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## Case report

# Difficulties in the differential diagnosis between Takayasu arteritis and rheumatic fever: case report<sup>☆</sup>



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### ABSTRACT

In this article, we present the case of a patient with heart failure with biological aortic valve prosthesis and multiple vascular changes consistent with Takayasu arteritis (TA) who was seen in our department receiving corticosteroids and secondary prevention of rheumatic fever (RF); it was not possible to exclude the association between both diseases.

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### Dificuldades no diagnóstico diferencial entre arterite de Takayasu e febre reumática: relato de caso

### RESUMO

Apresentamos o caso de uma paciente portadora de insuficiência cardíaca com prótese valvar aórtica biológica e alterações vasculares compatíveis com arterite de Takayasu (AT) que chegou ao serviço em uso de corticoides e em profilaxia para febre reumática (FR). Não foi possível afastar a associação entre ambas as enfermidades.

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## Introduction

Takayasu arteritis (TA) is a large-vessel vasculitis of unknown etiology, affecting the aorta and its main branches. This disease primarily affects females around the third decade of life, in different parts of the world.<sup>1</sup> The diagnosis associates clinical findings and inflammatory laboratory parameters with imaging studies, given that, to date, no specific biomarkers were identified.<sup>2</sup> A critical issue concerns its pathophysiology; an association with tuberculosis has been suggested, since both diseases show granulomatous lesions and present a similar geographic distribution, being more prevalent in Asia, Africa and South America.<sup>3</sup>

Rheumatic fever (RF) is an inflammatory systemic disease determined by an immune response to infection by group A beta-hemolytic *Streptococcus pyogenes* in genetically predisposed individuals after infection of upper airways,<sup>4</sup> and generally affects children and young adults in economically disadvantaged populations.<sup>5</sup> The Jones criteria<sup>6</sup> are used for diagnosis, which must be established early to ensure immediate treatment in order to prevent carditis, its most severe form, which may follow a chronic course and cause significant morbidity and mortality.<sup>7</sup>

RF patients may suffer pancarditis, and endocardial involvement is the most severe consequence, because the valve lesions may progress to permanent damage, determining the clinical picture and the prognosis of the disease. The mitral and aortic valves are most often affected, with regurgitation in the acute phase, and stenosis with progression of the disease.<sup>7</sup>

In this paper, we present the case of a female patient admitted to the Hospital de Clinicas, Universidade Federal do Triangulo Mineiro (HC-UFTM) with heart failure (HF) decompensation, referring a previous diagnosis of TA and RF and with an unsystematic treatment for both diseases.

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## Case report

DPS, female, 37 years old, Caucasian, was admitted to the HC-UFTM in January 2013 with a decompensated HF. She reported that at the age of 15 started progressively with exertional dyspnea, asthenia, generalized arthralgia, daily high fever, swelling in the lower limbs and large joints, and a difficult-to-control hypertension, having been diagnosed with RF and started secondary prevention with benzathine penicillin in addition to prednisone (intravenously and then maintenance doses of 80 mg/day on average) and captopril, digoxin, furosemide, spironolactone, nifedipine and amiodarone. At the age of 21 she presented a new decompensation, being diagnosed with TA with aortic, renal, carotid and subclavian involvement; indicated a non-specified, non-performed surgical procedure, opting to keep the current clinical treatment at that time. At the age of 28, the patient was submitted to an aortic valve replacement procedure with biological prosthesis. She refers that, throughout this period, she remained on prednisone (20 mg/day on average), benzathine penicillin and the other drugs mentioned above. At her last admission, she started presenting with chest pain, palpitation, exertional

dyspnea, asthenia, fainting, lower limb edema and hypotension. Physical examination revealed large discrepancies of blood pressure and pulses, as follows: right upper limb: 60/40; pulses present – left upper limb: blood pressure and unidentified pulses – right lower limb: 180/70; pulses present – left lower limb: 120/70, thin pulses. She also presented an aortic and mitral systolic murmur, aortic diastolic murmur, and bilateral carotid and renal bruits, especially on the left side. The patient was admitted to the ICU, when clinical treatment was introduced for HF, with improvement of her clinical picture.

The patient brought with her several old imaging studies; one of these tests was a coronary angiography carried out in 2003, showing carotid (both), subclavian and aorta involvement – findings suggestive of TA and of severe aortic regurgitation. An echocardiogram (ECHO) carried out in 2011 found moderate mitral regurgitation and double lesion in her aortic valve prosthesis. The patient also brought a biopsy report of her native aortic valve, to which we had access only to this report (and not to the slide), showing “strong fibro-hyalinosis, chronic inflammation and edema focuses compatible with valve degeneration.” Of the tests performed during hospitalization, blood count, biochemistry and protein electrophoresis were normal, and inflammatory markers were always negative; ECHO confirmed the previous findings and a progression of HF with an ejection fraction (EF) dropping from 79% to 35%; the coronary angiography revealed, in addition to preexisting lesions, an ostial occlusion of right coronary artery; and the arteriography displayed an aortic bioprosthesis with discrete failure and an intra-prosthesis saccular image suggestive of pseudo-aneurysm or dissection, as well as severe bilateral involvement of subclavian and carotid vessels, with vicarious vertebral arteries.

Although the patient had an indication for surgical approach, the procedure was contraindicated due to the high cardiovascular risk. She was assessed by the Rheumatology team, which confirmed the diagnosis of TA associated or not with RF. Anti-DNase B and inflammatory tests were ordered, all of them with negative results. Secondary prophylaxis with benzathine penicillin and oral treatment with prednisone were maintained, besides a careful follow-up.

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## Discussion

In both TA and RF, cardiac involvement is the major determinant of morbidity and mortality. The early clinical and epidemiological picture of this patient is common to both diseases,<sup>1</sup> and while TA occurs rarely, the prevalence of RF in our population makes it imperative that one always keeps this diagnosis in mind. In a recent study among Pediatric Rheumatologists in São Paulo, it was found that RF, albeit with a progressive reduction in incidence, was diagnosed more often in private health centers; on the other hand, TA and other vasculitides were diagnosed more often in public system.<sup>8</sup>

A diagnosis of TA was straightforward for this patient; the remaining doubts were whether the disease was active, or if the patient was suffering the sequels of previous outbreaks, and if there was an association with RF.

At the time, our patient had no evidence of inflammatory activity. These parameters can help in the diagnosis and monitoring of TA, but do not rule out disease activity; in this scenario, imaging studies are the gold standard, whereby frank disease progression was observed.

The greatest difficulty was in relation to the referred diagnosis of RF, since there was no way to confirm or refute this hypothesis at a time of such advanced cardiac lesions and the concomitant pathology determinant of structural heart damage. Although unlikely, we could not rule out the association of both diseases. In a study by Doi et al., a patient with coarctation of the aorta secondary to TA and mitral stenosis due to RF was described.<sup>9</sup> Castlemain et al. described a female patient with aortic regurgitation secondary to dilation of the aortic arch; these authors proposed the hypothesis of RF, and subsequently found that theirs was a case of TA.<sup>1</sup> Gangahanumaiah et al. described the case of a female patient aged 29 with HF, history suggestive of RF and with an ECHO showing severe mitral regurgitation, mild aortic regurgitation, pulmonary hypertension, with left ventricular function maintained. Both valves were replaced; and signs suggestive of TA were observed in pathological studies.<sup>10</sup> Ravelli et al. reported the case of a teenager with nonspecific symptoms for 2 years who developed aortic regurgitation; the primary diagnostic hypothesis proposed for this teenager was RF, and afterwards TA was diagnosed by imaging studies.<sup>11</sup>

Valve changes are not uncommon in patients with TA, and usually these problems stem from structural heart and vascular injuries.<sup>12</sup> In such cases, aortic regurgitation, followed by mitral regurgitation, occurs more frequently.<sup>13</sup> Abid-Allah et al. described heart valve involvement in 4 cases of TA, as follows: an isolated mitral regurgitation; two isolated aortic regurgitations; two associations of mitral and aortic regurgitation, with hypertension in all cases.<sup>12</sup> Brady et al. described the case of a female patient with TA and aortic regurgitation and heart failure with a normal mitral valve.<sup>14</sup> In a Brazilian series of patients with RF, carditis was the second most frequent major sign, predominantly occurring in females, and the most common valve change was mitral regurgitation.<sup>15</sup>

Difficulties in meeting diagnostic criteria in TA are constantly mentioned in the literature, and this contributes to hinder the differential diagnosis.<sup>16</sup> With regard to our patient, although we consider more likely that any changes are really due to TA, in our clinical and epidemiological context, we must always consider the hypothesis of RF in the differential diagnosis for all patients with inflammatory systemic signs and heart manifestations, especially when there is mitral valve involvement.

### Conflicts of interest

The authors declare no conflicts of interest.

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