Co-occurrence of Takayasu's arteritis and tuberculosis: Report of a Tunisian pediatric case

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ABSTRACT

Few reports on co-occurrence of Takayasu's arteritis (TA) and tuberculosis (Tb) have been published in childhood. A 12-year-old girl presented with 4-month's history of a dry cough, persistent fever, marked weakness, and weight loss. Physical examination revealed impalpable peripheral pulses and unrecordable blood pressure (BP) on upper limbs. In lower limbs, peripheral pulses were normal and BP reached respectively 160/90 and 140/87 mmHg. Laboratory investigations showed an erythrocyte sedimentation rate at 140 mm in the 1st h and microcytic anemia (8.6 g/dl). Doppler ultrasound and computed tomography angiography revealed significant thickening of the aortic-arch and both common carotid arteries wall, with luminal narrowing of the right common carotid and its branches and severe stenosis of the left subclavian artery. Simultaneously, the diagnosis of active pulmonary Tb was achieved based on radiological data, positive Mantoux test and successful response to antitubercular drugs. During follow-up, corticostetroids and methotrexate were required to control TA relapses.

Keywords: Child, takayasu arteritis, tuberculosis

INTRODUCTION

Takayasu's arteritis (TA) is a rare primary vasculitis, predominantly affecting the aorta and its main branches. The chronic and progressive vessel wall inflammation leads to concentric wall thickening and stenosis producing a variety of ischemic symptoms or aneurysms, with a high incidence of morbidity and a significant risk of early death.[1] The etiopathogenesis of this disease is still poorly understood, but an autoimmune basis is widely suggested. In addition, genetic and environmental factors also probably play an important role.[1] Among the environmental factors, evidence implicating *Mycobacterium tuberculosis* (MT) has been provided for more than five decades.[2-4] In spite of the clinical relationship between both conditions, no evident link has been proved until now. Until date, few reports on childhood TA associated with active tuberculosis (Tb) have been published.[3,4]

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We report here, the case of the co-occurrence of active pulmonary Tb and type I TA in a Tunisian girl; and we review published data analyzing the etiopathogenic link hypotheses between both conditions.

CASE REPORT

A 12-year-old girl was referred to the hospital for a 4-month's history of a dry cough, night sweats, persistent fever, marked weakness and weight loss of 3 kg. All these symptoms failed to respond to conventional antibiotics and inhaled corticosteroids. The patient was free from underlying diseases and had a record of Bacillus Calmette–Guérin vaccination at birth. There was no history of contact with Tb patient or family history of the vascular or rheumatic disorder.

On admission, she was afebrile and pale. Physical examination revealed impalpable peripheral pulses

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and inaudible blood pressure (BP) on upper limbs; BPs in right and left lower limbs were 160/90 mmHg and 140/87 mmHg, respectively. Auscultation showed heart rate at 108 beats/min with no added sound but revealed a systolic bruit along the path of the right external carotid artery. Peripheral pulses in lower limbs were full, and no bruit was detected over the abdomen or elsewhere. All other systemic examinations including pulmonary auscultation were normal.

Laboratory findings were: White blood cells at 8600/mm^3, hemoglobin at 8.6 g/dl, platelet counts at 522,000/mm^3, reticulocytes at 105,900 /mm^3, serum ferritin at 417 µg/l. Coombs test was negative. Erythrocyte sedimentation rate (ESR) was at 140 mm/h, C-reactive protein (CRP) was at 125 mg/L; fibrinogen was 7.12 g/L; albuminemia was at 21.1 g/l and α2- and γ-globulinemia were respectively at 15.2 g/l and 14 g/l. Serum electrolytes, liver and kidney function tests and urinary analysis were normal. Viral markers were negative for hepatitis B and C, human immunodeficiency virus, cytomegalovirus and Epstein-Barr virus. Antinuclear antibody, antineutrophil cytoplasmic antibodies, antiphospholipid and anticardiolipin antibodies were negative.

Doppler ultrasound and computed tomography (CT) angiography scans showed circumferential wall thickening of both common carotid arteries [Figure 1a] leading to stenosis of the right common carotid [Figure 1b] and its branches and severe stenosis of the left subclavian artery [Figure 2a and b] but excluded further vessel involvement of descending aorta, renal, or cerebral arteries. The ophthalmological examination was normal.

Investigations for Tb showed a strongly positive Mantoux test at 20 mm and positive Quantiferon-TB test. However, three specimens of sputum smear and culture for acid-fast bacilli were negative.

Chest X-ray/CT scans revealed numerous parenchymal nodes in both lungs associated to hilar lymphadenopathy suggesting active Tb [Figure 3a and b]. All these data were compatible with the diagnosis of TA according to the final EULAR/PRINTO/PRES TA criteria [Table 1] associated with active pulmonary Tb.[5]

The patient was placed then on antitubercular therapy, with oral prednisone (0.5 mg/kg/day) and low-dose aspirin for its antithromboxane effect. Within 4 months of treatment, the patient showed clinical recovery of fever, dry cough, and night sweats. However, inflammatory activity persisted (ESR: 79 mm/h; CRP: 91mg/dL; hemoglobin: 9.9g/dl). Immediately after stopping antitubercular drugs, the prednisone dose was increased to 2 mg/kg/day for 30 days. Then, prednisone dose was progressively decreased. Acute phase reactants returned to normal values. During 4 years of follow-up, subsequent relapses were observed whenever prednisone dose decreased to under 20 mg/day without new vessel involvement or progression of the previous vascular damage. Oral methotrexate (12.5 mg/m^2/week) was added then leading to relapse spacing and reduction of corticosteroids dose to 10 mg/kg each 2 days.

DISCUSSION

We report hereby the clinical findings of the co-occurrence of active pulmonary Tb and type I TA in a pediatric patient. In Tunisia, 2000 new cases of Tb are diagnosed each year with an incidence at 22.4/10^5 in 2010. However, an exhaustive electronic search found only 75 cases of TA published over 25 years, among them only one pediatric case in a 12-year-old boy who curiously has presented

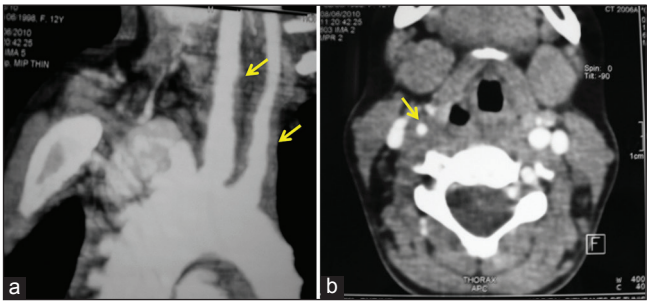

Figure 1: (a) Cervical computed tomography angiography scans (sagittal section) circumferential wall thickening of both common carotid arteries, (b) cervical computed tomography angiography scans (cross section) stenosis of the 2/3 vascular area of the right common carotid

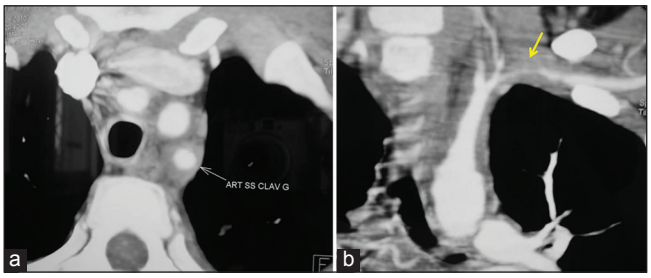

Figure 2: (a) Cervical computed tomography angiography scans (cross section), (b) cervical computed tomography angiography scans (sagittal section) a left subclavian artery, severe stenosis of two centimeters

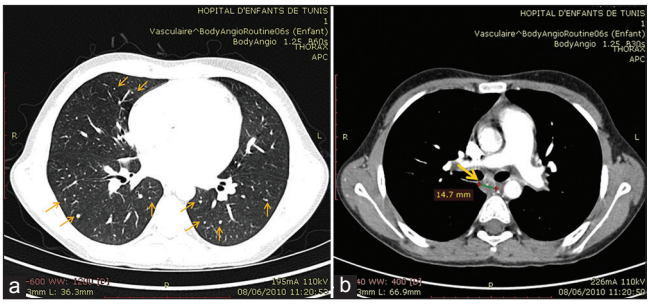

Figure 3: (a) Thoracic computed tomography angiography scans, bilateral pulmonary nodes, (b) thoracic computed tomography angiography scans (mediastinal window), hilary lymphadenopathy

Table 1: EULAR/PRINTO/PRES criteria and classification definition of Takayasu arteritis

	Mandatory criteria
Angiographic abnormality	Angiography (conventional, CT, and MRI) of the aorta, its main branches or pulmonary arteries showing aneurysm/dilatation, narrowing, occlusion, or thickened arterial wall, not due to any other causes
	Additional criteria (need one of the five)
Pulse deficit or claudication	Lost/decreased/unequal peripheral artery pulse Symptoms of claudication: focal muscle pain induced by physical activity
Blood pressure discrepancy	Discrepancy of four-limb systolic blood pressure >10 mmHg in any limb
Bruits	Audible murmurs or palpable thrills over large arteries
Hypertension	Systolic/diastolic blood pressure >95th centile for height
Acute phase reactant	Erythrocyte sedimentation rate (ESR) >20 mm per hour or C reactive protein (CRP) above normal

cervical Tb lymphadenitis 3 years prior to TA.[6]

Diagnosis and treatment of TA during childhood remain challenging entities.[1] The diagnosis is often established in advanced stages of the disease due to the nonspecific symptoms in this age.[2] Fever, weakness, and weight loss observed in TA are common symptoms in infectious diseases in childhood, especially in Tb. In our patient, clinicians were focused on respiratory symptoms and TA was diagnosed secondarily, 4 months later following a complete physical examination. At this time, the patient fulfilled all diagnostic criteria of the disease[5] with the coexistence of both inflammatory and fibrotic phase of the disease.

Nevertheless, we failed to prove active Tb upon positive culture for MT. Indeed, microbiological confirmation of childhood pulmonary Tb is not always achieved because of the difficulty of a collection of specimens and low sensitivity of smear microscopy. Among 15 studies, including 4768 respiratory specimens in 3640 children investigated for pulmonary Tb, Detjen *et al.*, found only 12% positive culture tests.[7] In our report, the diagnosis of Tb was highly probable upon combined criteria for a high index of presumption. In addition to clinical symptoms with a chronic cough and fever, positive Mantoux test and Quantiferon-TB and suggestive radiological abnormalities, the patient showed complete recovery of all these symptoms with antitubercular drugs. Furthermore, chronic cough has not been cited in the literature as a diagnostic criterion of TA[2,5] and pulmonary involvement, results in wall thickening and luminal stenosis or occlusion of pulmonary artery on computed tomography angiography scans.[8]

The natural history of this arteritis is highly variable. The response of TA to anti-tubercular drugs remains controversial among authors; Pantell and Goodman[4] described the case of a complete symptomatic remission as well as the return of pulses simultaneous with anti-Tb therapy. However, most reports on co-occurrence of active Tb and TA combined antitubercular drugs and corticosteroids. In our report, antitubercular drugs, had no effect on TA vasculitis and did not prevent new relapses. Hahn *et al.*[9] reported that 90% of their patients had strongly positive Mantoux tests, usually without active Tb, suggesting an autoimmune trigger.

The literature currently hypothesizes an autoimmune basis[10] and not a direct role of MT. Indeed, Arnaud *et al.*[11] failed to detect MT in arterial lesions of either active or inactive TA but did not exclude the possibility of a cross-reaction between mycobacterial and arterial antigens. Aggarwal *et al.*[12] showed that patients with TA have heightened humoral response to mycobacterial antigens, including the 65 kDa fraction, a heat shock protein that has also been found to be expressed in the arterial wall of TA patients. Recently, Soto *et al.*[13] identified in a case and control study a higher frequency of IS6110 and hupB gene sequences of MT and bovis in the aortic tissue of TA patients and in Tb compared to patients with atherosclerosis with important statistical differences suggesting that arterial damage could occur due to the previous infection with MT. Finally, the exact pathogenic sequence between TA and Tb remains to be elucidated.

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Conflicts of interest

There are no conflicts of interest.

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