A Rare Vasculitis of Childhood, Takayasu Arteritis

Aydın Ece, Velat Şen, Sevgi Yavuz, Ali Güneş, Ünal Uluca, Cahit Şahin

ABSTRACT

Takayasu arteritis is a potentially life threatening vasculitis that characterized by granulomatous inflammation of large vessels including aorta, its major branches and pulmonary arteries. True incidence of TA is not known in children, since TA is very rare; however, incidence of TA has been estimated as 0.8-2.6 per million children. Making a diagnosis is more difficult in childhood compared with adults due to non-specific clinical findings. The diagnosis of TA is done based on clinical criteria, laboratory investigations support and radiologic images confirm the diagnosis. Corticosteroids with other immunosuppressive drugs are used for treatment and biological agents are given to resistant cases. In this report, it was aimed to draw attention to a potentially fatal disease that frequently diagnostic delays and therapeutic difficulties occur. We, herein reported signs, symptoms, imaging methods and treatment modalities of two children, a 12 year-old male and a 13 year-old female patients, that presented with non-specific initial symptoms and diagnosed as TA with clinical findings and radiological images

Key words: *Takayasu arteritis, child, vasculitis, diagnosis, treatment*

Çocukluk çağının nadir vasküliti, Takayasu Arteriti

ÖZET

Takayasu arteriti aorta, aortanın ana dalları ve pulmoner arterler gibi büyük damarların granülomatöz enflamasyonuyla karakterize potansiyel olarak hayatı tehdit eden bir vaskülitidir. Çocuklarda çok nadir görüldüğünden gerçek sıklığı bilinmemekle birlikte, TA insidansı milyonda 0,8-2,6 arasında olarak tahmin edilmektedir. Çocukluk çağında klinik bulgular erişkinlere göre daha az spesifik olduğu için tanı koymak daha güçtür. Hastalığın tanısı klinik kriterlere göre konur, laboratuvar testleri tanıyı destekler ve radyolojik görüntüleme yöntemleri tanıyı teyid eder. Tedavide kortikosteroidlerle birlikte diğer immunsupresan ilaçlar kullanılmakta, dirençli vakalarda biyolojik ajanlar uygulanmaktadır. Bu yazıda çocuklarda sıklıkla tanı gecikmeleri ve tedavi zorlukları yaşanan ve ölümcül olabilen bir hastalığa dikkat çekilmesi amaçlandı. Nonspesifik semptomlarla başlayan ve klinik bulgularla ve görüntüleme yöntemleri ile Takayasu arteriti tanısı konulan biri 13 yaşında kız ve diğeri 12 yaşında erkek iki olguyu belirti, bulgu, uygulanan görüntüleme yöntemleri ve tedavileriyle birlikte sunduk.

Anahtar kelimeler: *Takayasu arteriti, çocuk, vaskülit, tanı, tedavi*

INTRODUCTION

Takayasu arteritis (TA) also known as "pulseless disease" is a chronic, idiopathic granulomatous vasculitis that involves large vessels. The average presentation age is 11.4 years and 20% of cases are diagnosed before the age of 19 years. Usually 19 months of delay occur in the diagnosis of TA cases. Early diagnosis and effective treatment can prevent compliactions related to the disease (1). Takayasu arteritis is a potentially life threatening vasculitis with the approximately mortality rate of 35% in children (2). The disease has an acute early phase with non-specific symptoms, such as hypertension, headache, fever, muscle pain, arthralgia, night sweats and weight loss. Nearly one-third of children present with inactive disease in which there are vascular sequels instead of active vasculitis.

Because of non-specific symptoms and absence of a specific diagnostic laboratory test, the disease is often un-

Dicle University Medical School, Department of Pediatrics, Diyarbakır, Turkey

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Correspondence: Dr. Aydın Ece
Dicle University Medical School, Department of Pediatrics, Diyarbakır, Turkey
E-mail: draydinece@hotmail.com

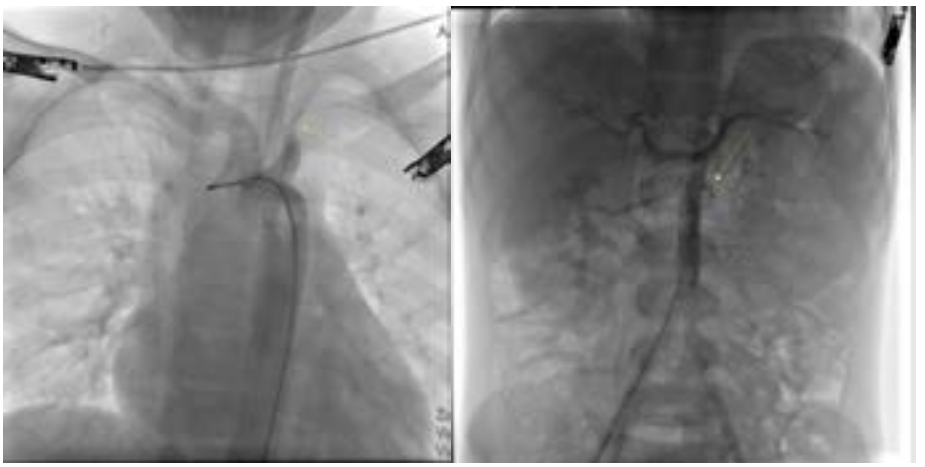

***Figure 1**. Classical angiographic appearances of case 2*

recognized in the early acute phase. If untreated, the next phase affects the aorta and its main branches so that affected vessels may become stenotic and aneurysms may develop (2,3). Presenting symptoms at the second stage usually reflect end-organ ischemia with cold extremities, poor or absent of arterial pulses and claudication (2).

The incidence of TA in adults estimated to be 0.8-2.6/1.000.000 in different countries. Although the incidence of TA in childhood is not known in one series 30% of all cases were children (Brunner). Diagnosis of TA is done according to EULAR/PRINTO/PRES (Eurepean League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/ Paediatric Rheumatology) criteria included angiographic abnormalities, peripheral pulse alterations, systolic blood pressure difference of extremities, arterial hypertension and elevated acute phase reactants (4). Few studies on childhood TA have been published up to date and reports on TA in children are still scarce. Thus, we herein, reported two pediatric patients with TA that diagnosed and followed up at the Pediatrics Clinics of Dicle University Hospital. Our aim is to report clinical, laboratory and radiologic image finding of two TA pediatric patients, in order to improve the knowledge of clinicians about TA in childhood, allowing early diagnosis and better patient outcome.

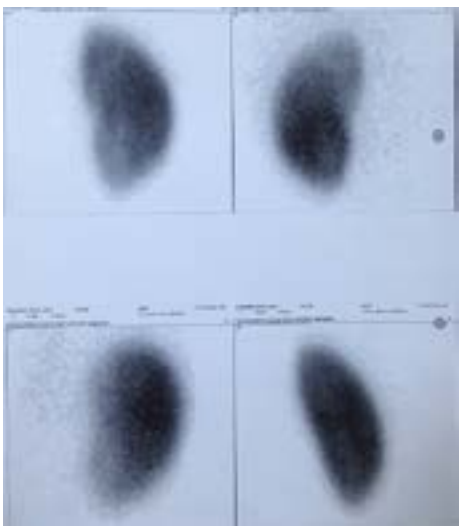

***Figure 2**. DMSA of Case 2 showed non-functional left kidney*

CASE 1

A 12 year-old boy admitted with weakness, fatigue, weight loss, headache and abdominal pain for the last three months. Body weight was 30 kg (3. percentile), height 135 cm (3-10. percentile) and body temperature was normal. The physical examination revealed that left brachial and radial pulses could not be felt by palpation and there were bruits over carotid artery and on abdominal region. Right upper extremity blood pressure was 200/100 mmHg and the left arm blood pressure was

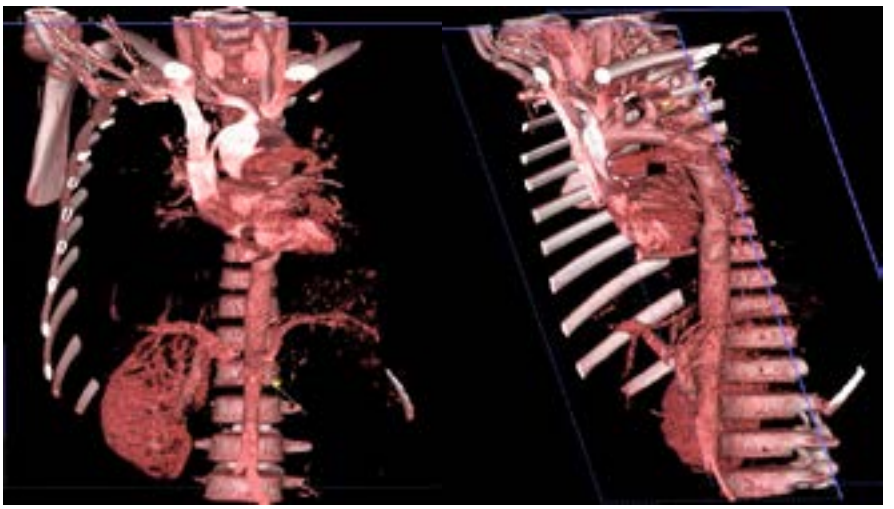

***Figure 3**. Magnetic resonance images of case 2*

so low that could not be measured. Laboratory investigation results were as follows: white blood count (WBC) 15.600/ mm^3, platelet count 543.000/ mm^3 and hemoglobin 10.3 g/dl. Liver and kidney functions and other blood chemistry were within normal limits, except for blood urea of 70 mg/dl (N<40). Elevated acute phase reactants were detected as erythrocyte sedimentation rate (ESR) 44 mm/h (0-15) and C-reactive protein (CRP) 1.3 mg/dl (0-0.8). Viral markers including hepatitis viruses, Epstein-Barr virus and cytomegalovirus were negative. Anti-nuclear antibody (ANA) and anti-neutrophil cytoplasmic antibodies (c-ANCA, p-ANCA) were negative and complement factor 3 (C3) and C4 were normal. Urinalysis revealed proteinuria (+++) and hematuria (++). Doppler ultrasound revealed increased resistive index in left kidney and intimal hyperplasia and occlusion of proximal and middle portions of left subclavian artery. Conventional angiography showed occlusion of left subclavian artery at 23 mm of exit cite of aorta and in left vertebral artery. Additionally, left renal artery was seen as nearly fully occluded (Figure 1). DMSA scan also showed non-functional left kidney (Figure 2). Magnetic resonance imaging (MRI) angiography demonstrated that left subclavian artery was completely occluded and circulation was maintained with the collateral vessels and left renal artery was narrowed from the proximal segment and its wall thickened. Additionally, left kidney perfusion was clearly decreased and left kidney was seen as hypodense (Figure 3).

The patient received TA diagnosis based on above findings and therefore treatment initiated with prednisolone (2 mg/kg/d) and acetyl salicylic acid (3 mg/kg/d) together with anti-hypertensive drugs (nifedipin 30 mg, BID, doxazosin 2 mg/d and enalapril 0.1 mg/kg/d). High blood pressures and elevated acute phase reactants returned to normal limits and complaints of patient disappeared within two weeks. He is currently asymptomatic and under regular follow up controls.

CASE 2

A 13 year-old girl was admitted to hospital with complaints of fever, fatigue, malaise, headache, weight loss, pain and coldness in right arm and in two feet and incapability to walk for the last 6 months. She has been investigated by various health centers with no clear diagnosis and treatment during the last 6 months. Physical examination revealed cold right hand and both feet, weight 47 kg (10.-25. percentile), height 159 cm (25.-50. percentile), body temperature 38.3°C. Blood pressure of right and left arms were 155/80 mmHg and 80/40 mmHg, respectively. Right radial artery pulse could not be felt. Bruit was heard at carotid artery region and there was hepatosplenomegaly 3 cm below the costa.

Laboratory test results were as follows: WBC 12300/ mm^3, hemoglobin 11.7 g/dl, platelet count 293.000/ mm^3, ESR 35 mm/h (N: 0-15) and CRP 3.7 mg/dl (N: 0-0.8). Viral markers including markers of hepatitis B, hepatitis C, cytomegalovirus and Epstein-Barr virus were

all negative. Serum biochemical analyses and urinalysis were normal. Anti-nuclear antibody and c-ANCA and p-ANCA were also negative. Abdominal ultrasound showed hepatosplenomegaly and Doppler ultrasound revealed narrowing of right radial artery lumen, a flow pattern with low resistance and decreased peak systolic rate. Flow rates of bilateral ulnar and left radial arteries were lower than normal values. MRI angiography showed narrowing of left subclavian and brachial arteries.

The diagnosis of TA was done according to clinical criteria and radiological images. Intravenous high dose methylprednisolone (30 mg/kg/d, maximum 1 g/d) was initiated and this followed by oral prednisolone (1 mg/kg/d), oral cyclophosphamide (2 mg/kg/d for 3 months), aspirin (100 mg/d) and anti-hypertensive drugs (nifedipine 30 mg B.I.D, enalapril 5 mg/d, doxazosin 2 mg/d). Angioplasty was performed to left brachial artery. Claudication and cold extremities were got better and acute phase reactants were returned to normal levels. The patient, now continue to come to follow up examinations in a better health status, though some complaints continue.

DISCUSSION

Takayasu arteritis represents 1.5% of vasculitis in children. Disease course is variable and may have multiple relapses despite treatment (1,2). Although, etiology and pathogenesis of TA is not known, immune and genetic factors may have role in the pathogenesis of the disease (1-3). The diagnosis of TA is usually difficult for physicians and an average of 19 months of diagnostic delay has been reported (1). It is likely that the non-specific clinical presentation of TA at early period contributes to delay in diagnosis. Our patients had also 6 months and 3 months delay in diagnosis.

The diagnosis of TA was done in our patients based on EULAR/PRINTO/PRES criteria, which included following features: Angiographic abnormalities of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation (mandatory criterion) plus one of the five following criteria: 1) pulse deficit or claudication, 2) four limbs blood pressure discrepancy, 3) bruits, 4) hypertension, and 5) elevated acute phase reactants (4). Fatigue has been reported as the most common presentation of TA in children, and other signs and symptoms are hypertension (83%), headache (31%), weight loss (22%), arthritis/arthralgia (14%) and fever (2%) (1-5). Both of our patients had fatigue, hypertension, weight loss and headache.

The most frequently involved vessels are renal arteries (73%), subclavian arteries (57%), and carotid arteries (52%). The thoracic or abdominal aorta was affected in nearly 50% of children. Coronary, vertebral, brachial and axillar arteries are involved with less frequency (1,3). Our male patient had left subclavian artery and renal artery involvement, while our female patient had subclavian and brachial artery involvements.

Although there is no specific diagnostic laboratory test for TA, elevated ESR and CRP levels can be seen during active disease (6). However, classical inflammatory markers have limited sensitivity and lack of specifity in TA. In a study, elevated ESR was found in 100% of children with TA, decrease in peripheral pulses in 58% and bruits in 26% (5). Both of our patients had high ESR and CRP levels and decrease pulses, and bruits were heard at carotid artery and/or at abdominal region.

A combination of imaging modalities is commonly necessary for diagnosis of childhood TA. These radiological imaging methods are conventional angiography, magnetic resonance angiography, computed tomographic angiography and Doppler ultrasound. The gold standard is conventional radiography. The most frequently detected vascular abnormalities are stenosis, occlusion, dilatation and aneurysm (7-9). Our first patient showed narrowing occlusions in left subclavian and renal arteries and thick subclavian and renal artery walls by Doppler ultrasound, conventional angiography and MRI angiography. Second patient had narrowing of right radial artery, left subclavian and brachial arteries that showed by imaging methods.

Treatment of TA is based on the use of glucocorticoids and immunosuppressive agents and surgical correction with angioplasty, in order to prevent irreversible vessel damage with resultant insufficiency of vital organs. Remission has been achieved in 60% of patients treated with glucocorticoids alone (1,10). Percutaneous transluminal angioplasty (PTA) is the most common palliative procedure. However, endovascular revascularization procedures (by-pass grafts, patchy angioplasty, endarterectomy, PTA, stent placement) are associated with high failure rates in patients with TA (2). We gave corticosteroids (high dose bolus followed by daily oral doses), acetyl salicylic acid, cyclophosphamide and anti-

hypertensive drugs to our patients and both of patients benefited from treatment.

In conclusion, diagnosis and treatment of TA in children is considerably difficult. Because of few cases of TA have been reported in pediatric age group, the report of more TA cases may help to improve awareness of physicians and provide early diagnosis and better therapeutic results. We supposed that the report of these two cases helps to improve the knowledge of clinicians about TA in childhood.

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