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Review

Small vessel involvement in Takayasu's arteritis

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ABSTRACT

Objectives: To describe the small retinal and systemic vessel involvement in Takayasu's arteritis.
Methods: We described 3 patients with Takayasu's arteritis and small retinal vessel occlusion seen in our department between 2004 and 2011. We performed an extensive literature review and provided a global analysis of small retinal vessel involvement in Takayasu arteritis (i.e., total number of patients analyzed = 9).
Results: Seven patients had small retinal artery occlusion, and two had venous involvement. Four cases were inaugural of the disease (44.4%). Takayasu's arteritis was extended (Type V) in the majority of patients presenting with small retinal vessel occlusion (5/9, 55.6%), and 8/9 reported cases (88.9%) presented with involvement of the supra-aortic branches. Immunosuppressive regimen allowed an improvement in 5/9 patients and stabilization in 1/9, but the situation worsened in 3/9 patients. The visual outcome was severe, and 3/9 patients (33.3%) experienced irreversible blindness.
Conclusion: Occlusion of small retinal vessels is a rare and severe microcirculatory complication in Takayasu's arteritis, as well as necrotizing cutaneous vasculitis or myocarditis. Small retinal vessel involvement can be inaugural of the disease and seriously impact the visual prognosis in TA patients.

Contents

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1. Introduction

Takayasu's arteritis (TA) is a large vessel vasculitis of unknown origin, leading to multiple organ damages because of tissue hypoperfusion, and secondary chronic ischemia. The disease preferentially occurs in young women, especially in Asia and Middle East, but has a worldwide repartition [1]. The main pathological features are granulomatous inflammatory panarteritis, with intimal proliferation and disruption of the elastic lamina. Although the pathogenesis is unclear, an acute vascular inflammation is observed. This may be due to the activation of the MICA/NKG2D pathway in response to an unknown stimulus, resulting in activation of T and NK cells recruited to the vascular wall. Secondary production of pro-inflammatory cytokines and interferon-γ by Th1 lymphocytes induces activation of macrophages, release of VEGF and PDGF, and intimal proliferation [2]. This results in luminal reduction of the large vessels, mostly in the subclavian arteries and the aortic arch branches, but can occur in any segment [1,3]. The diagnosis of large vessel arteritis is usually suspected clinically and confirmed with international criteria [4], along with biological inflammation. MRI can be performed at diagnosis to assess vascular inflammation instead of the classical angiography. However, its performance in monitoring disease activity is not good [5], and non invasive PET scan has to be preferred [6]. Usual therapies consist in cortisteroids and immunosuppressive drugs (such as methotrexate) in severe or refractory cases. However, failure of these conventional regimens can occur. In such patients, a good efficacy of anti-TNFa agents has been assessed on large vessel involvement [7].

In the course of Takayasu's arteritis, ocular manifestations are described in 8.1–68% of cases in TA [1,8,9], especially in the late course of the disease. They are usually associated with ischemic lesions secondary to chronic hypoxia due to common carotid involvement. Several ocular lesions have been reported (i.e., uveitis, scleritis, glaucoma, retinopathies), and most of the published cases come from Asian countries [8,10–21]. The retinal manifestations are the most frequently reported ocular lesions in TA (up to 35% patients) and were the most extensively studied [8,19,20].

One of the major retinal involvement is the so-called “Takayasu's retinopathy”, a specific manifestation secondary to carotid involvement with hypoperfusion of the eye [22]. Patients may also present with hypertensive retinopathy, mostly attributed to renovascular chronic systemic hypertension due to renal artery occlusion. Like Takayasu's retinopathy, hypertensive retinopathy may preferentially occur in chronic state, when systemic damages have already occurred [8,19].

Besides these two “classical” patterns of retinal lesions in TA, small retinal vessel occlusion has been exceptionally described, with only few case reports in the literature. Importantly, these manifestations can be inaugural of the disease, remain often misdiagnosed and seriously impact the visual prognosis in TA patients.

We here propose the detailed analysis and outcome of three consecutive patients seen in our hospital between 2004 and 2011 who presented with atypical retinal vessel occlusion related to TA. We also reviewed available data from the literature on small retinal vessel occlusion in TA and found 6 additional cases. Lastly, we aimed to provide a large review of the prevalence and clinical spectrum of ocular lesions in TA.

2. Patients and methods

2.1. Patients

Between 2004 and 2011, among 90 patients diagnosed with Takayasu's arteritis and followed in our department of Internal Medicine, three (3.3%) were referred to the department of Ophthalmology for small retinal vessel occlusion. The systemic and ophthalmological data were retrospectively extracted from their medical files (NN and NB) and are described below. All patients fulfilled the ACR criteria [4]. The criteria included: an age<40 years at disease onset, claudication of extremities, a decreased brachial artery pulse, a blood pressure>10 mm Hg between arms, an audible bruit over subclavian arteries or aorta, an abnormal arteriography (at least 3 of the 6 proposed criteria required for diagnosis).

2.2. Definitions

2.2.1. Classification of TA

We used the International Classification [23] in order to standardize the extent of the arterial involvement of our patients, as follows: Type I: branches of the aortic arch; Type IIa: ascending aorta, aortic arch, and branches of the aortic arch; Type IIb: ascending aorta, aortic arch, and its branches and thoracic descending aorta; Type III: thoracic descending aorta, abdominal aorta, and/or renal arteries; Type IV: abdominal aorta and/or renal arteries and Type V: features of Type IIb and Type IV. However, some patients of the literature could have been classified with the previous Ueno and Lupi-Herrera classification [24] because of the publication date.

2.2.2. Disease activity assessment

Disease activity at the time of ocular manifestations and during follow-up was assessed by the NIH score, including four criteria: presence of ischemic signs (claudication, absence of pulses, carotidodynia, SBP difference), abnormal angiography, systemic symptoms (fever, arthralgia) and inflammatory disorders (i.e., elevated ESR or CRP), two of these features being new or worse [1].

Visual acuity was quantified using the Logarithm of the Minimum Angle of Resolution (LogMAR) scale. Indeed, the visual acuity is represented as the reciprocal of the minimal angle of resolution (the smallest letters resolved) at a given distance and at high contrast, and its evaluation may differ between scales (i.e., Snellen's, Vernier's…). Using the LogMAR scale allows comparison between examination and standardization of the values [25]. Ophthalmological remission and stabilization were defined as the resolution or the persistence without worsening of the clinical symptoms, respectively.

2.2.3. Small retinal vessel involvement

Small retinal vessel involvement was suspected by history of sudden blindness, amaurosis fugax or blurring of the vision. It was confirmed by fundus ophthalmoscopy and/or fluorescein angiography (i.e., prolonged filling time of the concerned vessel or absence of dye transit).

2.2.4. Literature review methods

In order to provide a global analysis of the small retinal vessel involvement in TA, and to describe the general ocular involvement in this disease, we performed a review of the literature using MEDLINE

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