

## Atypical presentation of Takayasu's arteritis in an adolescent

### Bir ergende Takayasu arteritinin atipik presentasyonu

Kıymet K. BİNNETOĞLU, Elif KARAKOÇ AYDINER, Safa BARIŞ, Ahmet ÖZEN, Ayşe İrem ZÖHRE, Feyyaz BALTACIOĞLU, Haner DİRESKENELİ, Işıl BARLAN

#### ABSTRACT

Takayasu's arteritis is rarely seen in childhood. In addition, symptoms are nonspecific and diagnostic laboratory marker is unavailable. We hereby described an adolescent with an atypical presentation of Takayasu's arteritis. A 15-year-old girl was admitted to our clinic with the symptoms of weight loss, fever, back pain, and malaise since 2 months. Physical examination ended with normal vital signs, centiles and no other pathological findings. Laboratory findings showed increased acute phase reactants. Irregularities in the aortic wall and luminal narrowing of aorta were detected in magnetic resonance angiography. In conclusion, children with Takayasu's arteritis present with nonspecific symptoms. No laboratory test is diagnostic, whereas abnormalities in large vessels in radiology are specific for the disease. Mainstay of treatment is systemic steroids and immunosuppressants and outcome is worse in children than in adults.

**Keywords:** Adolescent, HLAB51, Takayasu's arteritis, Vasculitis

#### ÖZET

Takayasu arteriti çocuklarda nadir görülen bir hastalıktır. Klinik bulgular özgün değildir ve tanısal bir laboratuvar test mevcut değildir. Burada, atipik bir klinikle başvuran bir ergende Takayasu arteriti sunulmaktadır. Onbeş yaşında kız çocuk kliniğimize 2 aydır süren kilo kaybı, ateş, halsizlik ve sırt ağrısı ile başvurdu. Fizik muayenede büyüme gelişmesi normal olan hastada patolojik bulguya rastlanmadı. Laboratuvar testlerinde akut faz reaktanları yüksek bulundu. Manyetik rezonans ile anjiyografik görüntülemelerde aorta duvarında düzensizlik ve daralmalar saptandı. Sonuç olarak, çocuklarda Takayasu arteritinde non-spesifik bulgular görülmektedir. Laboratuvar testleri tanısal olmamakla beraber radyolojik bulgular oldukça özgündür. Tedavide sistemik steroidler ve immüsupresanlar kullanılmakta ancak çocuklarda seyir erişkinlerden daha ağır olmaktadır.

**Anahtar kelimeler:** Ergen, HLAB51, Takayasu arteriti, Vaskülit

Kıymet K. Binnetoğlu (✉), Ayşe İrem Zöhre, Işıl Barlan  
Department of Pediatrics, School of Medicine, Marmara University,  
Istanbul, Turkey  
e-mail: drkiymetbinnet@gmail.com

Elif Karakoç Aydın, Safa Barış, Ahmet Özen  
Sub-department of Pediatric Allergy and Immunology, Department of  
Child Health and Pediatrics, School of Medicine, Marmara University,  
Istanbul, Turkey

Feyyaz Baltacıoğlu  
Department of Radiology, School of Medicine, Marmara University,  
Istanbul, Turkey

Haner Direskeneli  
Sub-department of Rheumatology, Department of Internal Medicine,  
School of Medicine, Marmara University, Istanbul, Turkey

Submitted/Gönderme: 13.04.2015 Accepted/Kabul: 21.05.2015

#### Introduction

Fever of unknown origin in childhood has broad categories of illnesses as underlying causes. More common etiologies should be searched initially such as systemic or localized infections followed by malignancies. Rheumatologic diseases are less common in etiology. Among those Takayasu's arteritis is very rarely seen in childhood. In addition, symptoms are nonspecific and a diagnostic laboratory marker is unavailable [1-3]. Early diagnosis and treatment is vital especially in children for a better outcome.

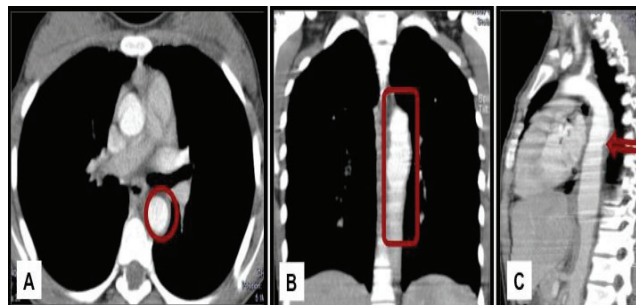
We hereby described an adolescent with an atypical presentation of Takayasu's arteritis at an early phase of this disease.

## Case Report

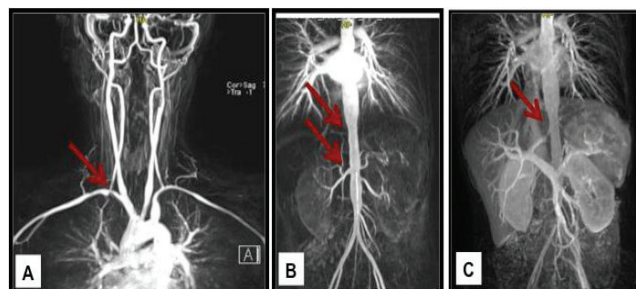
A 15-year-old girl was admitted with the symptoms of weight loss, fever, back pain, fatigue and malaise for the last 2 months. Past medical history revealed hospital admission with vomiting and diarrhea due to *Entamoeba histolytica*. Her family history revealed Behçet's disease in an uncle. Physical examination ended with normal vital signs and centiles. Laboratory findings showed increased acute phase reactants; WBC:  $9.2 \times 10^3/\mu\text{L}$ , absolute neutrophile count:  $5.500/\mu\text{L}$ , ESR: 98 mm/hour and CRP:  $54\text{mg/l}$  ( $0-5\text{mg/l}$ ). Differential diagnosis was not compatible with blastic transformation. Procalcitonine level was  $0.06\text{pg/mL}$  ( $<10\text{pg/mL}$ ) which was not indicative of an infectious etiology. Blood and urine biochemistries were in normal range for the age. Following the initial work-up, she necessitated further evaluation for weight loss and night fever primarily for infectious agents such as brucellosis, typhoid fever and tuberculosis. Wright, Gruber Widal, stool cultures, ppd and quantiferon assays were all negative. Viral serologies for CMV, EBV and HIV were also found to be negative. Cardiac examination, blood cultures and echocardiography were not suggestive for infective endocarditis. Connective tissue and inflammatory bowel diseases were also considered for this patient. Daily abdominal pain with a short duration of 10 minutes was the only positive finding in her history. On the other hand, patient had negative ANA, anti dsDNA, c-ANCA, p-ANCA with borderline positive rheumatoid factor:  $26.1\text{IU/ml}$  ( $<23\text{IU/ml}$ ). She had negative HLA-B27 but positive HLA-B51 titers with a negative pathergy testing. Abdominal and thoracic computed tomographies were performed to rule-out localized abscess or solid tumor. Interestingly, thorax tomography showed annular type thickening of great vessels' wall (Figure 1A, 1B, 1C) with normal pulmonary arteries. To explore those changes more, magnetic resonance angiography was performed. Irregularities in the aortic wall both in thoracic and abdominal section, luminal narrowing of aorta both above and below diaphragmatic level were detected (Figure 2A, 2B). These radiological findings in large arterial vessels were compatible with Takayasu's arteritis.

Putting all these subtle clinical and diagnostic radiological features together, patient most likely had early phase Takayasu's arteritis. Absence of hypertension in all extremities, headache, claudicating extremities, and audible bruit in this patient was compatible with the early phase and atypical presentation of this disease. She was treated with  $1\text{mg/kg/day}$  methylprednisolone. One week after the treatment, her symptoms regressed including malaise,

fatigue, and fever and she started to gain weight. In addition, ESR and CRP levels returned to normal range at the 1<sup>st</sup> month follow-up visit. Steroid therapy was continued for 1 month at a dose of  $1\text{mg/kg/day}$  and following schedule was as planned as 20% taper of steroid dose every two weeks. Steroid dose could not be tapered at 2<sup>nd</sup> month due to reversal of nonspecific symptoms and  $2\text{mg/kg/day}$  azathiopurine was added for steroid sparing effect.



**Figure 1.** A) Thickening of thoracic aorta wall at axial thoracic imaging, B) Luminal irregularities of the thoracic aorta wall at coronal thoracic imaging and C) Thoracoabdominal aortic wall tortuosity and thickening at sagittal thoracoabdominal imaging.



**Figure 2.** A) Wall thickening and narrowing of the right subclavian artery at the level of vertebral artery origin at contrast enhanced cervical imaging, B and C) Narrowing and wall irregularities at the diaphragmatic level and infrarenal abdominal aorta at contrast enhanced thoracoabdominal magnetic resonance imaging

## Discussion

Takayasu's arteritis is the most common, granulomatous inflammation of large arteries. Disease has an acute early phase, with non-specific symptoms such as hypertension, headache, fever, muscle pain, arthralgia, night sweats and weight loss. Due to the non-specific symptoms and the absence of specific laboratory parameters, the disease is often unrecognized in this phase. To date, Takayasu's arteritis is a rarely described disease in pediatric age group with only a few studies [1-3]. These patients were mostly admitted with less specific symptoms than in adults such as fever, arthralgias and hypertension [4]. For the initial admission in

children, the typical presenting symptoms and findings was reported to be headache (31%) and hypertension in physical examination (82%) [4,5]. The patient in this report did not complain about headache and had normal blood pressure in all extremities. These symptoms were atypical for Takayasu's arteritis. Rarely seen symptoms such as fever (29%), dyspnea (23%), weight loss (22%) and vomiting (20%) [4] were prominent in our patient at admission.

Ozen et al revised the diagnostic criteria of Takayasu's arteritis as follows in 2010; mandatory angiographic abnormalities of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation plus one of the five following criteria: 1.pulse deficit or claudication, 2.four limbs blood pressure discrepancy, 3.bruits, 4.hypertension, 5.elevated acute phase reactants [6]. According to those revised criteria, our patient met 2 of them: increased acute phase reactants and the mandatory and diagnostic radiological findings.

Regarding Takayasu's arteritis, human leukocyte antigen risk alleles for various populations are studied. Indian subjects were found to be associated with HLA-B5 and its two serological subtypes, B51 and B52 [7]. Recently Sahin et al described that Takayasu's arteritis was found to be associated with HLA-B\*52, but not with HLA-B\*51, in Turkey [8]. Our patient was positive for HLA B51 with a family history of Behçet's disease. Currently, human leukocyte antigen risk alleles do not provide diagnostic or prognostic features for patients with Takayasu's arteritis

Adequate therapy in Takayasu's arteritis is important to prevent irreversible vessel damage resulting with insufficiency of vital organs. Corticosteroids are still the mainstay of treatment [9]. In addition, other immunosuppressive agents such as methotrexate, azathiopurine and cyclophosphamide are other therapeutic options [10]. In about one-fourth of the treated patients, remission was not achieved but relapses observed. Addition of anti-TNF therapy may be a possible beneficial agent for these patients [11,12]. Despite providing short-term benefit, endovascular revascularization procedures (bypass grafts, patch angioplasty, endarterectomy, percutaneous transluminal angioplasty, stent placement) are associated with a high failure rate in patients with Takayasu's arteritis [13,14]. Patient reported here initially received steroid therapy which was followed by a systemic immunosuppressant agent (azathiopurine). She did not need anti-TNF or vascular intervention yet, but may be essential in the long term outcome.

Anti-inflammatory therapy can lead to dramatic improvement in symptoms of Takayasu's arteritis. Although improvement of symptoms usually follows glucocorticoid therapy, relapses usually occur with dosage reduction [15]. Five-year survival rate in adults is as high as 94% [15], whereas mortality rate in children is around 35% [2]. Mortality is related to hypertension, pulmonary vascular involvement, renal and cardiac failure [16]. In our patient, early diagnosis and initiation of steroid treatment rendered in remission of clinical symptoms and acute phase reactants, as expected. Follow-up of this patient revealed the need of azathiopurine as an immunosuppressant agent while steroid was tapering due to relapsing symptoms. Since the patient had been followed for only 3 months in our clinic, long term outcome is unavailable now. On the other hand, Goel et al reported that despite aggressive immunosuppression therapy, damage progressed in one-third of patients with childhood Takayasu's arteritis [17].

In conclusion, children with Takayasu's arteritis present with nonspecific symptoms. No laboratory test is diagnostic, but abnormalities in large vessels in radiology are specific for the disease. Mainstay of treatment is systemic steroid and outcome is worse in children than in adults.

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