm. Clinically this condition presents with acute flank pain, palpable flank mass and hypovolemic shock together known as 'Lenk's triad'. Historically, renal neoplasms followed by vascular diseases were the most common causes of Wunderlich syndrome. Our case was 50 years old woman. A spontaneous retroperitoneal hemorrhage patients who at night come to emergency with sudden abdominal pain. Wunderlich syndrome is cause of unexplained abdominal pain should be kept in mind.

1. Introduction

Spontaneous retroperitoneal bleeding (SRC) is a life-threatening clinical condition (Murphy et al., 2013). Wunderlich syndrome (WS) is a rare, spontaneous and non-traumatic retroperitoneal hemorrhage, firstly described by Wunderlich in 1856 (Virchow, 1856). The incidence is not known clearly (Vaddi et al., 2011; Murphy et al., 2013). The classic Lenk's triad is seen in WS. These findings are pain in the unilateral acute phalanx, palpable mass in examination with abdominal palpation and hypovolemic shock indicators. However, the findings are usually nonspecific and variable in the patients (Baishya et al., 2011; Katabathina et al., 2011). There are renal (tumor, vascular and inflammatory diseases) and extrarenal (adrenal diseases, abdominal aortic aneurysm) diseases in the etiology of WS. The most common causes of WS are renal cell carcinoma and angiomyolipoma (Daskalopoulos et al., 2003). It should also be kept in mind that WS can be seen without the use of anticoagulants and trauma. The diagnosis is made by radiological imaging with clinical suspicion (Kendall et al., 1988; Zhang et al., 2002). The aim of presenting this case is to emphasize the importance of advanced imaging in unexplained abdominal pain to detect rare cases for life-threatening clinical conditions. As a result, it is to increase the awareness of emergency physicians for rare fatal conditions.

2. Case

A 50-year-old female patient was admitted to the emergency service with a sudden onset pain in her right upper and lower quadrants. Nausea and vomiting were

accompanied by persistent pain. The patient's medical history included hypertension (HT) and right renal angiomyolipoma. It was learned that the patient was not taking regular medication for HT and was followed up for angiomyolipoma. At the time of presentation, the blood pressure was 135/85 mmHg, pulse rate was 95/min, and the other vital signs were normal. The electrocardiogram (ECG) was showed normal sinus rhythm. Physical examination revealed right upper and lower quadrant tenderness, defense and rebound in the abdomen. The other examination findings were normal. Oral intake of the patient was stopped and the patient was monitorized. 2 L/min oxygen was started with nasal cannula. Vascular access was opened and normal saline infusion was started at a rate of 100 ml/h. In the laboratory tests; Hemoglobin (Hgb) was 11.98 g/dL hematocrit (Htc) was 37.5%, platelet (Plt) was 219300 / uL, INR was 1.08 and the other blood parameters were normal. Control Hgb was measured as 11.3 g/dL. The abdominal x-ray was seemed as normal (Fig. 1). In abdominal ultrasonography (USG); There was no free fluid in the abdomen, the right kidney dimensions could not be evaluated clearly. In the USG which was taken one month ago; a hyperechogenic lesion with vascular structure was seen in the right kidney. The lesion was in size 44 × 23 mm and was properly limited. She underwent computerized abdominal tomography (ACT) with intravenous contrast injection. In the right kidney, approximately 12 × 6 cm hematoma area extending to the superior and inferior of the kidney was seen in the ACT and there was a free fluid of 14 mm in the pelvic region (Fig. 2). The patient was consulted to the urology department because of the increased renal size due to bleeding. The patient underwent emergency surgery and right nephrectomy was performed. When her general condition improved, she was discharged with a plan of periodic follow-up.

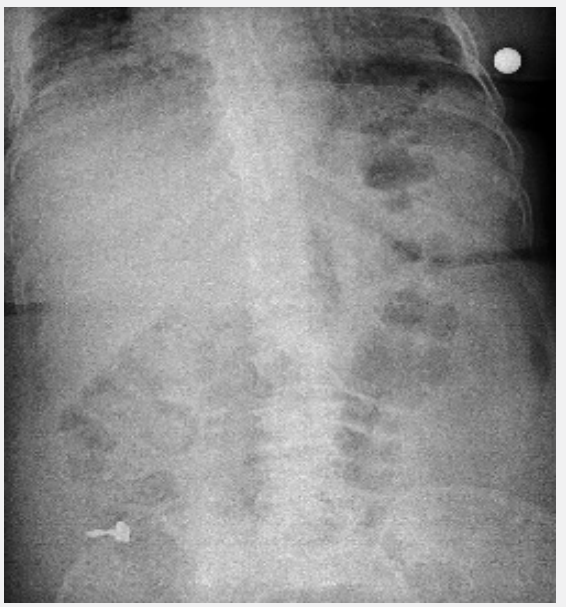

Fig. 1. Direct graphy.

Fig. 2. Computed tomography abdomen scan with contrast.

3. Discussion

Spontaneous retroperitoneal hemorrhage is a rare and fatal situation which is presenting to the ED with abdominal pain. (Murphy et al., 2013). Failure to diagnose can result in death. In general, the cases of WS are middle-aged previously in the literature. Kim et al. reported a case series with 28-case for WS. They found that the rate of women and men was the same, and the mean age was 48 years in the cases of WS. 35% of the patients had the diagnosis of HT. In the same study, 83% of patients had acute phalanx pain, 19% had hematuria and 11% had hypovolemic shock indicators (Kim et al., 2018). Our case was not compatible with Lenk's triad. In our report, the female patient was 50 years old and had a diagnosis of HT.

Daskalopoulos et al. reported a case series with 13-case of WS, They reported that 5 patients were diagnosed with only ACT and 7 patients were diagnosed with ACT after USG (Daskalopoulos et al., 2003). Zhang et al. reported 165 cases in a case-series(Zhang et al., 2002). They reported that 135 cases were diagnosed with ACT, 100 cases were diagnosed with USG, 5 with magnetic resonance imaging (MRI) and 81 with angiography. Computerized tomography is the gold standard in spontaneous retroperitoneal hemorrhage, but in the first tomography, a little more than half of the cases are diagnosed (Zhang et al., 2002). The first imaging method is usually abdominal x-ray and then USG. Direct abdominal radiography is generally used to exclude other possible pathologies (Murphy et al., 2013). The diagnostic value of x-ray is too lower than ACT (Zhang et al., 2002; Kim et al., 2018). In our case, due to obesity and intense intraabdominal gas, the diagnosis could not be done with USG. In the ACT

images, bleeding was observed in the retroperitoneal area beginning from kidney. Hemodynamic parameters were within normal limits despite bleeding.

The treatment algorithm in WS is not clear. Zhang's study reported that they performed total nephrectomy in 113 patients, partial nephrectomy in eight patients, drainage in 17 patients, embolization in six patients and clinical follow-up in 16 patients (Zhang et al., 2002). Kim et al. reported they performed total nephrectomy for 11 cases of 13 patients (Daskalopoulos et al., 2003; Kim et al. 2018). Early diagnosis may decrease mortality and prevent unnecessary nephrectomy (Zhang et al., 2002). Nephrectomy is performed in hemodynamically unstable cases, but embolization, radiofrequency ablation and cryoablation can be performed according to clinical condition (Flum et al., 2016). Nephrectomy was performed for our patient because the bleeding was opened to the retroperitoneal area.

Diseases in the patient's history may be a guide for rare clinical conditions. Therefore, advanced radiological imaging should be performed in the presence of clinical suspicion in unexplained abdominal pain.

This case is reported by obtaining consent from the patient and no support was provided from any institution.

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