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Takayasu Arteritis with Concurrent Cushing's Syndrome: A Case Report

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ABSTRACT

Takayasu arteritis (TAK) is a rare autoimmune condition, often called pulseless disease, characterized by chronic inflammation of the aorta and its major branches. The exact cause remains unknown, but it is classified as large-vessel vasculitis. The condition can result in ischemic symptoms, organ damage, and complications due to reduced blood flow. TAK can indeed lead to stenosis of arterial walls, which may weaken and lead to aneurysms, high blood pressure, and eventually heart failure or stroke. Treatment primarily involves immunosuppressive therapy, with corticosteroids playing a central role, although glucocorticoid-sparing agents such as methotrexate and biologics like TNF inhibitors are becoming more commonly utilized. This case discusses a 26-year-old female diagnosed with TAK who developed subsequent iatrogenic Cushing's syndrome as a major complication from extended corticosteroid use. CT angiography confirmed the presence of Takayasu arteritis along with an uncommon finding of bilateral renal artery stenosis. The complexities of managing Takayasu arteritis (TAK) are heightened in patients who also have concurrent metabolic disorders like Cushing's syndrome. This situation necessitates a multidisciplinary approach to ensure effective treatment and achieve optimal clinical outcomes

Keywords: Autoimmune disease, Iatrogenic Cushing's syndrome, Glucocorticoid-sparing agents, Large-vessel vasculitis, Renal artery stenosis, Takayasu arteritis.

INTRODUCTION

Takayasu arteritis (TAK), a rare chronic inflammatory disease that primarily affects the aorta and its main branches, is classified as large-vessel vasculitis. The inflammation can cause thickening, narrowing, and scarring of arterial walls, potentially leading to organ damage and complications due to reduced circulation.[1] The exact cause of TAK is unknown but is believed to involve an autoimmune cell-mediated mechanism, characterized by extensive intimal thickening, medial and adventitial hypertrophy, and the infiltration of mononuclear cells, sometimes including giant cells. The annual incidence of Takayasu arteritis is estimated at 0.4–3.4 cases per million individuals, with a female predominance. Its prevalence varies by region, with Japan reporting the highest at approximately 40 cases per million, compared to around 9 cases per million in the USA.[2,3] Early manifestations of TAK include systemic inflammatory responses, such as fever, fatigue, and weight loss. During the acute phase of the disease, vascular

complications arise, including loss of pulse, pulse discrepancies, vascular murmurs (bruits), and ischemic symptoms downstream from areas of arterial blockage or narrowing. The gold standard for diagnosing Takayasu's Arteritis is angiography. Doppler and non-invasive MRA, however, can also produce just as good results.[4] Oral corticosteroid therapy is the first-line treatment for Takayasu's arteritis. Immunosuppressive agents are often added to reduce dependence on steroids and prevent relapse. In the 2017 JCS guidelines, the use of Tocilizumab in TAK patients was a Class I recommendation and TNF-inhibitor (adalimumab) use was a Class IIa recommendation. The use of immunosuppressants such as methotrexate, and azathioprine is a Class IIa or IIb recommendation for treating TAK in combination with Glucocorticoid therapy.[5,6,7]

CASE DESCRIPTION

A 26-year-old female patient presented to the emergency department with postictal confusion and altered sensorium following 2 episodes of GTCS. She had complaints of 10-15 episodes of vomiting along with headache for 2 days and visual impairment for 10 days. On admission, her pulse rate was feeble with blood pressure 80/50 mmHg which was stabilized immediately using intravenous noradrenaline. Other vital signs were within normal ranges. Emergency MRI Brain showed bilateral posterior parietal and occipital infarcts with a chronic lacunar infarct in the right corona radiata, capsuloganglionic region. ANCA (antineutrophil cytoplasmic antibodies) test was detected negative. The patient was referred to vascular surgery for further management.

There was a remarkable difference in blood pressure between the upper and lower limbs. The blood pressure in both upper limbs was normal, while in both lower limbs, it was 160/90mmHg. CT Aortogram showed vessel wall thickening with luminal narrowing in both the right and left common carotid arteries (CCAs), right proximal subclavian artery (SCA), and left external carotid artery. Thrombus was noted in the distal brachiocephalic trunk extending into the proximal right SCA, and mid-right CCA causing complete luminal occlusion. Renal Artery Doppler showed increased peak systolic velocity (PSV) of bilateral main renal and segmental arteries with an increased acceleration time of the right main renal artery. 2D Echo finding showed Concentric LVH, Gr-II Diastolic dysfunction (DDF) normal Left ventricular (LV) Systolic function (EF-50%). Laboratory findings revealed an increased (ESR) erythrocyte sedimentation rate (60 mm/hr) and C-reactive protein (22 mg/L).

Initially, the patient was treated with a 5-day course of pulse dose of intravenous Methylprednisolone 500 mg o.d. and switched to oral application with 60mg q.d. for 7 days. Initiation of glucocorticoid-sparing therapy with T. Methotrexate 15 mg once weekly was opted. This approach facilitated a gradual reduction in the prednisolone dosage to 20 mg per day, followed by further tapering. The patient's discharge medication otherwise included tablets of aspirin (75 mg o.d.), pantoprazole (40 mg o.d.), levetiracetam (500 mg b.d.), pregabalin (75 mg o.d.), atorvastatin (40 mg h/s), folic acid (5 mg alt days), vitamin D and calcium supplements.

Four months after discharge, the patient reported an ITAS (Indian Takayasu Arteritis Score) of 4, indicating mild disease activity, often reflecting disease alleviation. However, the patient complained of severe visual impairment, facial puffiness (moon face) with redness, skin itching, hirsutism, fatigue, and toothache associated with a cavity, suggestive of iatrogenic Cushing's syndrome. The patient's treatment plan was reviewed and potential adjustments were made. As the ITAS was 4, indicating mild-to-moderate disease activity, biologics were not considered at this stage. Instead, steroid-sparing agents were optimized, given the patient's tolerance to methotrexate, enabling a reduction in steroid use. The methotrexate dose was increased to 25mg per week and

prednisolone was reduced to 10mg per day. Close monitoring of endocrine therapy to mitigate Cushing's syndrome and regular ITAS scoring to guide adjustments was counseled. The patient was scheduled for follow-up appointments, including consultations with a rheumatologist, cardiologist, and endocrinologist.

Tests	Value
Hb	Normochromic, normocytes, and microcytes.
RBC	
WBC	No significant infection
Platelets	Normal
Blood urea	21 mg/dL
Serum Creatinine	0.48 mg/dL
Erythrocyte sedimentation rate	60 mm/hr
C- Reactive protein	24 (positive)
Antineutrophil cytoplasmic antibodies	Negative
D-Dimer	0.591 ng/ml
PT	14.6
INR	1.2

DISCUSSION

TAK is also called pulseless disease, aortic arch syndrome, young female arteritis, idiopathic aortitis, or Martorell syndrome.[8] The diagnosis of Takayasu arteritis is often delayed, typically being established months after the initial symptoms. To advance diagnosis and treatment in younger patients, a thorough clinical examination is recommended. In this case, the patient's presentation with multiple organ involvement, including cerebrovascular events, renal artery stenosis, and elevated inflammatory markers, is characteristic of TAK. The diagnostic workup confirmed the diagnosis, including imaging studies and laboratory tests. The patient received appropriate initial treatment with high-dose corticosteroids to control disease activity. However, prolonged corticosteroid use led to the development of iatrogenic Cushing's syndrome. The challenge lies in balancing disease control while maintaining immune function and minimizing corticosteroid side effects. In this case, a stepwise reduction in corticosteroid dosage was implemented to reduce the risk of adrenal insufficiency, along with optimization of steroid-sparing therapy with methotrexate. Since this patient has mild disease activity (ITAS score of 4) after four months post-discharge, biologic therapy (such as TNF inhibitors) would not be the first-line choice at this stage. The focus should remain on optimizing the steroid-sparing regimen, as steroid use is a key concern, especially given the development of iatrogenic Cushing's syndrome. Regular monitoring and continued use of methotrexate or other steroid-sparing agents can help reduce the need for corticosteroids and may prevent further flare-ups. Currently, there are several disease-modifying anti-rheumatic drugs available to help manage the side effects associated with high-dose systemic glucocorticoid therapy, which is typically used as the first-line treatment for acute TAK.[7,9]

Both conditions and their treatments can often cause cardiovascular risks, metabolic abnormalities, osteoporosis, and infections. TAK patients often face complications like hypertension, particularly if renal arteries are involved. In this case, the patient had discrepancies in blood pressure between the upper and lower limbs, highlighting the need for tailored BP control. Use of atorvastatin (40 mg) in the patient's regimen supports cardiovascular health by managing lipid profiles, alongside, aspirin (75 mg) is included to prevent thrombotic events. Vitamin D and calcium were prescribed to counteract corticosteroid-induced osteoporosis and improve bone health. Regular ITAS scoring helps guide treatment

adjustments and identify potential relapses. The Indian Takayasu Arteritis Score (ITAS2010) is a widely used tool to assess disease activity in Takayasu Arteritis. It evaluates both the systemic and vascular manifestations of the disease, including both clinical symptoms and laboratory markers (like ESR and CRP) to measure disease activity. The score helps in guiding treatment decisions, especially in determining when to introduce more aggressive therapies such as biologics.[10] If the patient's disease activity persists or worsens despite optimal medical therapy, consideration may be given to biologic therapies, such as tocilizumab or adalimumab, in consultation with a rheumatologist. Instructing the patient on recognizing signs of Cushing's syndrome, managing medication side effects, and adhering to follow-up appointments is vital. The management of TA and its complications requires close coordination between specialists to help mitigate these risks and ensure comprehensive patient care.

CONCLUSION

Takayasu arteritis and steroid-induced Cushing's syndrome are both complex conditions that require careful diagnosis and management. The interplay between these two conditions, where steroid therapy used to control TAK may induce Cushing's syndrome, necessitates careful steroid dose management, use of adjunct therapies to reduce steroid dependency, and close monitoring of clinical symptoms. While biologics like TNF inhibitors are an option for refractory cases or those with severe organ involvement, they should generally be reserved for patients who fail to respond to conventional therapies. Close monitoring, including regular assessment using tools like the Indian Takayasu Arteritis Score (ITAS2010), is crucial to guide treatment adjustments to prevent disease relapses and minimize long-term complications, such as organ damage and cardiovascular risks. This case emphasizes the importance of a thorough clinical evaluation and adjusting treatment strategies based on disease progression and side effects. Effective management of both conditions requires a personalized, patient-centered approach, improving quality of life and preventing long-term complications.

Declaration by Authors

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Abbreviations

ANCA: Antineutrophil cytoplasmic antibodies, CCA: common carotid artery, CRP: C-reactive protein, DDF: Diastolic dysfunction EF: Ejection fraction, ESR: erythrocyte sedimentation rate, GTCS: generalized tonic-clonic seizures, ITAS: Indian Takayasu Arteritis Score, JCS: Japanese Circulation Society, LV: left ventricular, MRA: Magnetic Resonance Angiography, PSV: Peak systolic velocity, SCA: subclavian artery, TAK: Takayasu arteritis, TNF: Tumor necrosis factor.

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