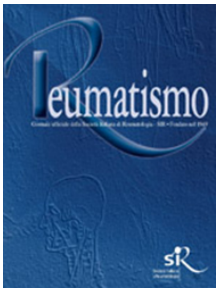

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Inflammatory back pain as an unusual manifestation of Takayasu arteritis: a case report

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Summary
Takayasu arteritis and spondyloarthritis are two rheumatological diseases whose co-existence is well-documented in the literature. Data on the presence of inflammatory back pain in Takayasu arteritis without a diagnosis of spondyloarthritis, however, is scarce. Here, we present a 33-year-old man who was admitted to the emergency department with acute-onset chest pain associated with left carotidynia, carotid bruit, and left arm claudication, normal electrocardiogram and computed tomography angiographic features suggesting Takayasu arteritis, including stenosis and occlusion of the aorta and its branches. Two years prior, he had undergone a clinical work-up for an inflammatory back pain accompanied by alternating buttocks pain, morning stiffness lasting more than half an hour, and heel pain. HLA-B27 status and magnetic resonance imaging of the sacroiliac joints were both negative. He was prescribed non-steroidal anti-inflammatory drugs and was placed on adalimumab 40 mg SC every two weeks but had to switch to etanercept two months before his emergency admission due to supply issues. Oral prednisolone was initiated at a dose of 60 mg/day with symptomatic improvement in both his inflammatory back pain and his chest pain, but he had to be switched to methotrexate and infliximab due to steroid side effects. Inflammatory aortitis should be considered as a possibility during the assessment of inflammatory back pain to mitigate the risks of delayed diagnosis.

Introduction

Takayasu arteritis (TA) is a granulomatous inflammatory condition of unknown etiology affecting large arterial vessels, causing occlusion, stenosis, or aneurysmal dilatation (1, 2). The disease was first described in Japan, where the incidence is estimated to be 150 cases per million per year (3). In Iraq, no official records have been published. However, the incidence estimate in Turkey, a neighboring country, was 3.4 cases per million per year (4). Although the co-existence of TA and spondyloarthritis (SpA) is well documented in the literature (4-6), the presence of inflammatory back pain (IBP) in TA without a diagnosis of SpA has been scarcely reported (7). Here, we present a case of TA with IBP not fulfilling the Assessment of Spondyloarthritis International Society (ASAS) criteria for SpA.

Case Report

In July 2021, a 31-year-old man presented to the rheumatology clinic with inflammatory low back pain (fulfilling the ASAS definition) of 5 years duration (8). It was accompanied by alternating buttocks pain, morning stiffness lasting more than half an hour, heel pain, sleep disturbances, and fatigue. Additionally, the patient has been experiencing a headache and left-sided neck pain for a few years. The patient denied any history of red eyes, painful digits or peripheral joints, dysuria, or skin lesions but reported chronic mucus-containing, painless diarrhea once a week. Family history of the same condition or the above-mentioned clinical features was negative.

Musculoskeletal examination revealed positive provocative tests for the sacroiliac joints (compression, distraction, and FABER) and tenderness at the attachments of the Achilles tendon. Investigations showed a normal complete blood count, an elevated erythrocyte sedimentation rate (ESR) of 128 mm/1st hr, and negative serological tests (anti- double stranded DNA and anti-cyclic citrullinated peptide antibodies). HLA-B27 status was negative. Inflammatory bowel disease was suspected; therefore, an endoscopy was performed. However, the biopsy only showed mild, non-specific ileitis. The X-ray and magnetic resonance imaging (MRI) of the sacroiliac joint were not significant.

He was considered a case of enthesitis-related SpA and was given a trial of two types of non-steroidal anti-inflammatory drugs (NSAIDs) 2 weeks apart. However, due to a very mild symptomatic response, the decision was made to start adalimumab 40 mg SC every 2 weeks, which resulted in an improvement in his back pain severity from 8 to 2 on the visual analog scale (VAS) score.

Five months before the above presentation, the patient experienced new-onset palpitations, for which a cardiologist's opinion was sought. His blood pressure was elevated to above 160/90 mmHg. An echocardiographic study (Figure 1) revealed mild to moderate aortic regurgitation due to a functionally bicuspid valve and dilated aortic root from the sinus and proximal ascending aorta (37, 43, and 47 mm) with an arch measuring 41 mm in diameter. Mild concentric left ventricular hypertrophy with grade I diastolic dysfunction consistent with hypertensive heart disease was also noted. He was prescribed antihypertensive medications and placed on a 6-month follow-up but was non-compliant with both.

On January 19, 2023, he was switched from adalimumab to etanercept 50 mg/week SC due to supply issues.

In March 2023, the patient presented to the emergency room with acute-onset severe central chest pain and left upper limb pain extending to the fingers, accompanied by exertional dyspnea and sweating. His pulse was weaker on the left side, with left-sided carotidynia, bruit, and a blowing diastolic murmur heard best at the left lower sternal border. Baseline and follow-up electrocardiograms showed no ischemic changes, and his serum troponin was 0.1 mg/dL (N: 0.0-0.6 mg/dL).

His inflammatory markers were elevated (ESR: 90 mm/1st hr, C-reactive protein: 48 mg/dL), and he also reported an increase in the severity of his back pain in the weeks leading up to the emergency room admission. An echocardiogram showed that his condition has worsened since 2021 (Figure 1), with the aortic root and sinus dilating to 43, 44, and 49-50 mm, respectively. In light of the patient's previous medical history, the presence of inflammatory aortitis was considered, and he was referred to the

rheumatology department of Baghdad Teaching Hospital. Computed tomography (CT) angiography revealed circumferential medial thickening of the aorta (ascending, descending, and arch), celiac axis, and superior mesenteric artery, as well as occlusion of the right common carotid artery and stenosis of vertebral and subclavian arteries, bilaterally (Figure 2). A new MRI of the sacroiliac joints and lower lumbar spine was ordered and resulted negative. He was diagnosed with TA according to the classification criteria of the American College of Rheumatology (9), and oral prednisolone was initiated at 60 mg/day.

Two weeks after steroids were initiated, he had an ESR of 55mm/1st hr, and his IBP severity had gone from 7 to 4 on the VAS score. Methotrexate was added at 15 mg/week, steroids were down-titrated to reduce side effects (impotence and acne), and infliximab at a dose of 5 mg/kg IV was then initiated with the reduction of ESR to 35 mm/1st hr by the end of April. Surgery for aortic regurgitation is pending until his inflammatory condition is stabilized.

Discussion

SpA is a group of heterogeneous but overlapping disorders whose diagnosis depends largely on specific clinical features that are present in widely variable combinations in different patients, supported by radiology of the sacroiliac joint and spine, genetic status, and inflammatory markers. It is generally divided into axial SpA and peripheral SpA. IBP is a leading symptom in axial SpA.

The prevalence, epidemiology, and genetic characteristics of SpA vary among countries; in ankylosing spondylitis (AS), for example, the male-to-female ratio is 9:1 in Iraq but 2-3:1 in Europe (3). Additionally, HLA-B27 status is positive in 8% of the general population and 90% of those with AS in Europe; in contrast, it is positive in 2.1% of the general population and 55% of AS patients in Iraq (10-12), making it less sensitive as a diagnostic tool in Iraq. Furthermore, HLA-B27-negative AS patients are more likely to have a negative MRI (13). Positive ASAS classification criteria for axial SpA require either positive radiology (MRI or X-ray) or HLA-B27 status (8). Hence, AS is expected to be diagnosed with difficulty in countries like Iraq in the absence of modified criteria. The co-existence of TA with SpA has been reported in the literature on several occasions (4-6). However, data on the occurrence of IBP in aortitis or TA without a diagnosis of SpA is scarce. To our knowledge, there is only one paper reporting the presence of IBP without SpA in patients with TA (4). It described the prevalence of concomitant rheumatological disorders or isolated rheumatological symptoms in 198 patients with TA. The most common isolated rheumatological symptom after the exclusion of concomitant diagnoses (*e.g.*, AS) was IBP (24.7%) (4). However, this study did not elaborate on whether the back pain was a presenting symptom or not. Another paper has aimed at reporting clinical features of non-infectious aortitis caused by different rheumatological disorders (including TA and giant cell arteritis) in 32 patients (7). Although the only patient with TA in this group did not complain of IBP, the overall prevalence of IBP in the group was 28% (7).

Although enthesitis is included as an entry criterion in the ASAS criteria for peripheral SpA, when axial symptoms are present, such as IBP, it is recommended to use the axial SpA criteria to make the diagnosis (14). However, a diagnosis of axial SpA cannot be made either, because of the negative HLA-B27 and absence of sacroiliitis on imaging, which are entry criteria for axial SpA according to ASAS (8). In addition, the patient showed atypical features that make SpA less likely, namely, a poor response to NSAIDs and the absence of a family history. The presence of subtle symptoms of TA at presentation to the rheumatology clinic (*e.g.*, neck pain) and the recent diagnosis of hypertension (which might explain the headache) and aortic regurgitation in this young patient should make TA part of the differential diagnosis. Furthermore, the reduction in his IBP after the initiation of steroid treatment and the elimination of alternative potential causes of back pain, such as infections or tumors with MRI, point toward inflammatory aortitis as the cause of the IBP. It is worth mentioning that tumor necrosis factor inhibitors have been found to be effective in managing inflammation in patients with TA. However,

studies examining their protective effects against disease progression and the development of structural damage have shown contradictory results. Treatment with adalimumab in this patient might have masked symptoms of TA and discontinuing adalimumab and replacing it with etanercept could explain the TA relapse that followed shortly after (15). Further studies are needed to explore the association between TA and IBP.

The presence of IBP in the context of aortic regurgitation would probably raise suspicion of SpA-related aortitis rather than TA; however, given the evidence from the literature on the co-occurrence of TA and SpA, in addition to the presence of carotidynia, TA should not be disregarded.

The patient in this case report experienced a delay of at least 3 years in the diagnosis of TA, which may have contributed to the development of aortic regurgitation requiring surgery (1). Had the diagnosis of TA been considered (given the past medical history of IBP, hypertension, and carotidynia), a fludeoxyglucose F18 positron emission tomography-CT scan or angiography would have been ordered, and corticosteroids could have been initiated earlier and the complication prevented.

Conclusions

Inflammatory aortitis should be considered as a possibility during the assessment of IBP. Additional clinical manifestations such as an asymmetrical peripheral pulse, aortic regurgitation, carotidynia, and bruits should be actively sought to heighten the clinical suspicion of TA and mitigate the risk of a delayed diagnosis.

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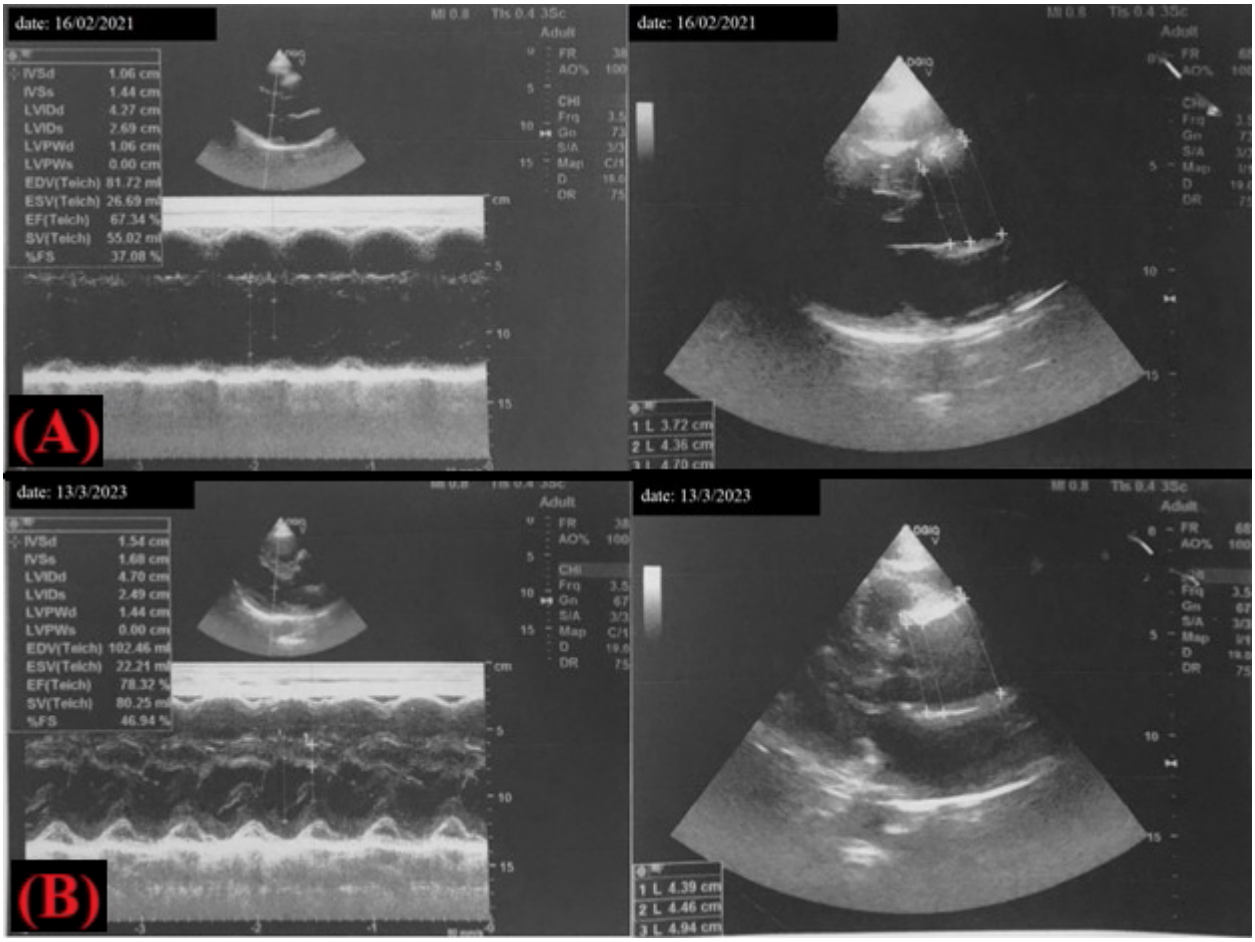

Figure 1. Echocardiogram studies. A) Baseline echocardiogram showing dilated aortic root from the sinus and proximal ascending aorta measuring 37 mm, 43 mm, and 47 mm, respectively; B) follow-up echocardiogram showing aortic root and sinus measuring 43, 44, and 49-50 mm, respectively.

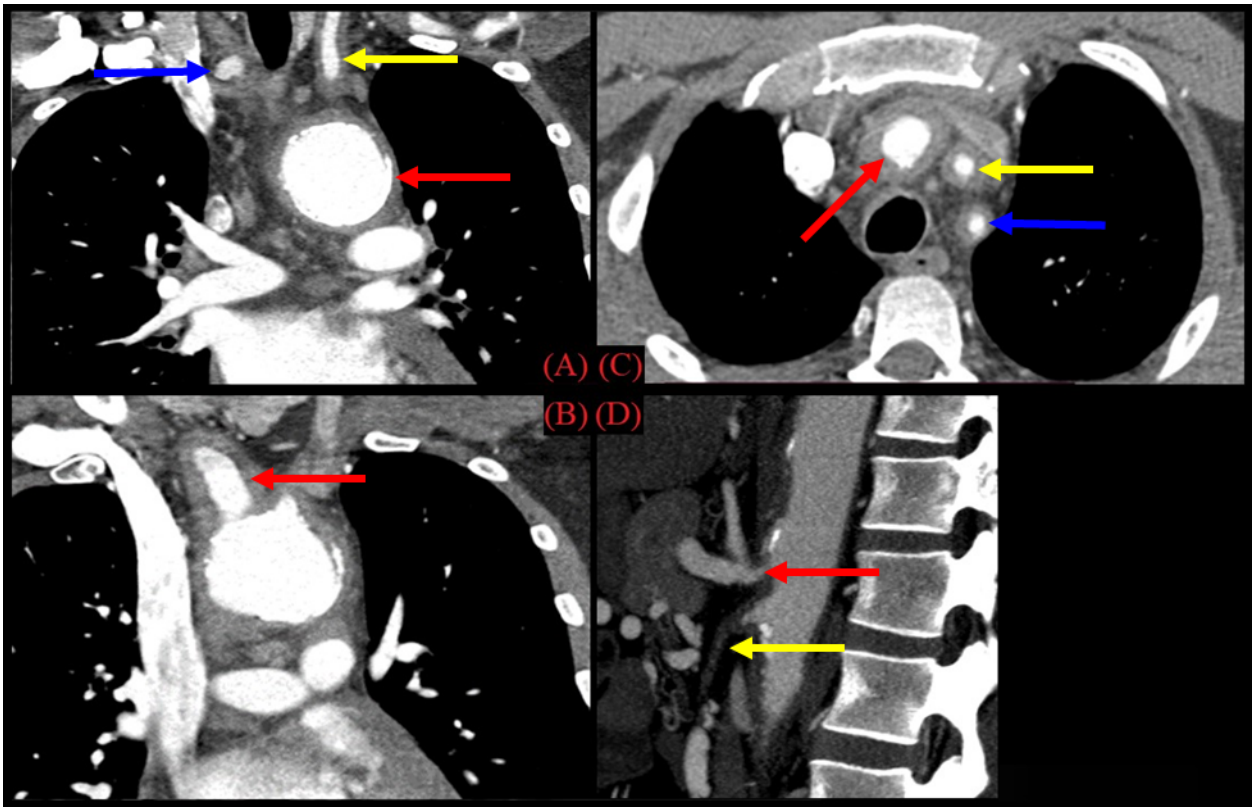

Figure 2. CT Angiogram. A) Aortic arc ectasia (red arrow) with occluded right brachiocephalic artery lacking contrast (blue arrow) and thickening of the left common carotid (blue arrow); B) ectasis and thickening of the right brachiocephalic artery (red arrow) with nearly 30% right subclavian artery stenosis; C) circumferential thickening of the origin of the left brachiocephalic (red arrow), left common carotid (yellow arrow), and left subclavian (blue arrow) arteries; D) near 75% celiac axis origin stenosis (red arrow) with occluded celiac axis (yellow arrow).