Takayasu's arteritis in children and adolescents: report of three cases
Ana Karina Soares Nascif¹, Marcelo Delboni Lemos², Norma Suely Oliveira¹, Paula Campos Perim², Ana Costa Cordeiro², Mariana Quintino²

ABSTRACT
Takayasu’s arteritis (TA) is a systemic vasculitis that affects mainly the aorta and its major branches. Despite being the third most frequent vasculitis in childhood, the occurrence of TA in the pediatric age group is scarce. We report three cases of TA in children, emphasizing signs and symptoms, angiographic alterations and therapeutics.

Keywords: Takayasu’s arteritis, pediatrics, signs and symptoms, therapeutics.

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INTRODUCTION
Takayasu’s arteritis (TA) is a systemic granulomatous vasculitis of large vessels that mainly affects the aorta and its large branches. It is the third most frequent vasculitis of childhood.¹ Most patients diagnosed are women in third decade of life;¹ however, the disease has been reported in children as young as seven months of age.²

The diagnosis of TA is based on the EULAR/PRINTO/PRES criteria, that comprises: angiographic abnormalities, alterations in peripheral arterial pulses, systolic blood pressure (BP) discrepancy in any limb, arterial hypertension, large artery bruits, and elevated acute phase reactant.³

The treatment of TA requires the use of corticosteroids, which can be associated with immunosuppressive or biological agents. Some cases benefit from surgical intervention.¹

Despite the increasing identification of children and adolescents with TA, reports of disease in this population are still scarce among us.⁴ Thus, we report three patients with TA diagnosed according to the established criteria⁵ and followed-up at the outpatient clinics of Pediatric Rheumatology of the Service of Rheumatology of the Hospital Universitário Cassiano Antônio Moraes of the Universidade Federal do Espírito Santo (HUCAM/UFES), from December 2007 to January 2010. Data were obtained from medical record review after written informed consent was provided.

CASE REPORT
Case 1
The 15-year-old female patient was admitted in October 2007 complaining of fatigue, headache and intermittent claudication of upper limbs for one year. Symptoms were attributed to chronic anemia. The physical examination revealed the following: impalpable peripheral pulses and inaudible blood pressure (BP) on upper limbs; systemic BP measured on right and left lower limbs of 220/110 mmHg and 160/90 mmHg, respectively; and bilateral carotid bruit. The laboratory tests
showed inflammatory activity, and imaging studies suggested TA.

In December 2007, because of extensive arterial impairment and clinical severity, monthly pulse therapy with methylprednisolone (MTP) was initiated in association with pulse therapy with cyclophosphamide (CTX) and oral prednisone (1 mg/day), in addition to anti-hypertensive drugs. The patient did not respond to the immunosuppression instituted, which was changed to subcutaneous methotrexate (SC MTX) 25 mg/week, associated with oral corticoid. Due to the persistence of symptoms and arterial hypertension 18 months after beginning therapy, six infusions of infliximab (5 mg/kg/dose) were prescribed. After starting biologic therapy, the patient evolved with symptom remission, and oral corticoid could be progressively reduced. Systemic arterial hypertension (SAH), however, persisted despite the use of five anti-hypertensive drugs.

**Case 2**

A 16-year-old female patient was admitted in June 2009 complaining of fatigue for five years, chronic anemia, and recently diagnosed arterial hypertension. She had a previous echocardiographic diagnosis of coarctation of the aorta (CoAo). The physical examination revealed carotid and abdominal bruits, and SAH with BP discrepancy in the limbs as follows: right upper limb (RUL), 180/130 mmHg; left upper limb (LUL), 160/120 mmHg; and lower limbs, 200/140 mmHg. The laboratory tests evidenced increased erythrocyte sedimentation rate (ESR) and C-reactive protein (PCR), and imaging studies suggested TA and excluded CoAo.

Monthly pulse therapy with MTP and oral prednisone (1 mg/kg/day) was prescribed in association with anti-hypertensive drugs. In November 2009, due to arterial hypertension of difficult control, the patient underwent percutaneous transluminal angioplasty with stent placement in the left renal artery and aneurysm embolization with fiber coils. The images before and after the procedure are shown in Figure 1. After the procedure, pulse therapy was suspended, and SC MTX (25 mg/week) was associated, allowing for a gradual reduction in oral corticotherapy. The patient evolved with a partial reduction in BP and kept using four classes of anti-hypertensive drugs.

**Case 3**

Female patient who, at the age of 8 years, began complaining of daily headache and abdominal pain, being then diagnosed with abdominal migraine. At the age of 10 years, she was referred to the Rheumatology Service due to arterial hypertension and the echographic finding of ascending aortic aneurysm. On physical examination: SAH, significant discrepancy in BP between the upper limbs (LUL, 170/100 mmHg; RUL, 150/90 mmHg), reduced left radial pulse amplitude and diastolic bruit over the aortic area. The laboratory tests evidenced increased inflammatory activity. The imaging studies suggested TA.

Pulse therapy was initiated with MTP associated with oral prednisone (1 mg/kg/day), subsequently changed to pulse therapy with CTX due to partial response to corticoid. The
patient evolved with partial remission of symptoms, but developed exogenous Cushing syndrome with SAH refractory to the use of five anti-hypertensive drugs. Immunosuppressive therapy with SC MTX (25 mg/week) was maintained.

Table 1 lists the inflammatory activity tests, at diagnosis and after treatment, and the patients’ radiological findings at diagnosis.

**DISCUSSION**

TA is rarely described in the pediatric age group, especially among us. In the international literature, a recent review article reported a total of 241 TA cases published in the pediatric age group.5 So far, to our knowledge, 21 pediatric cases have been published in Brazil.5-9 We report three patients with TA, corresponding to 14.2% of the national cases published.

Table 1 lists the inflammatory activity tests, at diagnosis and after treatment, and the patients’ radiological findings at diagnosis.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Inflammatory activity tests and radiologic findings</th>
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<tbody>
<tr>
<td></td>
<td>Case 1</td>
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<tr>
<td>ESR at diagnosis</td>
<td>107 mm/1st hour</td>
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<tr>
<td>CRP at diagnosis</td>
<td>74.2 mg/L</td>
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<tr>
<td>ESR after treatment</td>
<td>6 mm/1st hour</td>
</tr>
<tr>
<td>CRP after treatment</td>
<td>Negative</td>
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ESR: erythrocyte sedimentation rate; PCR: C-reactive protein.

In childhood, headache is the most frequent initial non-specific symptom of TA, occurring in 31% of cases.1,10 Our three patients had headache, emphasizing the inclusion of TA in the differential etiological diagnosis. Two patients reported fatigue, a common complaint in the literature, which corroborates the need for giving attention to that complaint. One patient reported claudication of the upper limbs, which is highly specific for TA.1 Abdominal pain occurs in 5% to 50% of the cases10 and was reported in our younger patient.

Arterial hypertension is the most common finding on physical examination of children and adolescents with TA (82.6%), and often suggests the diagnosis.10 All patients were hypertensive at the diagnosis, which led to the referral of two of them. In literature, the prevalence of such findings varies greatly, occurring in 5% to 58% of patients, probably due to the small number of cases published.

The tests of inflammatory activity are elevated in most cases,3,10 similarly to our results. In our cases, this finding and their clinical features supported the request for imaging studies and helped to establish our patients’ diagnosis.

The characteristic finding on angiography is the diffuse involvement of the aorta. The most commonly found lesion is stenosis (53%), followed by occlusion (21%), and aneurysm (10%). The most affected arteries are the renal arteries (73%).10 Our cases are in accordance with those in literature: two patients had stenosis, occlusion, and aneurysm, and one patient had stenosis and diffuse occlusion of the aorta. All patients had impairment of the renal artery.

The treatment of TA consists of prescribing corticosteroids, which can be associated, initially or during the evolution, with either CTX or MTX in cases of progressive disease, or biologic agents in resistant cases. Surgical intervention may have good results in cases of severe renovascular hypertension.1,10 All patients received initial treatment with corticosteroids, and subsequent association of MTX. Only the patient of case 2 did not receive CTX, because she underwent the intravascular procedure. The patient of case 1 received infliximab because of resistance to immunosuppressive drugs. All our patients had a good response to therapy and had their inflammatory activity normalized, maintaining SAH despite the use of anti-hypertensive drugs.

The report of rare cases, such as the ones in this article, helps to improve the knowledge of pediatricians and rheumatologists about TA in childhood, allowing early diagnosis and better therapeutic results.
REFERENCES


