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Case Report

Acute Infliximab-Related Infusion Reaction in a Takayasu Arteritis Patient

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Introduction

Vasculitis is a pathologic process that results in damage and inflammation to blood vessels [1]. Takayasu Arteritis (TAK) is a chronic autoimmune vasculitis of large and medium sized arteries, most prevalent in the aortic arch and proximal great vessels. It is a rare disease, with its incidence estimated to be 2.6 cases per million per year, predominantly affecting young Asian women [2,3]. TAK has been found to be the highest prevalence in Japan (40 cases /million), and the lowest in the United States (0.9 cases /million) [4]. TAK is often referred to as the "pulseless disease" with weak upper extremity pulses because of aortic arch involvement [5]. The vessels typically involved include the aorta and the subclavian, carotid, axillary, and renal arteries [6]. Vascular changes in the renal arteries may lead to renal artery stenosis and resulting hypertension [7]. Other reported complications include cardiomyopathy, cerebrovascular events, sensorineural hearing loss, interstitial pulmonary fibrosis, and pneumonia [6]. Other symptoms of TAK may include flu-like symptoms, including night sweats, fever, and myalgias, in addition to arthritis, skin nodules, and ocular disturbances.

The etiology of TAK is unknown. However, patients have been found to have increased immunoglobulin titers against *M tuberculosis*, implicating previous tuberculosis infection as a possible predisposing factor. Another hypothesis suggests TAK may result from an autoimmune complement dependent cytotoxicity mediated by anti-endothelial cell antibodies [8]. Diagnosis of TAK is difficult due to the heterogeneity and non-specificity of clinical presentation in patients. The most commonly used diagnostic criteria is the 1990 American College of Rheumatology Classification criteria, which requires three out of six of the following criteria: age <40 years at onset, claudication of an extremity, decreased brachial artery pulse, a difference of >10 mmHg in systolic blood pressure between arms, a bruit over the subclavian arteries or aorta, and arteriographic evidence of narrowing of the aorta, its branches, or large arteries in the proximal upper or lower extremities [9]. Patients with TAK are often found to present with increased inflammatory markers such as C-Reactive Protein (CRP), and Erythrocyte Sedimentation Rate (ESR) [10]. Imaging arteries is useful in diagnosing TAK, distinguishing locations of vascular lesions, and determining disease progression [10]. Treatment of TAK is dependent on disease progression. High dose glucocorticoids are the first line treatment for active TAK and may be tapered to a maintenance dose with control of acute inflammation [11]. Immunosuppressive therapy may be used in conjunction with glucocorticoids in advanced cases. These include non-biological agents such as methotrexate, cyclophosphamide, azathioprine, and mycophenolate mofetil [10]. Biological agents have become more frequently used, including Anti-Tumor Necrosis Factor Alpha (TNFα) agents, rituximab, and tocilizumab. These are used as adjunctive therapies to glucocorticoids [12].

Case Presentation

Patient Description

A 42-year-old male with a four-year history of Takayasu Arteritis

was admitted to the emergency department following a routine infusion of infliximab (Remicade). Within an hour of the infusion, the patient experienced shortness of breath with upper back pain, burning chest pain, Left Lower Quadrant (LLQ) abdominal pain, and diaphoresis. He stated that these are similar symptoms to his Takayasu Arteritis flares; however, his flares usually develop over 2-3 days, and this was very sudden in onset. The patient also stated the only deviation from his normal routine was that he ate prior to his last infliximab treatment. The patient is a Gulf War veteran with a history of PTSD/depression, fibromyalgia, hypertension, and a Cerebrovascular Accident (CVA) 2 months prior with residual left sided weakness. Surgical history includes vasectomy and right sided knee surgery.

The patient is taking Losartan 50 mg QD, Sertraline 125 mg QD, Aspirin 81 mg QD, Zolpidem PRN, and Cyclobenzaprine PRN. The patient is also taking daily Vitamin D and Folic Acid supplements. For his TAK, the patient had been on infliximab 700 mg Q6 weeks, methotrexate 20 mg/week, azathioprine 50 mg QD, and prednisone 10 mg QD. Upon admission to the ED, the patient received solumedrol 125 IV since he was not able to complete his infliximab infusion. He also received Acetaminophen 975 PO and Zofran 4mg. On physical exam, the patient was found to be alert and oriented, with vital signs within normal range, although slightly tachycardic at 107 bpm. Blood tests and radiography were unremarkable. The next day, as recommended by the rheumatologist, the patient was able to receive the rest of his infliximab infusion with no complications and was discharged home on prednisone 10mg and Tylenol PRN. Three days following the completion of Iv infusion treatment, the patient was doing well and was free of symptoms.

Tests and Imaging

CT Angiography of the chest was obtained to visualize the aorta and its branch vessels (Figure A, B). The imaging showed diffuse thickening of the wall of the aortic arch, the descending component, and the ascending aorta, with additional surrounding inflammation of the mediastinal fat. The distal abdominal aorta was thickened and inflamed to a level slightly above the bifurcation. There was no evidence of aortic dissection, strictures, or significant dilatation or aneurysm formation. Pulmonary vasculature was grossly unremarkable with no evidence of pulmonary embolism. Diffuse 2 to 5 mm micronodular infiltrates were found scattered throughout both lungs and were determined to likely be nonspecific inflammation.

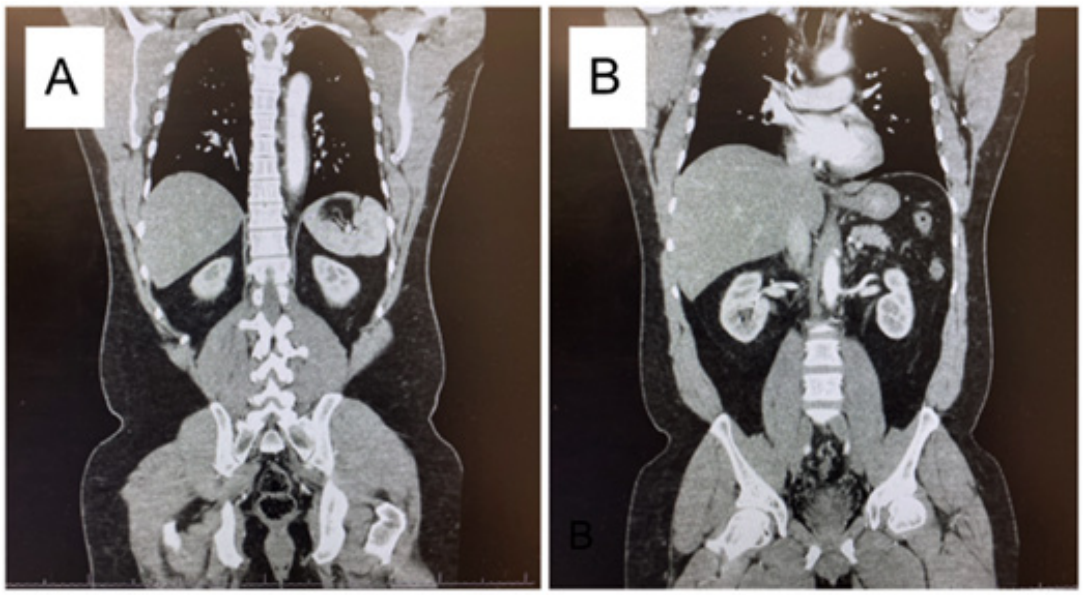

Figure:
A.CT angiography of the chest-diffuse thickening of the descending aorta.
B.CT angiography of the chest-thickening of the aortic arch and ascending components, with the distal abdominal aorta thickened to a level slightly above the bifurcation. There is surrounding inflammation of mediastinal fat as well.

Discussion

Infliximab is a monoclonal antibody that targets pro-inflammatory cytokine TNFα. Infusion-related reactions following infliximab administration have been thoroughly documented, although the etiology underlying these reactions are not well-defined. Infusion reactions are estimated to affect 5% to 20% of IBD patients receiving infliximab [13]. Although presentations of infliximab-related infusion reactions are widely heterogeneous and inconsistent, systematic reviews have been performed to suggest methods for preventing and managing infliximab-related infusion reactions [14]. Immediate infusion reactions to infliximab are classified as those that develop either during the infusion course or within 1 to 2 hours of completion of the dose. These reactions mostly occur during patients' initial infusions, and present with

symptoms such as pruritus (22.1%), flushing (9.95%), dyspnea (6.2%), chest discomfort (5.9%), and hypertension (5.9%) [14] Acute infusion reactions may be immune mediated type 1 hypersensitivity anaphylactic reactions, although this is rare. More common are non-immune-mediated reactions, which are thought to be related to infusion dosage rate.

Certain factors have been proposed as risk factors for infusion reactions. Episodic, irregular treatment with long intervals is associated with systemic reactions. Thus, it is suggested that patients should be initiated on infliximab using an induction series and regular bi-monthly scheduled infusions [15]. Additionally, concomitant immunosuppressive therapy such as systemic steroids and immunomodulators have been suggested to prevent the development of anti-infliximab antibodies. This hypothesis has been supported in trials demonstrating a positive association between combination immunosuppression and lower risks of infusion reactions [15]. This patient's sudden-onset reaction during his infliximab infusion closely aligns with the presentation of an acute non-immune-mediated infusion reaction. However, the presence of an infusion reaction in this patient is surprising as he was not susceptible to any of the proposed risk factors. He had been receiving regular infliximab at 6-week intervals for four years, in addition to multiple concomitant immunosuppressive therapies, including prednisone, methotrexate, and azathioprine.

Conclusion

In summary, this is a 42-year-old male with a four-year history of Takayasu Arteritis who presented to the Emergency Department after developing symptoms of a sudden onset aortitis flare after his infliximab infusion. The presence of an acute infliximab-related infusion reaction within the TAK patient is uncharacteristic due to his extensive history receiving regular treatment and multiple concomitant immunosuppressive therapies. Although immediate-type infusion reactions have been extensively reported in IBD patients, most reactions occur during the initial infusion. This case presentation is unique in that the patient had been receiving regular infliximab infusions for several years prior. There is a paucity of literature discussing infliximab infusion reactions in TAK patients or what factors may contribute to developing an immediate-type reaction to infliximab despite years of treatment.

Acknowledgements

None.

Conflict of Interest

None.

References

1. Langford CA, Fauci AS (2022) Vasculitis syndromes. McGraw Hill.
2. Mirouse A, Biard L, Comarmond C, Lambert M, Mekinian, et al. (2019) Overall survival and mortality risk factors in Takayasu's arteritis: A multicenter study of 318 patients. J Autoimmun 96: 35-39.
3. Ishikawa K (1988) Diagnostic approach and proposed criteria for the clinical diagnosis of Takayasu's arteriopathy. J Am Coll Cardiol 12(4): 964-972.
4. Cotch MF, Hoffmann GS (1995) The prevalence, epidemiology, and cost of hospitalizations for vasculitis in New York State 1986 to 1990. Arthritis Rheumatol 38: 225.
5. Kancherla H, Konduri G, Bollam A, Atla K, Injeti N, et al. (2022) Takayasu arteritis: A case report. Journal of Young Pharmacists 14(1): 130-132.
6. Manfrini O, Bugiardini R (2006) Takayasu's arteritis: A case report and a brief review of the literature. Heart international 2(1): 66.
7. Sharma BK, Jain S, Sagar S (1996) Systemic manifestations of Takayasu arteritis: the expanding spectrum. Int j cardiol 54 Suppl: S149-S154.
8. Tripathy NK, Upadhyaya S, Sinha N, Nityanand S (2001) Complement and cell mediated cytotoxicity by antiendothelial cell antibodies in Takayasu's arteritis. J Rheumatol 28(4): 805-808.
9. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, et al. (1990) The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 33(8): 1129-1134.
10. Podgorska D, Podgorski R, Aebisher D, Dabrowski P (2019) Takayasu arteritis-epidemiology, pathogenesis, diagnosis and treatment. J Appl Biomed 17(1): 20.
11. Koster MJ, Matteson EL, Warrington KJ (2016) Recent advances in the clinical management of giant cell arteritis and Takayasu arteritis. Curr Opin Rheumatol 28(3): 211–217.
12. Mekinian A, Comarmond C, Resche-Rigon M, Mirault T, Kahn JE, et al. (2015) Efficacy of Biological-Targeted Treatments in Takayasu Arteritis: Multicenter, Retrospective Study of 49 Patients. Circulation 132(18): 1693-1700.
13. Cullen Garrett, Adam S Cheifetz (2012) Infusion Reactions Related to Infliximab Therapy Are Not Usually Associated with Drug Discontinuation. J Rheumatol 39(8): 1500-1502.
14. Lev Lichtenstein, Yulia Ron, Shmuel Kivity, Shomron Ben Horin, Eran Israeli, et al. (2015) Infliximab-Related Infusion Reactions: Systematic Review. Journal of Crohn's and Colitis 9(9): 806-815.
15. H Fidder, F Schnitzler, M Ferrante, M Noman, K Katsanos, et al. (2008) Long-Term Safety of Infliximab for the Treatment of Inflammatory Bowel Disease: A Single-Centre Cohort Study. Gut 58(4): 501-508.