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Measurement of the knowledge of pediatric residents about the urinary tract infection in children

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Low body mass index versus obesity: Which is worse during cardiac surgery?

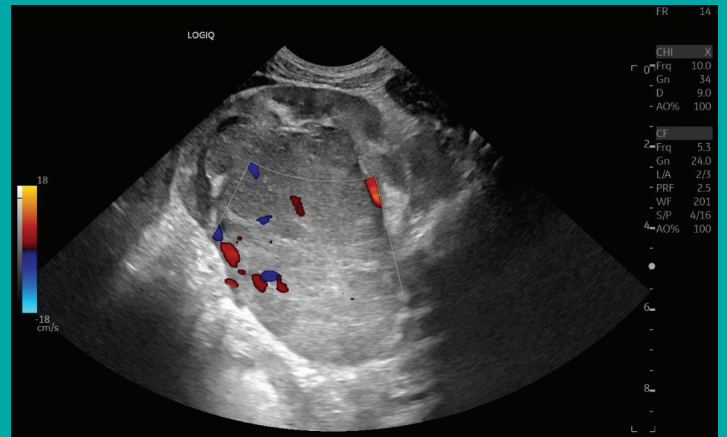
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Measurement of the Knowledge of Pediatric Residents about the Urinary Tract Infection in Children

ABSTRACT

Objectives: Urinary tract infection (UTI) is one of the most common infectious diseases in children. However, although several specific guidelines have been published, the management of UTI has not been standardized. In this study, we evaluated the knowledge of residents about UTI using an online questionnaire. It was aimed to increase the interest and attention of residents on UTI.

Methods: The questionnaire consisted of 42 multiple-choice and true/false questions prepared through "Google Forms." The questions were sent to resident physicians working in Ankara province through various "WhatsApp" groups. Participation in the survey was voluntary.

Results: Ninety-three research assistants participated in the survey. The proportion of physicians in the first 2 years of residency training was 29.1%, and in the last year was 54.9%. 25.8% of residents felt competent about UTI. Bladder-bowel dysfunction, vesicoureteral reflux, and obesity were confirmed as risk factors by 98.9% of residents. However, 35.5% of the residents stated that fever is not seen in lower urinary tract infection and 5.4% stated that pyuria is sufficient for the diagnosis of UTI. The use of prophylaxis was thought to prevent renal scarring by 78.5%. Probiotic/prebiotic use was reported to be protective by 40.9%.

Conclusion: UTI can be managed differently depending on the level of knowledge and experience of physicians. In addition to correct answers, incorrect/incomplete answers were also noteworthy in our survey. Collaboration among physicians caring for pediatric patients and agreement on common guidelines are thought to provide more appropriate management of pediatric UTIs.

Keywords: Pediatrics, prophylaxis, residency training, urinary tract infection

Urinary tract infection (UTI) is one of the most common infectious diseases in childhood. It is divided into two main groups according to the site of occurrence. Upper urinary tract infection is an infection of the renal pelvis and/or renal parenchyma, while lower urinary tract infection is limited to the bladder and urethra (1). The clinical picture is quite heterogeneous, and symptoms such as dysuria, frequent urination, and incontinence are observed in lower urinary tract infections, whereas fever and flank pain are usually present in upper urinary tract infections (2). UTI affects 2.8% of children each year, with a recurrence risk of up to 30% (3). The prevalence of UTIs shows a bimodal distribution, reaching peak levels in the first year of life and during toilet training between 2-4 years of age. In the first 6 months of life, UTI is more common in uncircumcised male infants, whereas it is more common in girls after the age of one year (4).

Urine sampling is very important for the diagnosis of UTI. The technique used to obtain a urine sample for urinalysis or culture affects the contamination rate and may lead to misinterpretation of the results. Suprapubic aspiration and bladder catheterization have low contamination rates, but being invasive procedures, they cause various difficulties in daily use. Obtaining a urine sample with a plastic bag attached to the genital area is the most commonly used method, but it is simple and noninvasive with a high contamination rate. Therefore, the bag method should not be used for urine culture (5). A positive urinalysis for nitrite or nitrite with leukocyte esterase has a high specificity for the diagnosis of UTI and initiation of empirical antibiotic treatment (6).

In terms of UTI treatment, most guidelines recommend different molecules for empirical treatment selection (7). The antibiotic to be used should be selected according to

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local resistance patterns. The most common bacterial cause of UTI in infants and children is *Escherichia coli* (*E. coli*). Approximately 50 percent of *E. coli* are resistant to amoxicillin or ampicillin. In addition, the frequency of *E. coli* producing extended-spectrum beta-lactamase is increasing, leading to higher rates of resistance to amoxicillin-clavulanate. Resistance rates to trimethoprim-sulfamethoxazole have also increased in some populations in recent years. Therefore, cephalosporin group antibiotics are recommended as first-line oral agents in the treatment of UTI in children (8). Antibiotic prophylaxis can be used in the presence of a history of recurrent UTI (≥ 3 episodes per year), in the presence of high-grade vesicoureteral reflux (VUR) (stage 4-5), or until voiding cystourethrography (VCUG) is performed when indicated. Although there has been a recent trend to decrease the use of prophylactic antibiotics, prophylaxis in selected cases may protect against long-term adverse outcomes (9).

Although several specific guidelines have been published in recent years, UTI management has not been standardized (10-14). In this study, we evaluated the knowledge level of residents working as research assistants in the Departments of Pediatrics in university and training and research hospitals in Ankara province in terms of diagnosis and treatment of UTI using an online questionnaire. It was aimed to increase the interest and attention of resident physicians on UTI by drawing attention to various guidelines on the subject.

METHODS

The questionnaire study, aimed at measuring the level of knowledge of residents working as research assistants in the Department of Pediatrics in terms of diagnosis, treatment, and follow-up of UTI, was a multicenter cohort study in Ankara province. The questionnaire consisted of 42 questions with multiple choice and true/false options prepared through "Google Forms." The questions could be answered in 10-15 minutes. The survey was sent to resident physicians via various "WhatsApp" groups. Participation in the survey was voluntary. Before starting to answer the survey questions, the participants were asked for their place of work information, and the data were stored electronically.

In the first part of the questionnaire, the participants were asked about the year of their residency training, whether they were working in the Pediatric Nephrology service or outpatient clinic, and whether they felt competent in terms of UTI management. In the following questions, their level of knowledge about the definition and risk factors of UTI, the gold standard method for urine sampling, the conditions required for definitive diagnosis of infection, treatment, imaging methods, indications for starting prophylaxis, and other preventive measures for UTI were questioned (10-14).

Ethical approval for the study was obtained by the Gazi University Ethics Commission on 05.10.2023 with the research code 2023-1135.

Statistical Analysis

In the presentation of descriptive statistics, categorical data were presented as number (percentage). Cross-tabular analyses and Fisher's exact Chi-square tests were used to compare the qualitative characteristics of the groups. The Shapiro Wilks test was used to determine the normal distribution of numerical measurements

Table 1. General characteristics of the pediatric residents who participated in the survey

Sex	%
Female	75.3
Time spent in specialized training	
0-1 year	14
1-2 years	15.1
2-3 years	16.1
3-4 years	54.8
Units in the Department of Pediatric Nephrology	
Pediatric Nephrology inpatient clinic	86
Pediatric Nephrology outpatient clinic	73.1
Both	67.7
Feeling competent in the diagnosis/treatment/prophylaxis of urinary tract infection	25.8

in the groups. Two groups were compared using independent samples t-test and Mann-Whitney U test for those not normally distributed. IBM SPSS Statistics version 22 package program was used for all statistical analyses. The significance level was taken as $p < 0.05$.

RESULTS

A total of 93 residents working as research assistants in the Department of Pediatrics in Ankara participated in the survey (Female/male: 3.2). The proportion of physicians in the first 2 years of residency training was 29.1% and 54.9% in the last year. The majority of the physicians worked in the Pediatric Nephrology service or Pediatric Nephrology outpatient clinic during their residency training (86% and 73.1%, respectively). The proportion of residents who had worked in both units was 67.7%. However, only 25.8% of the participants felt competent in the diagnosis, treatment, and follow-up of UTI (Table 1).

Bladder-bowel dysfunction, VUR, and obesity were confirmed as risk factors for UTI by 98.9% of the residents. However, 45.2% of the residents stated that the frequency of UTI was higher in girls in the first year of life, 35.5% stated that fever was not seen in lower urinary tract infection, and 5.4% stated that pyuria alone was sufficient for the diagnosis of UTI. When evaluated according to the duration of residency training, physicians in the first year of residency gave more incorrect answers to these questions than physicians in the last year of residency, although not statistically significant [46.4% versus 37.3% ($p=0.329$), 43.1% versus 30.8% ($p=0.369$), and 15.4% versus 5.9% ($p=0.237$), respectively].

Suprapubic aspiration as the gold standard for diagnosis was correctly answered by 72%. While 15.1% of the participants stated that urine sampling by urethral catheterization and 12.9% stated that midstream urine sampling was the gold standard, no physician chose the bag urine method. In the evaluation according to the duration of specialty training, although not statistically significant, physicians in the first year of specialty training correctly accepted suprapubic aspiration as the gold standard at a lower rate than physicians in the last year of specialty training (61.5% vs. 74.5%, $p=0.905$). These percentages were similar between physicians who had not yet worked in the Department of Pediatric Nephrology and

physicians who had worked in this department (66.7% vs. 74.6%, $p=0.691$).

More than one-third of the participants ($n=34$, 36.6%) thought that the growth of 100,000 colonies of bacteria per mL in a bagged urine sample was accurate for the definitive diagnosis of UTI. In cases of pyuria in midstream urinalysis, 52.7% and 60.2% of the residents answered correctly that the growth of 50,000 colonies of bacteria per mL in culture and 1,000-10,000 colonies of bacteria in urethral catheterization would be sufficient for the diagnosis of UTI. More than one-fifth of the participants ($n=21$, 22.6%) reported that asymptomatic bacteriuria should be treated. Residents in their first year of residency training were more likely to have incorrect knowledge on this topic than those in their final year of training (46.2% vs. 19.6%, $p=0.159$). Residents who had worked in the Department of Pediatric Nephrology were more likely to know that asymptomatic bacteriuria did not need to be treated than those who had not yet worked in the department (77.6% vs. 62.5%, $p=0.335$). Almost all residents correctly answered that indications for intravenous treatment include severe patient presentation, vomiting and/or non-compliance with oral therapy, and that neonates and infants younger than 2 months should be treated parenterally due to the risk of urosepsis and severe pyelonephritis (97.8% and 96.8%, respectively).

It was known by 57% of the participants that all pyelonephritis cases should be evaluated with urinary tract ultrasonography (USG) after the first UTI. This was significantly higher among last year residents than first year residents (70.6% vs. 38.5%, $p=0.016$). Similarly, physicians who had worked in both the Pediatric Nephrology outpatient clinic and the Pediatric Nephrology service were more likely to confirm the need for urinary tract USG after pyelonephritis than physicians who had not worked in these departments (65.1% vs. 40%, $p=0.022$). Almost all participants correctly answered that VCUG can detect changes consistent with VUR, urethral obstruction due to posterior urethral valves, ureterocele, and/or neurogenic bladder (93.5%).

The rate of residents who thought that prophylactic antibiotics should be initiated in patients with 3 or more UTIs per year was 80.6%. No significant difference was found in the evaluations comparing the necessity of initiating prophylactic antibiotics in patients with recurrent UTI in terms of the time spent in the specialty training process, and the rates of physicians who stated that prophylaxis was necessary were numerically similar (84.6% among residents in the first year of specialty training, 78.6% among residents in 1-2 years, 73.3% among residents in 2-3 years, and 82.4% among residents in the last year of training, $p=0.855$). Almost all of the participants were aware that prophylactic antibiotics should be initiated in patients with stage 4-5 VUR on VCUG (95.7%). However, the necessity of short-term prophylaxis due to VCUG was correctly answered by 23.7%. This rate was 23.1% and 25.5% in first and last year residents, and although not statistically significant, it was similar in all groups ($p=0.969$). The rate of residents who reported that every patient undergoing clean intermittent catheterization should receive long-term prophylaxis was 80.6%. The proportion of residents in the first year of residency training who thought that long-term prophylaxis should be used in every patient was higher compared to residents in the last year of residency training (92.3% vs. 76.5%, $p=0.586$).

Almost all residents correctly recognized that amoxicillin, trimethoprim/sulfamethoxazole, or nitrofurantoin are the antibiotic options for long-term prophylaxis (96.7%). However, the rate of physicians who thought that trimethoprim/sulfamethoxazole should be used for prophylaxis in the first two months of life was 31.2%. Prophylaxis is thought to prevent renal scarring by 78.5%. This misconception was slightly higher among first-year residents compared to last-year residents (84.6% vs. 72.5%, $p=0.483$). While 23.5% of the residents who had worked in a pediatric nephrology service or outpatient clinic knew that antibiotic prophylaxis does not prevent renal scarring, none of the residents who had not yet worked in this department answered this question correctly ($p=0.043$). Vitamin A supplementation can be used to reduce scar formation was known by 22.6% of the participants. In the comparisons made among residents in terms of this knowledge, it was observed that the duration of specialty training or whether or not they worked in the Pediatric Nephrology department did not make a significant difference (14.3% among residents in the first year of specialty training, 28.6% between 1-2 years, 19.4% between 2-3 years, 23.5% among residents in the last year, $p=0.153$; 22.5% among physicians who had worked in the Pediatric Nephrology service and 23.1% among physicians who had not, $p=0.604$; 19.1% among physicians who had worked in the Pediatric Nephrology outpatient clinic and 32% among physicians who had not, $p=0.188$).

When other factors other than antibiotic prophylaxis that may be protective in terms of UTI were questioned, prevention of constipation and circumcision in male patients with recurrent UTI or high-grade VUR were known to prevent the development of infection by the majority of the physicians surveyed (94.6% and 88.2%, respectively). Consumption of cranberry fruit/juice, probiotic/prebiotic use, and short-term application of local steroid cream to the tip of the penis in boys with physiologic phimosis were correctly recognized by 26.9%, 40.9%, and 22.6%, respectively.

The correct and incorrect statements among the items asked to the Pediatric Health and Diseases resident physicians in order to measure their level of knowledge about the diagnosis, treatment, and prophylaxis of urinary tract infections are presented in Table 2 and Table 3, respectively.

DISCUSSION

UTI, which is a very common bacterial infection in the pediatric population, constitutes an important cause of antibiotic use and hospitalization in children. It is known that the risk of UTI in infants up to the age of one year is higher in boys, especially in uncircumcised male infants, and after the age of one year, the male-female ratio reverses (7). However, approximately half of the resident physicians who participated in our survey stated that the frequency of UTI was higher in girls in the first year of life, suggesting that their level of knowledge about gender distribution in UTI was insufficient.

The diagnosis of pediatric UTI is challenging due to its non-specific clinical presentation. Fever may be the sole clinical symptom, particularly in young children. UTI should be considered in the differential diagnosis of children presenting with fever without an apparent source (15). Neonates and infants under three months typically present with non-specific symptoms such as feeding difficulties, restlessness, jaundice, or vomiting, and sometimes hypothermia. Older

Table 2. Correct statements and the proportion of participants selecting the relevant option when asked to measure their level of knowledge about the diagnosis, treatment and prophylaxis of urinary tract infections by pediatric residents

General Informations Related to Urinary Tract Infection:	%
Bladder-bowel dysfunction, vesicoureteral reflux, and obesity are some of the risk factors for urinary tract infections.	98.9
Newly developed enuresis nocturna with a diagnosis of urinary tract infection suggests lower urinary tract infection.	75.3
A fever of 38.5°C and above is indicative of pyelonephritis.	97.8
Informations Directed for the Diagnosis of Urinary Tract Infection:	
The presence of 100,000 colony-forming units of bacteria per milliliter (mL) in midstream urine confirms the diagnosis of urinary tract infection.	77.4
In the presence of pyuria, the presence of 50,000 colony-forming units of bacteria per milliliter (mL) in midstream urine confirms the diagnosis of urinary tract infection.	52.7
The presence of 1,000 to 10,000 colony-forming units of bacteria per milliliter (mL) in urethral catheterization confirms the diagnosis of urinary tract infection.	60.2
In infants under 4 months of age, the presence of 1,000 colony-forming units of bacteria per milliliter (mL) in urine obtained by urethral catheterization confirms the diagnosis of urinary tract infection.	31.2
Informations Directed for the Treatment of Urinary Tract Infection:	
Indications for intravenous therapy include the appearance of a severely ill patient, vomiting, and/or non-compliance with oral therapy.	97.8
Newborns and infants under 2 months of age should be treated parenterally due to the risks of urosepsis and severe pyelonephritis.	96.8
If sensitive according to the antibiogram, no antibiotic has superiority over another.	53.8
There is no difference in efficacy between starting with parenteral treatment and switching to oral treatment after the third day.	61.3
Informations Directed for Imaging Methods after Urinary Tract Infection:	
In patients diagnosed with urinary tract infection, imaging should be performed in the presence of pseudohypoaldosteronism to assess obstructive uropathy.	36.6
All cases of pyelonephritis should be evaluated with urinary system ultrasonography (USG) after the first infection.	57
Voiding cystourethrography (VCUG) can detect changes consistent with vesicoureteral reflux (VUR), posterior urethral valves (PUV) in male children, ureterocele, and/or neurogenic bladder.	93.5
Informations Directed for Prophylaxis of Urinary Tract Infection:	
Planning for VCUG is one of the indications for starting antibiotic prophylaxis.	23.7
Detection of grade 4-5 VUR in VCUG is one of the indications for starting antibiotic prophylaxis.	95.7
Having a history of 3 or more urinary tract infections per year is one of the indications for starting antibiotic prophylaxis.	80.6
Vitamin A prophylaxis reduces scar formation after urinary tract infection.	22.6
Options for antibiotic prophylaxis include amoxicillin, trimethoprim/sulfamethoxazole, and nitrofurantoin.	96.7
Nitrofurantoin and cotrimoxazole doses can be applied as 2 mg/kg/day.	58.1
In cases where urinary tract infection occurs 2 or more times under prophylaxis, the active substance used in prophylaxis should be changed.	80.6
Informations Items Directed for Factors That Can Be Protective against Urinary Tract Infection:	
Circumcision in male patients with recurrent urinary tract infections or high-grade VUR is protective against urinary tract infections.	88.2
The use of topical steroid cream on the tip of the penis in male children with phimosis is protective against urinary tract infections.	22.6
Consumption of cranberry juice/fruit is protective against urinary tract infections.	26.9
The use of probiotics/prebiotics is protective against urinary tract infections.	40.9
Prevention of constipation is protective against urinary tract infections.	94.6

children may exhibit lower urinary tract symptoms like increased frequency of urination, dysuria, and continence disorders, along with complaints of abdominal pain and lower back pain. The risk of upper urinary tract infection is higher if the patient has a fever of 38°C or higher, but fever can also occur in lower urinary tract infections. Therefore, in many pediatric cases, it is not possible to clearly distinguish between upper or lower urinary tract infections (1). In our

survey, approximately one-third of our resident physicians stated that fever would not be observed in lower urinary tract infections, indicating insufficient knowledge regarding UTI symptoms.

The role of urine dipstick examination in diagnosing UTI remains contentious. The specificity of nitrite positivity or positive nitrite results with leukocyte esterase is high enough to diagnose UTI and initiate empirical treatment (16). The National Institute for

Table 3. Incorrect statements directed towards pediatric health and disease assistant physicians to measure their knowledge levels regarding diagnosis, treatment, and prophylaxis of urinary tract infections, and the rate of participants choosing the relevant option

General Informations Regarding Urinary Tract Infection:	%
The prevalence is higher in girls within the first year of life.	45.2
Fever is not observed in lower urinary tract infections such as cystitis.	35.5
The presence of pyuria in urine is sufficient for the diagnosis of urinary tract infection.	5.4
<i>Enterococcus faecalis</i> is the causative agent in the majority of cases.	15.1
Having ≥ 2 urinary tract infections in the past year is defined as recurrent urinary tract infection.	67.7
Informations Directed for the Definite Diagnosis of Urinary Tract Infection:	
The presence of 100,000 colony-forming units of bacteria per milliliter (mL) in bag urine is one of the definite diagnostic criteria for urinary tract infection.	36.6
Informations Directed for the Treatment of Urinary Tract Infection:	
Asymptomatic bacteriuria should be treated due to the risks it carries.	27.3
In the treatment of uncomplicated lower urinary tract infections, 7-10 days of oral treatment is superior to 3-7 days of oral treatment.	26.9
Informations Directed for Imaging Methods after Urinary Tract Infection:	
The detection of abnormal ultrasound findings after the first pyelonephritis or a history of recurrent febrile urinary tract infections encompasses all indications for voiding cystourethrography (VCUG).	55.9
If a pathogen other than enteropathogenic E.coli is detected, VCUG is not necessary.	4.3
Informations Items Directed for Prophylaxis of Urinary Tract Infection:	
Intermittent clean catheterization due to neurogenic bladder or posterior urethral valves is one of the indications for starting antibiotic prophylaxis.	80.6
Long-term prophylactic antibiotic use reduces the frequency of febrile urinary tract infections more in boys under 2 years of age compared to girls.	54.8
Long-term prophylactic antibiotic use significantly prevents renal scar formation in both sexes.	78.5
Trimethoprim-sulfamethoxazole should be used for antibiotic prophylaxis in the neonatal period.	31.2
Informations Directed for Factors That Can Be Protective against Urinary Tract Infection:	
Reducing fluid intake is protective against urinary tract infection.	5.4

Health and Care Excellence (NICE) guidelines recommend urine culture only for patients at risk of severe illness or with a history of recurrent UTIs, and treatment planning based on nitrite/leukocyte esterase results in other patients (14). Conversely, guidelines from the Italian Society of Pediatric Nephrology (SINePe) and the European Society of Urology/European Association of Pediatric Urology (EAU/ESPU) strongly advise that urine culture should always be performed in the case of nitrite/leukocyte esterase positivity on dipstick (11,12). In our study, 5.4% of the resident physicians stated that pyuria alone was sufficient for the diagnosis of UTI, which may result from the discrepancies in UTI diagnostic criteria among the guidelines that the residents apply.

Urine sampling for urine culture is critical for diagnosing UTI. Different techniques are employed in daily practice. The technique used to obtain urine for urinalysis or culture influences the contamination rate, which may hinder accurate evaluation of the results, especially in early infancy (17). Suprapubic aspiration and bladder catheterization have low contamination rates but are invasive procedures that raise concerns, especially among parents. Consequently, a plastic bag attached to the genital area has become the most commonly used technique for urine collection in daily practice, but despite being simple and noninvasive, it has a high contamination rate of up to 63% and should not be

used for culture (18,19). However, in our survey, more than one-third of the physicians stated that growth in urine culture obtained by the bag method was sufficient for the definitive diagnosis of UTI. Recent updates in different guidelines have generally lowered the thresholds for defining a significant positive urine culture. A threshold of 50,000 CFU/mL is typically considered significant, but this threshold varies depending on the urine collection technique. Some guidelines recommend lower thresholds for urine obtained by suprapubic aspiration or urethral catheterization and higher thresholds for the clean capture/midstream method (10,20). More than half of the physicians in our survey reported that they consider 50,000 colonies of bacteria per mL in culture to be significant in the presence of pyuria in midstream urinalysis and 1,000-10,000 colonies of bacteria in urethral catheterization.

Empiric therapy for pediatric UTI is a contentious area, and most guidelines recommend a broad range of molecules as appropriate empiric therapies. Thus, the choice of initial antibiotic often depends on personal experience. The misuse and overuse of antibiotics are the primary causes of the alarming spread of antibiotic resistance in community-acquired pediatric UTIs, which further increases the risk of resistance development by promoting the empirical use of broad-spectrum molecules (1,21). The situation is similar for prophylactic antibiotics used without a real indication. Although pro-

phylactic antibiotics reduce the frequency of recurrent UTI by up to 50%, they are not effective in preventing new renal scar formation (22,23). In our survey, the rate of physicians who believed that antibiotic prophylaxis prevented new renal scar formation was quite high. This finding suggests that resident physicians lack knowledge about the necessity of prophylaxis. In the presence of low-grade VUR, the complications of prophylaxis outweigh the benefits, and prophylaxis is not recommended in patients with low-grade VUR (24). In our survey, almost all participants reported that prophylaxis should be used in patients with high-grade VUR.

Prophylactic non-antibiotic preventive measures classically include increasing fluid intake, ensuring genital hygiene, correction of bladder-bowel dysfunction and voiding dysfunction, and circumcision for male infants younger than 1 year and diagnosed with recurrent UTI (25). In addition, cranberry, vitamin A supplementation, and probiotic/prebiotic use have also been shown to reduce the frequency of UTIs and prevent renal scar formation (26-28). Approximately one-quarter of the resident physicians who participated in our survey were aware of the benefits of cranberry and vitamin A in terms of UTI. The protective properties of probiotic/prebiotic use were known by 40.9% of our physicians.

In conclusion, since UTI is a common problem for primary care pediatricians and a major cause of pediatric emergency department visits, collaboration among pediatricians and agreement on common guidelines are essential for the appropriate management of pediatric UTIs. Although several specific and well-established guidelines have been published in recent years, the management of pediatric UTI remains controversial. UTI may be managed differently depending on the level of knowledge and experience of physicians. In our study, we observed that residents who were in the last year of their residency training and/or had worked in pediatric nephrology units were more knowledgeable about the diagnosis, treatment, and follow-up of UTIs than residents who were at the beginning of their training and had not yet done a pediatric nephrology rotation. In addition to correct answers, incorrect/incomplete answers were also noteworthy in our survey. At some points, it was observed that the awareness and knowledge levels of the participants were low. However, the fact that the resident physicians who participated in the survey were at different stages of their specialty training and that different recommendations regarding UTI management were given in various guidelines should not be ignored. In conclusion, it is thought that updating the knowledge of residents on UTI management in every period of their training with new guidelines is extremely important to eliminate the long-term negative consequences of pediatric UTIs.

Ethics Committee Approval: This study was conducted with the permission of the Gazi University Local Ethics Committee (decision no: 2023-1135, date: 15.10.2023).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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Low Body Mass Index Versus Obesity: Which is Worse During Cardiac Surgery?

ABSTRACT

Objectives: Obesity can cause many diseases and leads to poor prognosis in the course of many diseases. Some researchers report that obesity positively affects cardiac surgery, and they refer to this phenomenon as the “obesity paradox.” Although there are many articles in the literature on obesity, there are no detailed studies on low BMI, especially in cardiac surgery. We wonder whether an extremely low body mass index is a risk factor, similar to obesity, in cardiac surgery patients.

Methods: We conducted an analysis of the data from 786 patients who underwent elective isolated coronary artery bypass surgery in the last two years. The patients were categorized into four groups based on their BMI: Low BMI (<18.5 kg/m², n=72), Normal BMI (18.5-24.9 kg/m², n=228), Overweight BMI (25.0-29.9 kg/m², n=321), and Obese BMI (≥30.0 kg/m², n=166). Demographic data, co-existing diseases, surgical techniques, cross-clamp times, postoperative bleeding, ICU stay, and extubation times were recorded and compared across the groups. The bleeding index and the transfusion index were calculated and compared.

Results: Although the number of grafts used was the same for all groups, the cross-clamp and total operation times were significantly longer for obese patients. During the postoperative intensive care follow-up, intubation times were also much longer for obese patients. Similarly, the amount of postoperative drainage was statistically significantly higher in obese patients. On the other hand, it was observed that the “bleeding index” was significantly higher in patients with LBMI (p<0.001). When comparing blood products, it was found that fresh frozen plasma and erythrocyte suspension were used in significantly higher numbers in the OBMI group (p<0.001).

Conclusion: Obesity remains an independent risk factor in cardiac surgery. In light of the information obtained in our current study, the bleeding index in patients with low BMI (BMI<18.5 kg/m²) is much higher than in obese patients. Patients with lower BMI require more blood transfusions than obese patients, indicating that low BMI is also a risk factor in cardiac surgery.

Keywords: Cardiac surgery, low body mass index, obesity

Obesity can cause many diseases and leads to poor prognosis in the course of many diseases. According to WHO sources, in 2022, one in every eight people in the world was living with obesity. Obesity is known to be an essential risk factor, especially for cardiovascular diseases (1).

While obesity causes diseases that require cardiac surgery, some publications report conflicting results stating that obese patients undergoing cardiac surgery have a better prognosis than normal-weight patients (2,3). Some researchers have concluded that obesity positively affects cardiac surgery and have termed this phenomenon the “obesity paradox” (4,5). On the other hand, some researchers, unlike others, have concluded that obesity is a significant risk factor for cardiac surgery and that there is no obesity paradox (6).

However, a lower-than-normal BMI may also have negative consequences and be an important risk factor in cardiac surgery patients. Although there are many articles in the literature on obesity, there are no detailed studies on low BMI, especially in cardiac surgery. We wonder whether an extremely low body mass index is a risk factor, similar to obesity, in cardiac surgery patients. For this purpose, we aimed to investigate whether the obesity paradox exists in cardiac surgery or whether low BMI is a risk factor, and to elucidate the possible reasons.

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Table 1. Demographic data of the patients

	Low BMI (n=72)	Normal BMI (n=228)	Overweight BMI (n=321)	Obese BMI (n=166)	r value
Age	63.01 (\pm 12.1)	63.37 (\pm 10.9)	61.84 (\pm 10.4)	62.14 (\pm 11.1)	0.333
F/M	27/45	92/135	126/195	74/92	0.665
BMI	18.03 (\pm 0.49)	23.47 (\pm 0.89)	27.36 (\pm 1.27)	33.26 (\pm 2.47)	N.A.
Diabetes	18 (25.0%)	53 (23.2%)	100 (31.2%)	59 (35.5%)	0.039
COPD	22 (30.5%)	42 (18.4%)	67 (20.9%)	60 (36.1%)	<0.001
PAD	11 (15.3%)	21 (9.2%)	22 (6.9%)	24 (14.5%)	0.022
Renal disease					
Smoking	25 (34.7%)	102 (44.7%)	139 (43.3%)	59 (35.7%)	0.158
Hypertension	34 (42.7%)	103 (45.2%)	136 (42.4)	78 (44.6%)	0.738
LVEF	45.70 (\pm 9.2)	45.78 (\pm 9.1)	46.10 (\pm 9.4)	46.24 (\pm 9.3)	0.948

COPD: Chronic obstructive pulmonary disease; PAD: Peripheral artery disease; LVEF: Left ventricular ejection fraction. N.A.: Not applicable.

PATIENTS AND METHODS

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Etlik City Hospital. We retrospectively examined the data of 786 patients who underwent elective isolated coronary artery bypass surgery in our clinic in the last two years. Patients who underwent different surgical interventions, such as ascending aortic and heart valve surgery, were excluded from this study to explore a more isolated patient group. Patients who were receiving dual antiplatelet therapy in the last five days before the surgery and patients who were loaded with these medications due to the diagnosis of acute coronary syndrome were also excluded from the study because they may affect the results regarding bleeding. Patients included in the study within these criteria were divided into four groups according to their body mass index (BMI). Those with BMI < 18.5 kg/m² were considered as the low BMI group (LBMI, n=72), those with 18.5 kg/m² ≤ BMI < 24.9 kg/m² were considered as the normal BMI group (NBMI, n=228), those with 25.0 kg/m² ≤ BMI < 29.9 kg/m² were considered as the overweight BMI group (OWBMI, n=321), and those with 30.0 kg/m² ≤ BMI were considered as the obese BMI group (OBMI, n=166). The preoperative demographic data of the patients are shown in Table 1. Operative and postoperative data are given in Table 2. Demographic data, co-existing diseases, surgical techniques, cross-clamp times, postoperative bleeding, ICU stay, and extubation times were recorded and compared across the groups. One of the critical calculations involved dividing the amount of bleeding by BMI to determine “the bleeding index.” Additionally, the blood products administered to patients due to bleeding were recorded, and “the transfusion index” was determined by dividing the average number of erythrocyte suspensions given by BMI.

Statistical Analysis

Categorical data were shown as percentages and continuous data were provided as mean \pm SD. A χ^2 test was used to test categorical variables. The allocation of the variables was normal. Variables were compared using one-way ANOVA and a Tukey HSD test as a post hoc test. A p-value less than 0.05 was considered statistically significant. The Bonferroni correction was applied for multiple comparisons. Data analysis was performed using the SPSS (version 27.0.1.0; SPSS Inc, Chicago, IL) statistical package for Mac.

RESULTS

This study included 786 patients; the patients' demographic data are shown in Table 1. No statistically significant difference was observed between the groups regarding age and gender. While diabetes mellitus (DM) and chronic obstructive pulmonary disease (COPD) were observed to be statistically significantly higher in obese patients (p=0.039 and p<0.001, respectively), peripheral artery disease was significantly higher in the low BMI group (p=0.022). Left ventricle ejection fraction, smoking, and hypertension results were similar in the four groups. There were also significant differences between operative and postoperative data. Off-pump surgery rates in all groups were between 14.5-18.7%, and there was no statistically significant difference in terms of surgical techniques applied between the groups (Table 2). Although there was no difference in the number of grafts used for all groups, cross-clamp and total operation times were significantly longer in obese patients. During postoperative intensive care follow-up, intubation times were significantly longer in obese patients (Table 2). Similarly, the amount of postoperative drainage was much higher in obese patients (p<0.001). The amount of drainage was calculated to be statistically significantly higher in obese patients. Conversely, it was observed that the “bleeding index” obtained by dividing the bleeding amount by BMI was statistically significantly higher in patients with LBMI. When the blood products were compared, it was observed that fresh frozen plasma and erythrocyte suspension were used in significantly higher numbers in the OBMI group (p<0.001). Finally, when the mortality rates were evaluated, it was observed that there was no statistically significant difference in the comparison of the four groups.

DISCUSSION

Whether obesity is a risk factor for cardiac surgery has been the subject of many studies for years. While at first glance, the operative and postoperative data of obese patients were expected to be poor, many studies conducted on obese patients showed that the results were much better, and they termed this phenomenon “the obesity paradox” (4). After the emergence of this idea, many articles were written on this subject, and it was reported in these articles that such a paradox did not exist and that the results were worse

Table 2. Operative and postoperative findings of the patients.

	Low BMI (n=72)	Normal BMI (n=228)	Overweight BMI (n=321)	Obese BMI (n=166)	r value
Off-pump	12 (16.7%)	33 (14.5%)	65 (20.2%)	31 (18.7%)	0.327
Operation time (min)	107.5 (±14.2)	117.4 (±11.2)	119.2 (±10.5)	123.5 (±10.7)	<0.001
X-clamp time (min)	30.4 n=60 (±5.4)	30.0 n=197 (±6.1)	31.0 n=256 (±5.9)	32.5 n=136 (±6.2)	0.021
CPB time (min)	55.2 (±8.7)	54.5 (±9.6)	56.8 (±9.6)	57.1 (±8.9)	0.505
Number of grafts	3.3 (±0.8)	3.4 (±0.8)	3.3 (±0.9)	3.4 (±0.7)	0.200
Duration of intubation (h)	6.1 (±1.3)	6.9 (±1.0)	7.1 (±1.1)	8.5 (±2.1)	<0.001
Total drainage (ml)	493 (±100.4)	491 (±128.4)	521 (±134.5)	611 (±144.8)	<0.001
Drainage/BMI (Bleeding index)	23.6 (±4.9)	19.8 (±5.4)	18.1 (±5.2)	15.08 (±4.7)	<0.001
Need for inotropic agent	16 (22.2%)	46 (20.2%)	66 (20.6%)	58 (34.6%)	0.002
IABP	4 (5.6%)	5 (2.2%)	7 (3.0%)	5 (3.0%)	0.425
Transfused blood products					
• FFP	0.50 (±0.5)	0.56 (±0.5)	0.78 (±0.6)	0.89 (±0.7)	<0.001
• ES	1.87 (±0.6)	2.04 (±0.6)	2.67 (±0.7)	2.89 (±0.7)	<0.001
ES/BMI (transfusion index)	0.103	0.086	0.097	0.086	<0.001
Surgical revision	1 (1.4%)	2 (0.9%)	3 (0.9%)	3 (1.8%)	0.818
ICU stay	1.9 (±0.5)	2.0 (±0.5)	1.9 (±0.6)	2.2 (±0.7)	<0.001
Hospital	5 (±1.1)	5.1 (±0.9)	5.2 (±1.1)	5.9 (±1.2)	<0.001
In hospital mortality	1 (1.4%)	0 (0%)	5 (1.6%)	2 (1.2%)	0.332

CPB: Cardiopulmonary bypass, IABP: Intra-aortic balloon pump, FFP: Fresh frozen plasma, ES: Erythrocyte suspension, ICU: Intensive care unit.

in obese patients (7,8). While the issue of obesity has been examined many times in scientific research, the situation of patients with lower-than-normal BMI has been somewhat overlooked, especially in cardiac surgery. In this study, we examined the consequences of low BMI, as well as obesity, in terms of patient outcomes in a more limited group of patients who underwent isolated coronary bypass surgery. In a recent UK-wide meta-analysis, it was observed that overweight and obese patients had less in-hospital mortality than normal-weight patients (4). In the same study, it was also observed that mortality was higher in underweight patients than in normal-weight patients. If we look at the results of this research from another perspective, it means that having a normal BMI is a risk factor for heart surgery.

Although the number of grafts was similar in our study, cross-clamp and operation times were significantly longer in the obese patient group (Table 2). We can explain this as technical difficulties due to the excess fatty tissue in both the myocardial and mediastinal regions. In obese patients, due to the excess of environmental fat tissues, there may be a partial slowdown at every stage, from sternotomy to bleeding control at the end of the surgery.

One of the most interesting issues in our research was the results regarding the amount of postoperative bleeding. As obesity increased, the amount of bleeding increased statistically significantly. On the other hand, when we adjusted the total bleeding amount to BMI, we calculated a kind of "bleeding index." We found the bleeding index was highest in patients with low BMI (23.6±4.9 ml/BMI in LBMI vs. 15.08±4.7 ml/BMI in OBMI, p<0.001). Thanks to this calculation, it was observed that patients with low BMI had much higher bleeding rates than obese patients. The first question

that comes to mind when we access bleeding index data is whether there was a statistical difference in blood transfusions between patient groups. According to the bleeding index, it was expected that OBMI patients would need less blood transfusion than LBMI patients. However, the result was the opposite: While OBMI patients were transfused an average of 2.89 units of erythrocyte suspension, it was calculated that 1.87 units of erythrocyte suspension were transfused to LBMI patients (p<0.001).

Similarly, we calculated "the transfusion index" by proportioning the amount of transfused ES to BMI. This rate was higher in the LBMI patient group than in OBMI patients (0.103 ES/BMI and 0.086 ES/BMI, respectively, p<0.001). The conclusion we reached after all these calculations is that LBMI patients are exposed to more bleeding and require more blood product transfusion.

Although Stamou et al. (5) stated that the results were better in obese patients, it is noteworthy that the obese patients in their study were younger than the other patients. In a recently published article, Wu et al. (7) reported that in patients who underwent robotic cardiac surgery, the intensive care period was prolonged, and postoperative kidney damage was higher in the obese patient group. Thus, they concluded that the obesity paradox did not exist. In our study, similar to the results of Wu et al. (7), the duration of intubation, ICU stay, and hospital stay in the OBMI patient group was significantly longer than that of all other groups. Apart from all these, postoperative surgical revision and even mortality rates were similar in all groups.

While discussions about the obesity paradox continue, Samuels et al. (9) reported their concerns about giving the wrong message to the public that obesity provides better results in terms of heart health.

It has been shown that obesity, especially severe obesity, increases cardiovascular, diabetic, cancer, and stroke risks and shortens life expectancy. While most publications investigate whether obesity is a risk factor for cardiac surgery, the issue of whether low BMI is also a risk factor has been somewhat neglected. In a recent study, Shi et al. (10) examined kidney damage in cardiac surgery and reported that low BMI was an important risk factor as high BMI. Reis et al. (11) also reported that low BMI was a risk factor according to early results after cardiac surgery. van Venrooij et al. (12) showed that patients with low BMI had more frequent lung infections in the postoperative period and that mortality was much higher in this patient group.

CONCLUSION

There are ongoing debates in the literature about whether there is an obesity paradox. However, recent publications indicate no such paradox and that obesity is still an important and independent risk factor in cardiac surgery. On the other hand, in light of the information we obtained in our current study, the bleeding index obtained by dividing the amount of bleeding by BMI in patients with low BMI (BMI<18.5 kg/m²) is much higher than in obese patients. Patients with lower BMI require more blood transfusions than obese patients, indicating that low BMI is also a risk factor. Prospective randomized studies are needed to better elucidate this situation.

Ethics Committee Approval: This study was conducted with the permission of the Ankara Etlik City Hospital Local Ethics Committee (decision no: AEŞH-BADEK-2024-300, date: 03.04.2024).

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Organization of Emergency Medical Services After an Earthquake: The Case of Adiyaman, Türkiye

ABSTRACT

Objectives: In this manuscript, we aimed the explanation of health organization of Adiyaman Province after the 5 day of earthquake.

Methods: The data presented herein were compiled from the experiences of emergency medicine specialists sent to Adiyaman Province by the Ankara Emergency Medical Services (EMS) Administration. We discuss the personnel and administrative management of Adiyaman Training and Research Hospital, the working system of Adiyaman EMS, patient transport to other provinces by land ambulances and air ambulances, establishment of tent hospitals, medical care point management, and environmental safety.

Results: After the earthquake, a total of 396 patients were transferred from Adiyaman to other provinces by aircraft. The average age of the patients was found 32.8 ± 17.6 years. The most common diagnosis was general body injuries. Patients were most frequently transferred to Ankara. The most commonly used aircraft for transportation was the Cargo Aircraft of the Turkish Armed Forces.

Conclusion: It should be considered that local administrators are also disaster victims. The fact that teams from other provinces undertake health management in the disaster area will facilitate the process. EMS management in the acute period is particularly important in terms of saving the lives of earthquake victims and preventing disabilities.

Keywords: Disaster, earthquake, Türkiye

On 06.02.2023, at 04:17, an earthquake of magnitude 7.7 occurred in the Pazarcık District of Kahramanmaraş Province. Before the area affected by the earthquake and the severity of the destruction were fully understood, a second major earthquake of 7.7 magnitude occurred in the Elbistan District of Kahramanmaraş Province at 13:24. The earthquake affected an area of 108,812 square kilometers covering 11 provinces (Kahramanmaraş, Hatay, Adiyaman, Gaziantep, Malatya, Kilis, Diyarbakır, Adana, Osmaniye, Şanlıurfa, and Elazığ) in Eastern and Southeastern Anatolia (1). A total of 11,020 aftershocks occurred (2). On 20.02.2023, an earthquake of 6.4 magnitude occurred in the Defne District of Hatay Province at 20:04 (3). The Ministry of Environment, Urbanization, and Climate Change conducted damage evaluation of 3,273,605 independent units in 830,783 buildings. In these evaluations, it was determined that 384,545 independent units in 105,794 buildings were heavily damaged and destroyed, and it was concluded that they should be demolished immediately. It was also determined that 133,575 independent units in 24,464 buildings were moderately damaged (4). According to the official statistics announced by the Disaster and Emergency Management Authority of the Ministry of the Interior on 23.03.2023, 50,096 people died and 107,204 people were injured in the earthquakes (5). It is known that the earthquakes also caused thousands of deaths and injuries in Syria (6).

The Republic of Türkiye declared a level 4 alarm, which is the highest emergency level and includes calls for help from international organizations and countries in emergencies such as natural disasters and epidemics for the earthquake region (7). In addition, while a state of emergency was declared for 3 months in 10 provinces affected by the earthquakes, the World Health Organization declared a level 3 emergency for the earthquakes that shook Türkiye (8).

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Table 1. Demographic characteristics of the patients transported from Adiyaman district

	n=396	%
Gender		
Men	197	49.7
Women	199	50.3
Age (Years)*		
All	32.8±17.6	31.0 (0.5-83.0)
Women	32.2±17.0	30.0 (1.5-65.0)
Men	33.4±18.2	31.0 (0.5-83.0)
Diagnostic Groups		
General Body Injuries	229	57.8
Lower Extremity Injuries	74	18.7
<i>Amputations</i>	11	2.8
Upper Extremity Injuries	16	4.0
<i>Amputations</i>	6	1.5
Crush Syndromes	20	5.1
Vertebral Fractures	14	3.5
Head Traumas	12	3.0
Pelvic Fractures	7	1.8
Chest Traumas	5	1.3
Pregnancies	2	0.5

*: Mean ± SD

In this manuscript, we aimed the explanation of health organization of Adiyaman Province after the 5 days of earthquake.

METHODS

The data presented herein were compiled from the experiences of emergency medicine specialists sent to Adiyaman Province by the Ankara Emergency Medical Services (EMS) Administration. We discuss the personnel and administrative management of Adiyaman Training and Research Hospital, the working system of Adiyaman EMS, patient transport to other provinces by land ambulances and air ambulances, establishment of tent hospitals, medical care point management, and environmental safety.

Findings

After the earthquake, a total of 396 patients were transferred from Adiyaman to other provinces by aircraft. The average age of the patients was found 32.8 ± 17.6 years. The most common diagnosis was general body injures (Table 1). Patients were most frequently transferred to Ankara. The most commonly used aircraft for transportation was the Cargo Aircraft of the Turkish Armed Forces (Table 2).

Day 1

After receiving the news of the earthquake at around 04.30 on the morning of 6 February, the provinces affected were determined at the meeting held at the Ministry of Health. Ankara EMS teams were assigned to Adiyaman Province. Two CN-235 CASA type ambulance aircraft belonging to the General Staff took off from Etimesgut Military Airport with a health team of 15 professionals (2 emergency

Table 2. Diagnoses of transferred patients, transferred provinces and aircraft types

	n	%
Province of the receiver hospital		
Ankara	275	69.4
İstanbul	58	14.6
İzmir	49	12.4
Malatya	12	3.0
Adana	1	0.3
Diyarbakır	1	0.3
Type of the aircraft		
Jet belonging to the Presidency of Turkey	22	5.6
Jet belonging to the Turkish Ministry of Health	33	8.3
Military Helicopter (Skorsky)	11	2.8
Aircraft Ambulance of the Turkish Armed Forces	71	17.9
Cargo Aircraft of the Turkish Armed Forces	259	65.4

medicine specialists, 3 general practitioners, and 10 paramedics) working in Ankara EMS. The aircraft could not land at Adiyaman Airport due to adverse weather conditions and landed at Adana İncirlik Military Airport. With the improvement in weather conditions, the aircraft departed at around 12:00 and reached Adiyaman Airport at around 13:00 (Figure 1A). The team was in Adiyaman during the second earthquake that took place in Elbistan in Kahramanmaraş Province.

When the team reached Adiyaman, there were many injured people in the hospital emergency room (on stretchers, in corridors, waiting chairs, and chairs). Physicians and nurses in the emergency room were trying to give medical attention to the injured. To determine the situation, the team met with the Provincial Health Director and the Chief of the Hospital. There was a shortage of medical personnel. There was no news from most of the hospital staff. Due to the large number of patients, intervention was difficult. There were patients in intensive care units and wards other than the emergency room. It was determined that there might be a gas leak in the operating room and therefore it was unsuitable for use. When the building was evaluated quickly, it was observed that the ceiling of the main entrance area had collapsed, and the walls were partially cracked, but the hospital was in good condition in general. Later, engineers from the Ministry of Health visited the hospital and confirmed that the building was in good condition.

Due to the high number of patients and the lack of health personnel, it was decided to transport the patients after their first intervention. The COVID polyclinic, a prefabricated building right next to the hospital emergency room, was transformed into a crisis center, and a provincial coordination desk was created there. The first patient transport was carried out by 2 ambulance aircraft (each had 6 stretchers) available at Adiyaman Airport. These aircraft were fully equipped air ambulances and could carry 6 intensive care patients at a time (Figure 1A). Then patients started to be transported to the surrounding provinces (Diyarbakır, Urfa, Gaziantep, and Elazığ) that were not affected by the earthquake or were less affected. Patient transport was started immediately



Figure 1. (A) CN-235 CASA type ambulance aircraft. (B) A C130 cargo plane which has 72 stretchers. (C) Jet engine ambulance planes. (D) Helicopter ambulance.

using the land ambulances available in Adiyaman. Then ambulances from neighboring provinces came to Adiyaman and took part in patient transport.

The team contacted the General Staff and requested more air ambulances so that the patients could be transported faster. Cargo planes were converted into ambulance planes by the General Staff. A C130 cargo plane (Figure 1B) was sent to Adiyaman Airport by the Air Operations Center of the Ministry of Health. The first C130 cargo plane landed at Adiyaman Airport at 17:30. This aircraft was inspected by our ambulance crews and it was concluded that although it had 72 stretchers, it would be appropriate to load 50 patients since medical intervention would be difficult because some stretchers were above head height. It was decided to transport patients who did not need intensive and urgent care on this plane (Picture 1a or 2). Working with the Adiyaman EMS Administration, the patients were sent to Adiyaman Airport in the existing ambulances in the province and loaded onto the C130 cargo plane. Then 3 jet engine ambulance planes (Figure 1C - one

with 4 stretchers, one with 2 stretcher ambulances, and one with a single stretcher) belonging to the Ministry of Health were sent to Adiyaman. These aircraft ambulances were fully equipped and were capable of transporting patients in need of critical care. After that, patient transport continued with CN235-CASA and C130 cargo planes, and ambulance planes belonging to the Ministry of Health.

The 1-1-2 Emergency Call Center building in Adiyaman was unusable due to damage. Therefore, emergency calls in Adiyaman were routed to the EMS Call Center in Eskişehir Province, which was not affected by the earthquake. Emergency requests received by Eskişehir EMS Call Center were sent to the EMS teams in Adiyaman by calling their mobile phones.

Support was requested by contacting the Ministry of Health in order to eliminate the health personnel shortage. Towards evening, many health personnel were sent to the region to help. These personnel included physicians from all branches such as general

practitioners, emergency medicine specialists, anesthesiologists, internists, orthopedists, general surgeons, thoracic surgeons, and cardiovascular surgeons. In addition, many nurses were assigned to the region. Many EMS and National Medical Rescue teams were deployed to Adiyaman.

The hospital was quite dirty due to dust from the walls and roofs that cracked during the earthquake. First, the operating room and intensive care units were cleaned by the cleaning staff. In the evening, as a result of the work of the technical teams, the gas problem in the operating room was solved and the operating room became usable.

Day 2

On the second day after the earthquake, new medical personnel continued to arrive in the region. It was decided to create a new organizational chart because the hospital administrators were also victims of the disaster. Accordingly, a new provincial coordinator, hospital coordinator, and hospital chief physician were assigned from the team. In addition, an administrative financial affairs manager, health care services manager, coordination officer, transport manager, intensive care manager, and emergency supervisors were appointed. A communication system was established between the intensive care unit, emergency room, wards, and crisis center. Thanks to the emergency room-intensive care unit-wards communication, the hospitalization of patients started. The hospital-crisis center communication also eased the transport of patients. The intensive care unit supervisor evaluated the transport requests from all intensive care units, determined the patients who needed to be transported first, and forwarded them to the transport center. In this way, triage was applied for transport. After determining the patients to be transported, it was determined which plane was suitable according to the conditions of the patients, and their transport was facilitated with that plane.

On the second day, the crisis coordination center started to be used more effectively. A human resources unit was established within the crisis coordination center to keep track of the personnel assigned to Adiyaman and to determine their duties. A transport coordination unit was established and the patients to be transported to other provinces were registered by this unit, and the transportation of patients by land or air ambulance was provided by this unit. In coordination with Adiyaman EMS Administration, ambulances in the province were grouped as 'transport ambulances' and 'emergency aid ambulances'. The transport ambulances were parked in the garden of the hospital, and they constantly transported patients to air ambulances and other provinces. Emergency ambulances were assigned to respond to earthquake victims when they were removed from the rubble.

Picture Archiving and Communication Systems (PACS) were activated in the hospital, and after CT scans were performed on patients, images were made to appear on the physicians' computers instead of the tomography computers. In this way, the crowding in the tomography unit was eliminated. The need for medicines and materials in the hospital was met by sourcing them from other provinces that were not affected by the earthquake. The hospital parking lot was converted into a warehouse to store incoming aid such as medicines, materials, food, and clothing. While pharmacists categorized drugs, warehouse managers categorized food

and clothing materials. The dialysis unit was activated and patients with crush syndrome started to be admitted.

To solve the resting needs of the personnel, they were accommodated in the crisis coordination center. In addition, 2 large sheltering tents were set up in the garden of the hospital for the accommodation needs of the personnel. In addition, tent cities started to be established for the shelter needs of the earthquake victims. Two field hospitals were established in Adiyaman (Figure 2A). These were fully equipped hospitals with operating rooms and intensive care units. While one hospital was planned as an adult hospital, the other hospital was planned as a gynecology, maternity, and children's hospital.

On the 2nd day, patient transfers continued with the C130 cargo plane, CASA ambulance plane, and ambulance planes belonging to the Ministry of Health. In addition, jets belonging to the Presidency provided the transport of patients who did not need emergency intervention.

Tent health facilities were established at 17 medical care points in order to provide health services to patients staying in tent cities and container cities (Figure 2B). A physician and 4 health workers were employed in these tents. Medical care points had medical devices and drugs that could be used to respond to emergencies. In addition, in these medical care tents, there were drugs to be used to treat the acute diseases of the earthquake victims and the drugs they needed for their existing chronic diseases. These drugs were provided to all patients in need.

Day 3

On the 3rd day, the numbers of personnel (doctors, nurses, paramedics, and National Medical Rescue Team personnel) and ambulances became sufficient. The radio communication system was activated and communication with the ambulances over the radio began.

Day 4

For infection control, 4 infection physicians and 5 infection nurses arrived at the hospital. Precautions were implemented based on their suggestions about intensive care units, operating rooms, and patients. Angiography began and patient admission started.

Day 5

Critically ill patients who were rescued from the wreckage and required urgent intervention were transported to neighboring cities by helicopter ambulances (Figure 1D). Water safety and environmental safety were ensured by monitoring of the water by public health teams. Malignant patients were transported to various hospitals in the province of Urfa, in consultation with the Urfa Provincial Health Directorate for chemotherapy treatments.

From the 5th day, it was observed that the personnel were both psychologically and physically worn out. Therefore, they were replaced by other personnel. The minimum number of personnel needed was determined, and a request for staff was made to the Ministry of Health. An aircraft was allocated by Turkish Airlines for the transfer of personnel and as of the 6th day personnel replacement began.

DISCUSSION

In the 7.0 magnitude earthquake that occurred in Haiti in 2010, 316,000 people were killed and 300,000 more were injured. After



Figure 2. (A) Field hospitals were established in Adiyaman. (B) Medical care points.

the earthquake, an international call for help was made and aid teams from abroad arrived in Haiti (9). In addition, many volunteers went to the region and helped the injured (10).

Many people were affected by the 7.8 magnitude earthquake that occurred in Nepal in 2015. It was reported that in the first aid center during the Nepal earthquake, there were patients on stretchers and on the ground, similar to the situation we experienced. In Nepal, as in our country, patients were transported by helicopters, but due to the large number, the patients were triaged (11).

In another study conducted on the earthquake in Türkiye, it was reported that patients were transported both by land and air not only from Adiyaman but also from other provinces affected by the earthquake (12). It has also been reported in other studies that medical aid was delivered to the disaster area in a short time by volunteer health workers (13).

CONCLUSION

It should be considered that local administrators are also disaster victims. The fact that teams from other provinces undertake

health management in the disaster area will facilitate the process. EMS management in the acute period is particularly important in terms of saving the lives of earthquake victims and preventing disabilities. In addition, we recommend that primary health care services, infection control, and treatment of chronic diseases throughout the province should not be ignored after the disaster.

Ethics Committee Approval: This study was conducted with the permission of the Ankara Bilkent City Hospital Local Ethics Committee (decision no: E2-23-4180, date: 26.05.2023).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Nt-proBNP in Pediatric Cardiac Surgery: A Correlation Study with the Postoperative Course and Morbidity

ABSTRACT

Objectives: B-type natriuretic peptides, synthesized by cardiac myocytes in response to increased ventricular wall stress, are secreted as prohormones and cleaved into biologically active hormone (BNP) and the inactive N-terminal fragment, known as Nt-proBNP. They possess diuretic, natriuretic, and vasodilatory effects. Recently, B-type natriuretic peptides have been identified as valuable parameters in detecting acute and chronic left ventricular dysfunction. This study aims to investigate the relationship between preoperative and postoperative Nt-proBNP levels, the postoperative course, and morbidity in congenital cardiac surgery patients.

Methods: Thirty-one patients, aged between 3 months and 16 years, undergoing open-heart surgery with cardiopulmonary bypass due to congenital heart disease, were examined. The patients had left-to-right shunt lesions or stenosis in the ventricular outflow tract. Patients were divided into two groups based on the need for high-dose (>5mcg/kg/min) inotropic therapy during the postoperative period: those requiring high-dose inotropic support and those requiring low-dose or no inotropic support. Nt-proBNP levels were measured preoperatively (T0), at 2 hours postoperatively (T1), and 24 hours postoperatively (T2). Additionally, postoperative inotropic support, cardiopulmonary bypass, cross-clamp, and mechanical ventilation durations were recorded.

Results: There was a statistically significant difference in cross-clamp durations between the groups. Statistically significant differences were also observed in the duration of inotropic therapy, mechanical ventilation, and length of stay in the intensive care unit. Our study revealed a correlation between the dose and duration of inotropic therapy administered during the postoperative period and Nt-proBNP levels, with patients requiring high-dose inotropic support showing a mean serum level of 1009.10 ± 1345.43 pg/ml. This finding suggests an association between elevated Nt-proBNP levels and increased postoperative inotropic requirements.

Conclusion: In the context of adult heart illnesses and cardiac surgery, serum Nt-proBNP levels are a biochemical marker that can effectively assess low functional capability and prognosis. Elevated levels of preoperative serum Nt-proBNP in individuals having cardiac surgery for congenital heart abnormalities offer crucial insights into myocardial function and the efficacy of medicinal interventions.

Keywords: Congenital cardiac surgery, inotrope, natriuretic peptide

Congenital heart diseases (CHDs) are conditions resulting from defects in the development of the heart and major blood vessels during fetal development. They are observed in approximately 0.8–1% of live births, with 1,035,795 live births recorded in Turkey in 2022 (1). In light of these data, it is estimated that approximately 10,000 babies are born with CHDs each year, and about one-fourth of them require surgical intervention within the first year of life (2). Moreover, the postoperative mortality rate in these patients exceeds 10% (2). Changes in cardiac output can rapidly occur in patients with CHDs, either in the preoperative period or, more commonly, in the postoperative period. Low cardiac output syndrome (LCOS) is a clinical syndrome characterized by a cardiac index below $2L/min/m^2$, resulting in inadequate oxygen delivery to tissues and terminal organs and failure to meet metabolic demands. LCOS significantly increases the risk of multiorgan dysfunction and is highly associated with mortality. The incidence of LCOS after surgery in children with CHDs ranges from 25% to 60%, typically manifesting 6 to 18 hours postoperatively, with a mortality rate exceeding 20% (3).

A variety of cardiac biomarkers have been reported in adults with heart failure. Since the measurability of natriuretic peptides in 2002, they have become essential for diagnos-

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Table 1. Diagnostic distribution of patients included in the study

Diagnosis	Number	Rate (%)
Atrial Septal Defect	4	12.9
Atrioventricular septal defect, Infundibular Pulmonary Stenosis	1	3.2
Tetralogy of Fallot	12	38.7
Partial Pulmonary Venous Return Anomaly	2	6.5
Transposition of the Great Artery Pulmonary Stenosis	1	3.2
Ventricular Septal Defect	11	35.5

tic and prognostic monitoring in patients with cardiac problems. The early elevation of BNP levels before the onset of heart failure symptoms enhances this peptide's diagnostic sensitivity and importance (4). Elevated BNP levels are observed not only in patients with heart failure due to systolic dysfunction but also in those with heart failure due to diastolic dysfunction (5). However, studies on biomarkers predicting preoperative and postoperative mortality and morbidity in children with CHDs are limited.

The aim of this study is to investigate the utility of serially measured Nt-proBNP levels in serum as a significant biomarker that predicts the early development of low cardiac output syndrome in congenital heart disease, thus contributing to the prevention of mortality and morbidity.

METHODS

After obtaining the approval of the hospital's education and planning committee and ethics committee, a prospective, randomized study was conducted at Dr. Sami Ulus Maternity and Child Health Research and Training Hospital in accordance with the Universal Code of Ethics contained in the Declaration of Helsinki. A total of 31 patients aged between 3 months and 16 years who underwent open-heart surgery with cardiopulmonary bypass due to congenital heart disease were included in the study. Patients with left-to-right shunt lesions and stenosis in the ventricular outflow tract were included in the study group. Patients who underwent single ventricle repair, had previously undergone palliative surgery, had residual defects, or received mechanical support therapy were excluded from the study.

Patients were categorized into two groups based on their postoperative need for inotropic medication: Patients in Group 1 needed high-dose inotropic support, which meant they needed at least 10 mcg/kg/min of dopamine or dobutamine, 0.1 mcg/kg/min of epinephrine or norepinephrine, or 0.5 mcg/kg/min of milrinone. In contrast, Group 2 consisted of patients not requiring inotropic therapy or receiving low-dose inotropic medication (<5 mcg/kg/min).

All patients discontinued oral intake 8 hours before surgery, and premedication was administered using 0.1 mg/kg midazolam 15 minutes before anesthesia induction. Patients were routinely monitored with two-lead ECG (DII-V5), pulse oximetry, and non-invasive blood pressure. Anesthesia induction was achieved with 15 mcg/kg fentanyl, 0.2–0.3 mg/kg midazolam, and 0.1mg/kg vecuronium. All patients were ventilated with $FiO_2 = 1.0$, tidal volume (TV) set at 15–20 ml/kg, respiratory rate adjusted according to age to maintain $PaCO_2$ at 35 mmHg, and an inspiration/expiration ratio of 1:2. Radial artery cannulation and right atrium catheterization

were performed using the Seldinger technique. Anesthesia maintenance included additional doses of 2 µcg/kg fentanyl, 0.1 mg/kg midazolam, and 0.05 mg/kg vecuronium as needed. Sevoflurane, at approximately 1 MAC, was added if necessary. Patients were cooled to 28–32°C according to their cardiac pathologies. Cardiac arrest was induced with antegrade hypothermic crystalloid cardioplegia, and corrective surgical procedures were performed under cardiopulmonary bypass.

All patients underwent preoperative transthoracic echocardiography to record their pathologies, and Nt-proBNP blood levels were measured one day before surgery (T0). Central venous pressure (CVP), heart rate (HR), systolic arterial blood pressure (SAB), diastolic arterial blood pressure (DAB), mean arterial blood pressure (MAB), postoperative inotropic support therapy durations and doses, and arterial blood gas samples were recorded after anesthesia induction.

For Nt-proBNP measurements, 3ml of venous blood was collected into EDTA-containing Lavender Vacutainer tubes 24 hours before surgery. The plasma was separated by centrifugation at 1600rpm for 15 minutes at +4°C and stored at -70°C in polypropylene tubes. Hemodynamic data, blood gas samples, and Nt-proBNP values were sampled again at 2 hours (T1) and 24 hours (T2) postoperatively. Postoperative inotropic therapy requirements and durations, cardiopulmonary bypass times (CPBT), cross-clamp (CC) times, mechanical ventilation times (MVT), and intensive care unit (ICU) stay durations were recorded. Plasma Nt-proBNP measurements were performed using the chemiluminescence method with Roche Diagnostic's Nt-proBNP kit on Elecsys 2010. The manufacturer's reference ranges for Nt-proBNP were accepted as 0–100 pg/mL for males and 0–150 pg/mL for females.

Statistical Analysis

Data were analyzed using the SPSS for Windows 22 statistical package. Comparisons were made using Student's t-test and Mann-Whitney U test. Pearson's correlation analysis was applied for correlation analysis, and $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the 31 patients included in the study was 5.87 ± 4.02 years (65% male, 35% female). The diagnostic distribution of patients is shown in Table 1.

Statistically significant differences were found in right ventricular pressure when examining preoperative hemodynamic data and Nt-proBNP levels between the two groups ($p < 0.05$). There were no statistically significant differences in left ventricular pressure,

Table 2. Preoperative hemodynamic data and Nt-proBNP level

	Shunt Lesion	Stenosis Lesion	Sensitivity
Right Ventricular Pressure	46.59±21.05	98.57±14.92	p<0.01
Left Ventricular Pressure	103.76±15.35	97.79±14.76	NS
Mean Pulmonary Artery Pressure	29.76±9.80		NS
Systemic/Pulmonary Flow Ratio	2.52±1.18		NS
Preoperative Nt-ProBNP Level	39.29±30.42	37.92±62.25	NS

NS: No significant difference

Table 3. Operative and postoperative data of the groups

	Group I	Group II	p
Cardiopulmonary bypass duration	51.62±26.72	81.40±48.00	NS
Cross-clamp duration	33.12±22.12	54.00±32.01	p<0.05
Duration of inotropic treatment	22.82±21.10	52.43±36.67	p<0.01
Duration of mechanical ventilation	6.25±6.52	14.93±11.55	p<0.01
Duration of Intensive Care	37.06±26.46	104.87±67.30	p<0.01

NS: No significant difference

Table 4. Postoperative 1st hour and 24th-hour NtproBNP levels of the groups

	Group I	Group II	p
Nt-ProBNP (1 st hour)	99.66±89.09	353.45±251.40	p<0.05
Nt-ProBNP (24 th hour)	144.41±128.94	1009.10±945.43	p<0.01

mean pulmonary artery pressure, systemic-pulmonary artery flow ratio, or preoperative Nt-proBNP levels (Table 2).

Statistically significant differences between the groups were found in cross-clamp times (p<0.05). There were statistically highly significant differences in the durations of inotropic therapy, mechanical ventilation, and ICU stay durations (p<0.01) (Table 3).

There was a statistically significant difference in postoperative 1-hour Nt-proBNP levels between the two groups (p<0.05), and a highly significant difference was observed in 24-hour Nt-proBNP levels (p<0.01) (Table 4).

There was a weakly significant positive correlation between the duration of inotropic therapy and serum Nt-proBNP levels at 1 hour postoperatively (r= 0.430, p<0.05). A moderately significant positive correlation was observed between the duration of inotropic therapy and serum Nt-proBNP levels at 24 hours postoperatively (r= 0.718, p<0.01).

There was a moderately significant positive correlation between serum Nt-proBNP levels at 24 hours postoperatively and mechanical ventilation duration (r= 0.619, p<0.01) and ICU stay duration (r= 0.484, p<0.01).

DISCUSSION

Type B natriuretic peptide (BNP) was first isolated from the porcine brain in 1988 by Sudoh and initially named brain natriuretic peptide (6). However, it was later shown that most circulating BNP originates from the ventricular myocardium. The brain natri-

uretic peptide exerts diuretic, natriuretic, and vasodilatory effects. It induces arterial and venous dilation by relaxing the vascular smooth muscle. It lowers peripheral vascular resistance, making the heart pump more blood and lowering filling and capillary wedge pressure (7). Unlike atrial natriuretic peptide, primarily produced in the atria and ventricles, BNP's main source is the ventricles. This renders BNP more sensitive and specific as a determinant of ventricular dysfunction compared to other natriuretic peptides (8).

After recognizing the heart's endocrine function, extensive studies have been conducted on the effects of natriuretic peptides, particularly in adult cardiac patients. Many studies have demonstrated that Nt-proBNP can be used in the diagnosis of symptomatic heart failure and correlates with the NYHA classification (9,10). In a study by Richards et al. (11), Nt-proBNP was shown to be an independent predictor of symptomatic heart failure and poor prognosis in patients with left ventricular systolic dysfunction following myocardial infarction. Lemos et al. (12) reported that detecting BNP serum levels in the early days following the onset of ischemic symptoms provides crucial information for risk stratification in acute coronary syndromes. Several studies have reported preoperative BNP plasma levels as determinants of postoperative left ventricular systolic function in patients undergoing coronary artery bypass surgery (13,14).

In a study conducted by Suda et al. (15) involving 59 patients with ventricular septal defects, a correlation was found between serum BNP levels and the left-to-right shunt, and a significant positive correlation was observed between the size of the shunt and serum

BNP levels ($r=0.45$, $p<0.01$). Kunii et al. (16) also demonstrated a positive correlation between serum BNP levels and the magnitude of left-to-right shunts ($r=0.45$, $p<0.01$), suggesting that plasma BNP levels could serve as a non-invasive method for determining the need for surgical treatment in left-to-right shunt lesions. However, in our study, although patients with left-to-right shunts had elevated serum Nt-proBNP levels in the preoperative period, no statistically significant correlation was found between the shunt magnitude and serum Nt-proBNP levels. This result was attributed to the preoperative cardiac evaluation of patients and the implementation of medical treatment to preserve myocardial function.

Our study observed a correlation between the dose and duration of inotropic therapy administered during the postoperative period and Nt-proBNP levels, with patients requiring high-dose inotropic support exhibiting an average serum level of 1009.10 ± 1345.43 pg/ml. This indicates that neurohumoral mechanisms increase endogenous compensatory activity to resolve myocardial dysfunction. Finding Nt-proBNP levels above 1000 pg/ml after surgery suggests a risk for low cardiac output syndrome, which means that the right treatment should be started right away.

CONCLUSION

In conclusion, serum Nt-proBNP levels, as a readily measurable biochemical parameter, can determine low functional capacity and prognosis, particularly in adult heart diseases and cardiac surgery. Preoperative serum Nt-proBNP levels in patients undergoing cardiac surgery due to congenital heart anomalies provide essential information about myocardial function and the effectiveness of medical treatment. Additionally, serum Nt-proBNP levels persistently elevated above 1000 pg/ml in the postoperative period serve as a warning sign for postoperative heart failure, low cardiac output, and residual defects, providing valuable insights into the effectiveness of cardiac support therapies.

Ethics Committee Approval: This study was conducted with the permission of the Ankara University, Faculty of Medicine Local Ethics Committee (decision no: 38-812, date: 24.01.2008).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Wilms Tumor Mimicking Renal Pelvis Hematoma in a Post-Traumatic Pediatric Patient: Case Report

ABSTRACT

Wilms' tumor (WT) is the most common renal tumor of childhood. Children with WT may present with a large, painless, abdominal mass and usually no constitutional symptoms. In our case, there were neither symptoms nor any physical examination findings that would lead us to WT. Herein, we report a 4-year-old male who presented to our clinic with concern for a traumatic lesion in abdomen. He was asymptomatic and had a small bruise on left upper quadrant. Ultrasound revealed a heterogeneous lesion which fills the renal pelvis. Renal pelvis hematoma and space-occupying lesions originating from the collecting system epithelium was considered as differential diagnoses. After kidney biopsy, the diagnosis of WT was confirmed. We present this case of WT to keep it in mind in the differential diagnosis of renal pelvis hematoma in a pediatric post-traumatic patient. We emphasise the importance of using multimodal approaches to make the correct diagnosis.

Keywords: Case report, post-traumatic patient, renal pelvis hematoma, Wilms tumor

Wilms' tumor (WT) is the most common renal tumor of childhood which influences nearly one child per 10,000 global under the age of 15 in one year (1). 80% of patients with WT are diagnosed between 1-5 years of age (2). Boys are generally diagnosed at a younger age than girls, while the frequency of WT is moderately higher in girls (3).

WT is a malignant embryonal renal tumor composed of variable amounts of embryonic renal elements (blastema, epithelium, and stroma) (2).

The most typical manifestation of WT is an asymptomatic abdominal mass. Abdominal pain, fever and microscopic hematuria are other common findings at diagnosis, while gross hematuria is rare (4).

In this case report, we report an unusual case in which a child presented with a clinical picture suggestive of a renal pelvis hematoma, however was instead found to have an intrapelvic WT extending to the proximal ureter.

CASE

A 4-year-old male patient was admitted to our clinic with a concern of traumatic lesion in the abdomen. It was learnt from his family that he fell on iron rods in a construction zone (Figure 1). On inspection, there was a small wound on the left upper quadrant (Figure 1). On physical examination, no abdominal mass was detected.

Renal ultrasonography revealed a heterogeneous-hypoechoic lesion which is approximately 82x60 mm in size, almost completely filling the renal pelvis. The lesion showed increased vascularity on colour doppler ultrasound (Figure 2). Left renal vein, left renal artery and inferior vena cava were patent. The lesion extended to the calyceal structures within the parenchyma and inferiorly to the ureteropelvic junction. In addition, there was a grade III increase in echogenicity in the upper pole of the left kidney due to venous engorgement secondary to a possible compression effect. In the differential diagnosis, space-occupying lesions originating from the collecting system epithelium, hematoma, angiomyolipoma with a connection to the collecting system and hydrophyonephrosis due to ureteropelvic stenosis were considered. Hence, CT (Computerized Tomography) scan and MRI (Magnetic Resonance Imaging) were performed.

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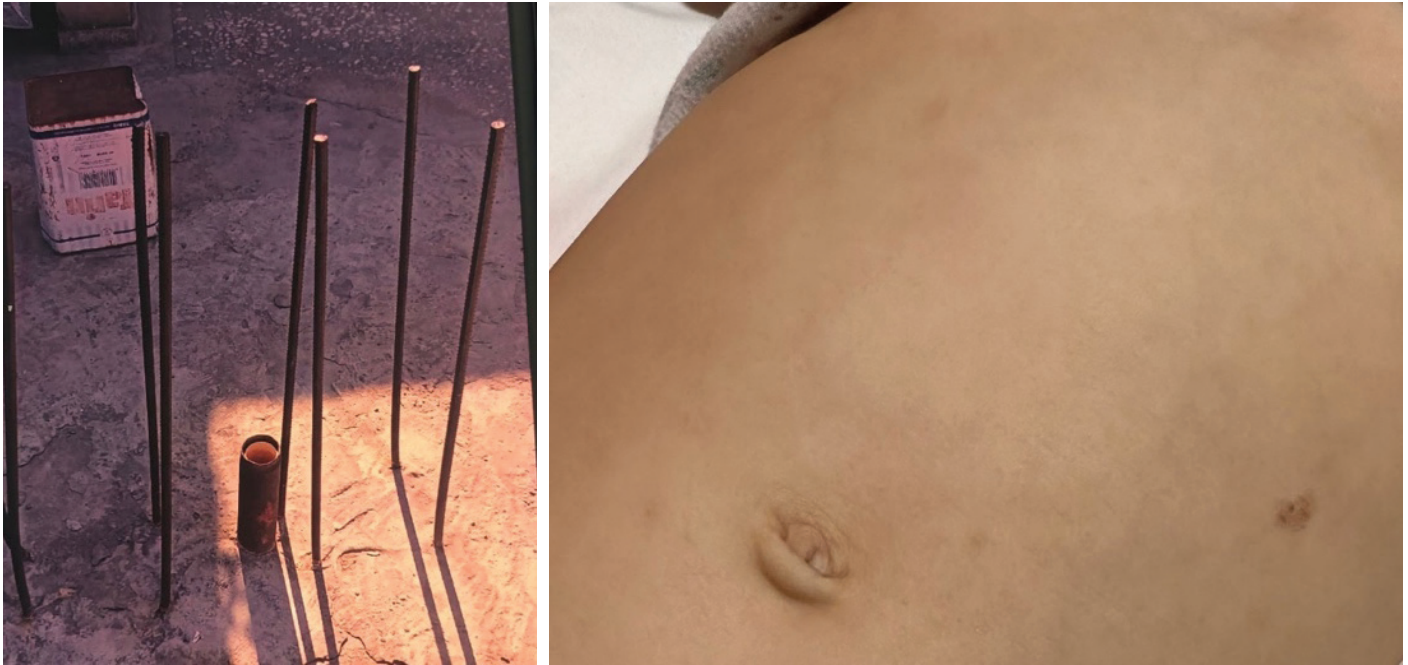


Figure 1. Small wound on the left upper quadrant from falling on iron rods in a construction zone.

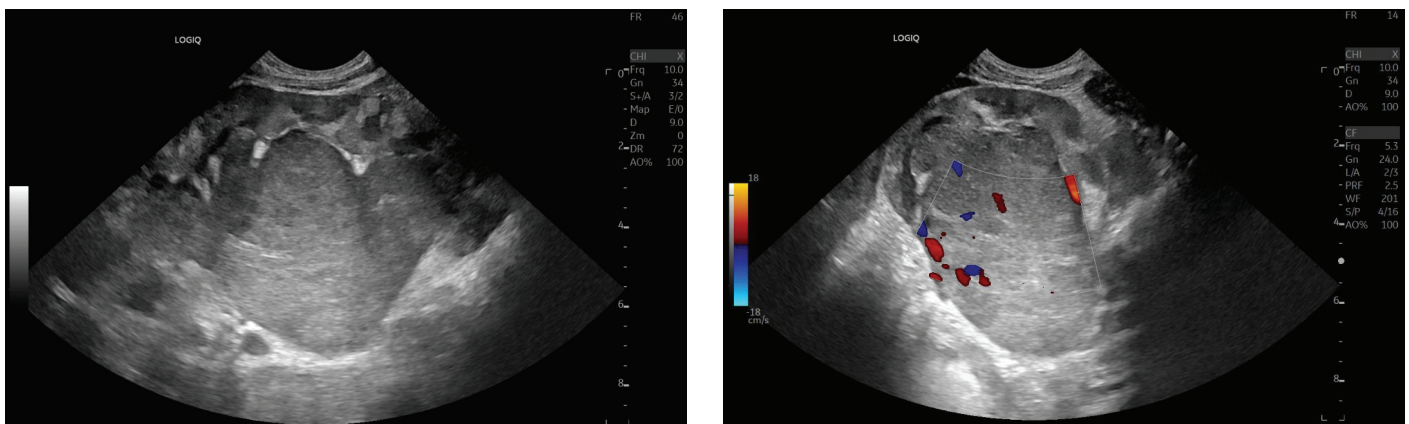


Figure 2. Gray-scale and color-doppler ultrasound images.

On CT examination, there was minimal contrast enhancement in the identified expansile mass. Delayed nephrogram phase was observed in the left kidney. In addition, in the late pyelography phase, no passage of contrast material into the left ureter was observed (Figure 3).

On MRI, the mass was observed within the left renal pelvis, filling the pelvicalyceal system almost completely, extending inferiorly to the proximal to the ureter in a polypoid manner. The mass was hypointense on T1 weighted images and hyperintense on T2 weighted images. After intravenous contrast injection, pathological contrast enhancement was observed in the defined mass (Figure 4). Diffusion-weighted imaging (DWI) ($b=800$) showed a pathological diffusion restriction in the mass (Figure 5).

CT and MRI demonstrated similar imaging findings. No accompanying lymphadenopathy was observed. In the light of all the findings, the diagnosis of botryoid WT originating from the left renal pelvis

was considered. Although renal pelvis hematoma was included in the differential diagnosis due to the patient's history of simultaneous falls, this clinical history was thought to be a coincidence due to the contrast enhancement of the lesion and other radiological findings.

Kidney biopsy was performed. A neoplastic structure with a biphasic appearance was observed. Histomorphological findings and immunohistochemical staining pattern suggested WT in the foreground in the case.

DISCUSSION

WT can be discovered after trauma as seen in our patient. In a review of 13 mass lesions found after trauma, malignancy was diagnosed in 6 patients. This study emphasised the importance of blunt abdominal trauma in revealing an occult cancer or hydro-nephrosis (5).

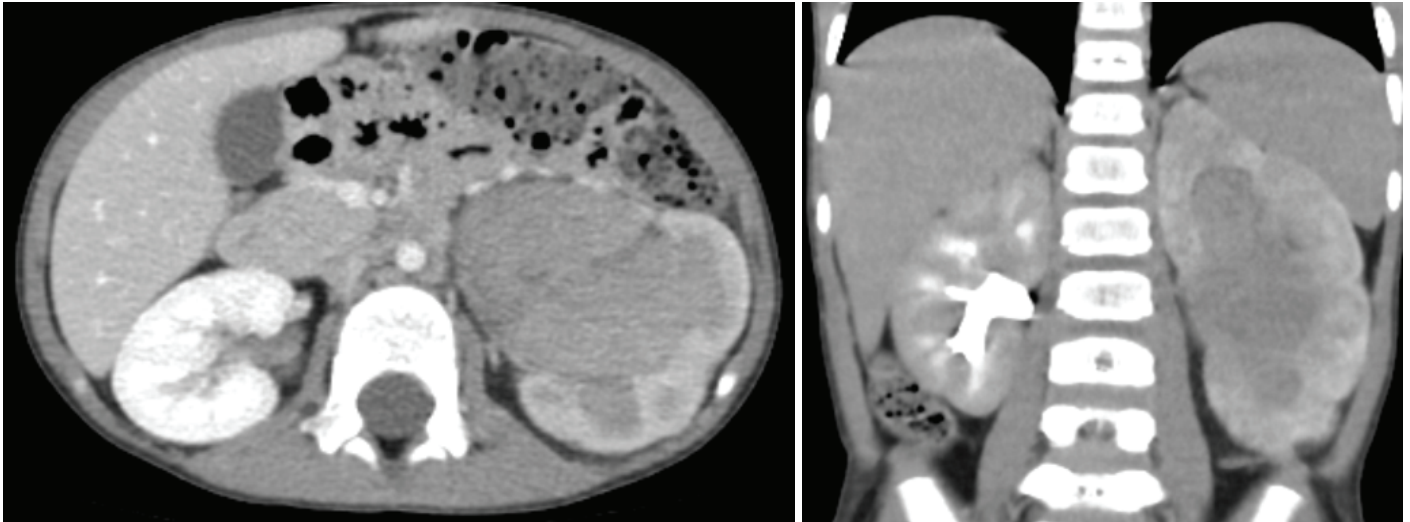


Figure 3. Axial (nephrogram phase) and coronal (pyelography phase) CT images.

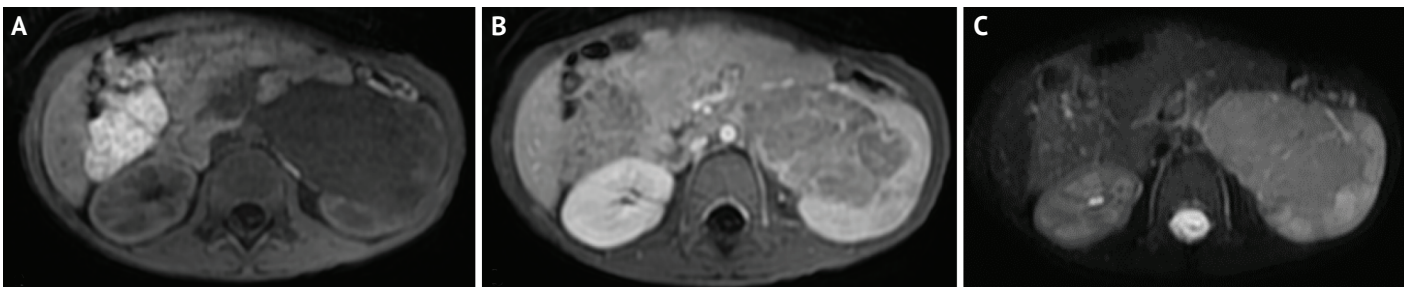


Figure 4. Pre-contrast (A) and post-contrast (B) T1 weighted images, (C) T2 weighted image-fat suppressed.

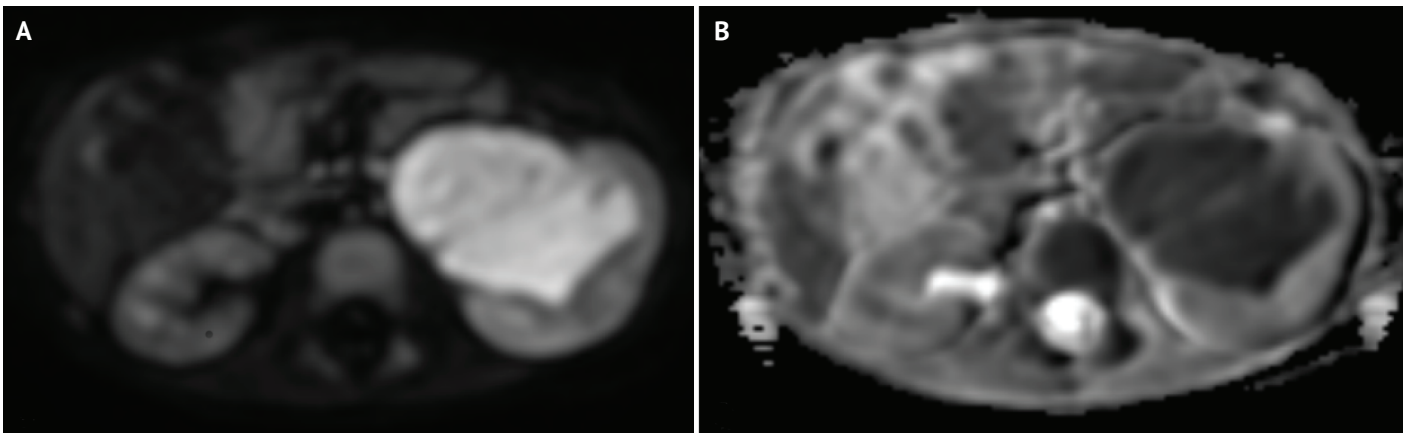


Figure 5. (A) Diffusion-weighted imaging (DWI) (b=800), (B) Apparent diffusion coefficient (ADC).

Approximately 7% of patients with WT have synchronous or metachronous bilateral renal tumors, so a thorough examination of the other kidney is required (6). If a mass was found in the contralateral kidney, we would have considered WT as a potential diagnosis, however in our case, the contralateral kidney was normal.

In cases with WT, abdominal ultrasound usually shows a predominantly solid but heterogeneous mass, with anechoic areas due to necrosis, hemorrhage or cyst formation. However, in our case,

a heterogeneous-hypoechoic lesion without anechoic areas was detected. On MR imaging, WT appears as a mass with low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences, as in our case (2).

It is important to consider angiomyolipoma with a connection to the collecting system in the differential diagnosis, since it may manifest as a hematoma. The tumor weakens the vessel walls and eventually forms aneurysms, which can result in hemorrhage. In children without tuberous sclerosis, angiomyolipomas are rare and

no microscopic fat was found in the mass on opposed-phase chemical shift MRI. Therefore, we excluded this diagnosis (7).

Renal pelvis hematoma is the most important disease in the differential diagnosis, because it usually presents in patients with pre-existing renal pathology or in the setting of trauma (8). Doppler ultrasound may be helpful to differentiate these two lesions. Renal hematoma doesn't have any vascular coding on doppler ultrasound, while WT mostly has vascular coding unless necrosis develops. Another clue that may suggest WT is the presence of lymphadenopathy along with a mass. The prognostic and therapeutic implications of lymph node involvement in children with WT are noteworthy. However, no lymphadenopathy was observed in our case (9).

CONCLUSION

Ultrasound is a fast, cheap and non-invasive diagnostic tool for the evaluation of renal lesions and must be used to evaluate every pediatric patient who had a trauma. This case emphasizes that WT should be kept in mind in the differential diagnosis of renal pelvic hematoma in a child with a history of trauma.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

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B.U., Ç.Ü.; Analysis and/or Interpretation – N.Ö.T., N.A.; Literature Search – N.Ö.T.; Writing – N.Ö.T., M.C.P.; Critical Review – M.C.P., N.A., B.U., Ç.Ü.

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Mönckeberg's Medial Sclerosis of the Thyroid: An Unusual Case Presentation

ABSTRACT

Mönckeberg sclerosis (MS) is an idiopathic and non-inflammatory vascular disease. It is characterized by calcification of the medium layer of muscle arteries. In contrast to atherosclerosis, MS does not cause narrowing of the vessel wall. In this study, we present a rare case who underwent total thyroidectomy due to Graves' Disease, and whose histopathological examination revealed the diagnosis of Mönckeberg Medial Sclerosis.

Keywords: Cardiovascular events, Mönckeberg's sclerosis, thyroid

Mönckeberg sclerosis, a vascular disease identified initially in 1903, is characterized by calcification of the medial layer of muscle arteries (1). Although it typically affects persons over 50 years of age who have type 2 diabetes and chronic kidney disease, it can also affect younger people who do not have any concomitant conditions. It is often found in peripheral arteries, giving rise to "pipestem" arteries (2). It usually does not cause clinical symptoms because, unlike atherosclerosis, it does not cause narrowing of the vascular lumen (3).

In this study, we present a patient who underwent total thyroidectomy due to Graves' Disease at Ankara Etilik City Hospital and was diagnosed with Mönckeberg Sclerosis as a result of the histopathological examination of the excised specimen.

CASE

A 50-year-old female patient has been under follow-up for Graves' Disease for two years. She presented to the Internal Medicine clinic with complaints of palpitations and weight loss. The patient did not have diabetes mellitus or chronic kidney disease. She had no known comorbidities.

There were no pressure symptoms or ophthalmopathy. Medical treatment was started for hyperthyroidism, and the patient was using propylthiouracil regularly for 6 months.

The physical examination was normal. Goitre or palpable nodules were not detected during the physical examination. Laboratory findings showed hyperthyroidism. Thyroid Stimulating Hormone (TSH): 0.26 mIU/L, Free T4: 2.14 ng/dL, Free T3: 6.55 ng/L, TSH Receptor Blocking Antibody (TRB): 11 IU/L

Ultrasound findings revealed the right lobe size of 20x32x44 mm. There was an isoechoic nodule measuring 6x5x6 mm. The size of the left lobe was 17x17x40 mm. There was a hypoechoic nodule measuring 2x3x3 mm in superior-anterior diameters, and a nodule with mixed echogenicity, measuring 7x8x9 mm, located in the middle. The size of the isthmus was 4 mm. The parenchyma was observed to have an extremely heterogeneous appearance. Parenchymal echogenicity was decreased. Fibrous bands and pseudonodular appearance were present in some places within the parenchyma. No lymph nodes of pathological shape and size were observed in either cervical anterior chain.

The patient underwent total thyroidectomy. Histopathologically, Mönckeberg sclerosis was reported. Mönckeberg's medial calcific sclerosis is seen in this artery to the right of thyroid tissue. This finding occurs most often in the elderly. Small muscular arteries in the pelvis, neck, and breast regions can be affected. Calcium deposits are mainly found in the media

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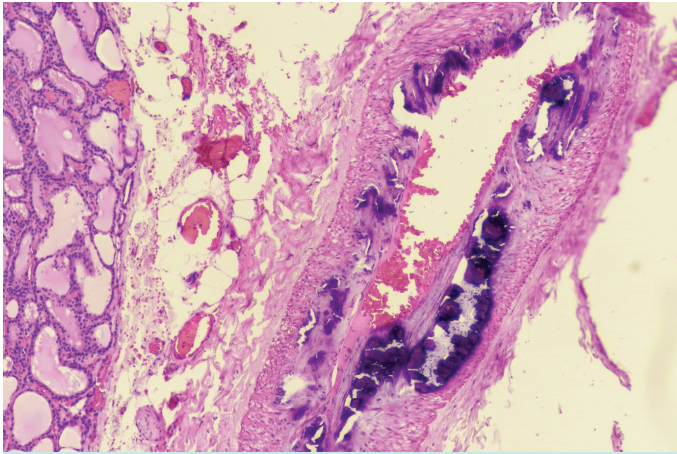


Figure 1. Calcium deposits mainly collect in the media of muscular arteries and as well both the media and internal elastic lamina are involved.

of muscular arteries. Some authors think that the media and internal elastic lamina are both involved (Figure 1). In addition to the obvious medial calcification, there is calcification of the internal elastic lamina (Figure 2).

The patient was consulted to the cardiology and cardiovascular surgery to rule out any comorbid-related diseases. The patient had no vascular or cardiac-related disease. The patient was discharged uneventfully after the second day of the operation.

DISCUSSION

The tunica media layer of the arteries to the extremities or visceral organs becomes dystrophically calcified in Mönckeberg's medial calcific sclerosis (4). The uterine, breast, and thyroid arteries in women have also been frequently mentioned, despite the fact that it was initially noticed in the lower limb arteries of aged men (5). According to Kröger et al. (6)'s study, its incidence in society was 6.9% for women and 13.3% for men. Despite the fact that its cause is unknown, Sato et al. (7)'s study provided evidence that physiological thyroid hormone concentration directly promotes MGP (Mönckeberg) gene expression in cells of smooth muscles via thyroid hormone nuclear receptors, preventing vascular calcification in vivo. In line with these findings, we have to mention that our patient had hyperthyroidism.

Mönckeberg sclerosis is thought to cause the loss of arterial flexibility, isolated systolic hypertension, hypertrophy of the left ventricle, and decreased myocardial perfusion, even though it was once assumed to be a harmless condition (8). MS-related decrease in arterial elasticity raises cardiovascular morbidity and mortality similar to non-insulin-dependent diabetes (9). Other areas of calcification should be carefully investigated, considering the rise in cardiovascular morbidity in people with this illness. To fully comprehend the connection between the thyroid gland, vascular calculi, and the related general disease, more research is required (10).

CONCLUSION

This case report is an unusual presentation of Mönckeberg sclerosis of the thyroid with hyperthyroidism. The diagnosis was con-

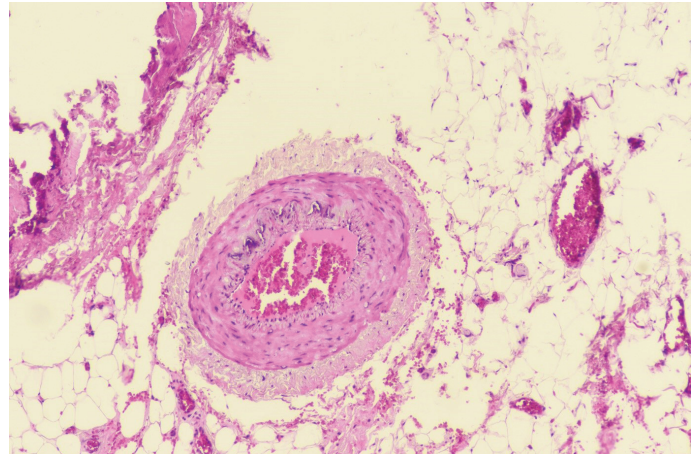


Figure 2. Early stages of calcification of the internal elastic lamina.

firmed with a pathological investigation of the surgical thyroidectomy specimen. Depending on the preponderance of the diseased areas, Mönckeberg sclerosis is a chronic degenerative disorder that affects the arteries and has a variety of clinical symptoms. People who are predisposed to systemic illnesses like diabetes and chronic kidney disease are more likely to develop the disease. Differential diagnosis is challenging because the condition is uncommon and asymptomatic.

Given that Mönckeberg sclerosis increases cardiovascular mortality and morbidity, additional testing should be conducted on patients who have a histological diagnosis of the condition to see if other large arteries are also involved.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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A Very Rare Cause of Bicytopenia; The Use of Vitex Acnu Castus

ABSTRACT

Vitex Agnu Castus dry extract BNO 1095 is used in many indications, mainly premenstrual syndrome. Nausea, headache, acne, etc. are the main side effects. The use of BNO 1095 was learned from the history of a 27-year-old female patient who was examined for bicytopenia etiology. Serological tests results were within normal limits and the bone marrow biopsy clonality result suggested that this might be related to non-neoplastic autoimmune processes. The response to methylprednisolone treatment was accepted as a finding supporting this result. Although there are many reasons in the etiology of bicytopenia, the use of herbal medicine should always be considered. This is the first case in the literature demonstrating that this herbal medicine causes bicytopenia.

Keywords: Bicytopenia, casticin, vitex agnu castus

Medicinal wild plants have been used as valuable tools in the management of different diseases for centuries due to their ease of use and cost effectiveness compared to chemical drugs obtained by synthesis (1).

Vitex agnus castus L. (VAC) is a bush type plant found in the Mediterranean parts of Europe and Central Asia. There are many conditions or diseases in which VAC extract is traditionally used, including menstrual disorders (amenorrhea, dysmenorrhea), premenstrual syndrome (PMS), corpus luteum failure, hyperprolactinemia, infertility, acne, menopause and impaired lactation (2). The various compounds in the chemical content of VAC are vitexilactone, rolundifuran, ketosteroids, diterpenoids (vitexlactam, vitexilactone, viteagnusin I and rotundifuran), flavonoids (orientin, kaempferol, penduletin, luteolin, artemetin, vitexin and casticin) and iridoids (agnusid, agnososid, agnucastosid A/B and aucubin) (1).

In the European Union herbal monograph, the posology commends that products containing VAC dry extracts are used for irregular menstruation, premenstrual syndrome and mastalgia at 4 to 20 mg/day. These dry extracts are standardized in the European Pharmacopoeia (EP) to contain not less than 0.01% casticin in the extract (3).

Casticin is a polymethylflavonide derived mainly from the Vitex species of the Verbenaceae family. This substance isolated from VAC leaves has potent anti-inflammatory and lipoxigenase inhibitory activity. The molecular mechanism of its anti-inflammatory action is the blockade of the NF- κ B, Akt and mitogen-activated protein kinase signaling pathway (4).

CASE

A 27-year-old female with no known chronic disease presented hospital with the complaints of weakness. The laboratory test results revealed bicytopenia: Leukocyte: 920/ μ L, neutrophil: 100/ μ L, hemoglobin: 10.6 g/dL, MCV: 68 fL, platelet: 211.000/ μ L. The patient was hospitalized for further examination. There were no B symptoms. Drug and herbal substance use was questioned and the patient reported having used BNO 1095 (generic name Agnucaston), which is a preparation of the dry extract of Fructus acnu casti for accessory breast, for 3 months and mpst recently 1 month ago.

Anemia parameters were within normal limits: Vitamin B12:231 ng/L, folat: 4.8 ug/L, ferritin: 72 ug/L. A peripheral blood smear was taken and evaluated. Anisocytosis was determined in the red blood cell morphology, leukocyte count compatible with complete blood count, and no atypical cells were seen. Viral hepatitis markers, TORCH panel, brucella, ANA,

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Table 1. Naranjo Advers drug reaction probability scale—items and score

To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score	Yes	No	Don't know	Score
Are there previous conclusion reports on this reaction?	+1	0	0	0
Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered?	+1	0	0	+1
Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	0
Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
Did the reaction reappear when a placebo was given?	-1	+1	0	0
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0	0
Was the adverse event confirmed by any objective evidence?	+1	0	0	0

→ Naranjo Score 5

→ Adverse drug reaction: Probable

Note: The Naranjo criteria classify the probability that an adverse event is related to drug therapy based on a list of weighted questions, which examine factors such as the temporal association of drug administration and event occurrence, alternative causes for the event, drug levels, dose-response relationships and previous patient experience with the medication. The ADR is assigned to a probability category from the total score as follows:

definite if the overall score is 9 or greater, probable for a score of 5–8, possible for 1–4 and doubtful if the score is 0. The Naranjo criteria do not take into account drug-drug interactions. Drugs are evaluated individually for causality, and points are deducted if another factor may have resulted in the adverse event, thereby weakening the causal association.

Anti-Ds DNA and SARS-COV2 PCR test were performed, and all were negative.

In the investigation of the etiology, ultrasound imaging showed a large number of cervical, axillary and inguinal lymph nodes, the largest of which were in the left axilla. This was a reactive lymph node in 20x6.7 mm size with an open hilum. Fine needle aspiration biopsy was performed on the right cervical lymph node, and it was reported as benign cytology.

Bone marrow aspiration and biopsy were performed. Flow cytometry was studied from the aspiration material. In the bone marrow aspiration evaluation; "normocellular bone marrow, megakaryocytes were found to be sufficient in number. Erythroid serial rate was increased (40%) and approximately 30% small, mature, narrow cytoplasmic atypical lymphoid cell infiltration was observed". The flow cytometry result was reported as: "Significant lymphocytosis and granulocytopenia, CD4 / CD8 ratio impaired in increased number of T lymphocytes [ratio 0.45, (reference range 1.3-3.6)]".

The bone marrow biopsy pathology was reported as "normocellular bone marrow showing increased CD3 (+) mature T cells, an increase in interstitial pattern containing interstitial multiple lymphoid aggregates" Considering possible lymphoproliferative or immunological processes, treatment initiated of 60 mg/day methylprednisolone.

The result of the clonality studied from the bone marrow biopsy were reported as; "Molecular findings supporting clonal T cell increase among polyclonal T cells are considered features supporting autoimmune neutropenia. Immunophenotypic and molecular findings observed in the bone marrow primarily suggest that the

increase in clonal cytotoxic T cells on a polyclonal basis may be associated with non-neoplastic autoimmune processes".

As a result of bone marrow clonality, the methylprednisolone dose was reduced and then discontinued. The patient remains under follow-up and the hemogram parameters are completely normal.

DISCUSSION

Over the last 50 years VAC has been used especially for the treatment of premenstrual syndrome and prevention of premenstrual mastalgia (5).

In a systemic review by Danielle et al. on the side effects of VAC treatment; the most commonly seen side effects were reported to be nausea, headache, gastrointestinal disturbances (nausea, vomiting, pressure sensation in the epigastric region, etc.), menstrual disorders, acne, itching and erythematous rash and these were seen to often be reversible (2).

Casticin is a potent immunomodulator and cytotoxic compound for which chemiluminescence, chemotaxis, T cell proliferation and cytotoxic activity have been tested in vitro. There has been reported to be a significant dose-dependent inhibitory effect on monocyte oxidative burst (6).

Casticin; decreases neutrophil, macrophage, and lymphocyte counts, proinflammatory cytokine and chemokine levels. It also significantly reduces the thickness of the epithelium and its infiltration by inflammatory cells (4).

Röhl et al., (7) showed that VAC dry extract BNO 1095 targets uterine myometrial tissue and inflammatory signaling molecules asso-

ciated with migratory / inflammatory cells. The same study also reported that BNO 1095 has a promising anti-inflammatory effect in in-vitro conditions through the strong inhibition of 5-lipoxygenase activity and leukotriene production and reduction of the production of inflammatory cytokines and reactive oxygen derivatives.

The patient presented in the paper had used fructus agni casti extract and the result of the bone marrow biopsy clonality suggested that it may be related to autoimmune processes. The hemogram parameters returned to normal in a short time after discontinuation of the extract, suggesting that this event was related to this extract.

The assessment of causality between fructus agni casti extract and bicytopenia using the Naranjo nomogram questionnaire yielded a score of 5, indicating that the side effect probably caused which means side-effect is probably caused by the fructus agni casti extract (Table 1) (8).

The aim of presenting this case was to emphasize that patients who are investigated for cytopenia should be questioned about the use of herbal substances in addition to medications and the possible side-effects of herbal products should be considered. This case also provides an example of the effectiveness of steroid therapy in the treatment of cytopenias triggered by autoimmunity.

There are no previous cases in the literature that this preparation causes bicytopenia. So this case report can be considered important due to its rarity and clinical significance.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

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