Caspian Journal of Internal Medicine 2024 (Autumn); 15(4): 729-734
DOI: 10.22088/cjim.15.4.729

Case Report

Multiple sclerosis in a patient with Takayasu's Arteritis: A case report

Mohammad Mehdi Emam (MD) [1¥]
Mahdiye Abiyarghamsari (MD) [2¥]
Muhanna Kazempour (MD) [1*]
Maryam Haghighi-Morad (MD) [3]
Farane Farsad (MD) [1]

1. Department of Rheumatology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Clinical Pharmacy, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Radiology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*** Correspondence:**
Muhanna Kazempour,
Department of Rheumatology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, 1333625445, Iran

E-mail:
muhannakazempour@gmail.com
Tel: +98 2155417243

¥ Mohammad Mehdi Emam and Mahdiye Abiyarghamsari contributed equally in this article.

Received: 5 March 2023
Revised: 17 Oct 2023
Accepted: 11 Nov 2023
Published: 9 Sep 2024

Abstract

Background: Multiple sclerosis (MS) and Takayasu's arteritis (TAK) are two autoimmune diseases that affect the Central nervous system (CNS), but the relationship between them has not been established.

Case Presentation: Here we report the emergence of MS during treatment. Takayasu's arteritis in a 24-year-old Iranian woman with a severe presentation. She was treated aggressively with IV methylprednisolone 1 g/day for 3 days and continued with oral prednisolone, also IV cyclophosphamide monthly. After 2 months, loss of vision led to a diagnosis of Optic neuritis (ON) caused by concomitant MS.

Conclusion: Differentiating CNS vasculitis associated with Takayasu's arthritis from coexisting MS affecting the CNS is challenging and what is important is to avoid giving a TNF inhibitor.

Keywords: Takayasu, Arteritis, Multiple sclerosis, Vision loss, Neurologic manifestations.

Citation:
Emam MM, Abiyarghamsari M, Kazempour M, Haghighi-Morad M, Farsad F. Multiple sclerosis in a patient with Takayasu's Arteritis: A case report. Caspian J Intern Med 2024; 15(4): 729-734.

Takayasu arteritis (TAK) is a rare, idiopathic, chronic inflammatory rheumatic disease that affects large vessels, mainly the aorta and its major branches, including the coronary, carotid, pulmonary, and renal arteries (1-3). Although this disease has a worldwide distribution, prevalence seems to vary geographically and appears highest in Asian countries and least in the North America (4-6). In 2021, the British Society for Rheumatology reported the incidence rate of TAK as 1.11 per million person-years although the heterogeneity in the data was extremely high (7).

Neurovascular complications occur in less than 20% of patients with TAK; however, they are a major source of morbidity in these patients (8). Vascular lesions and progression changes are quite different in TAK from those seen in ordinary atherosclerosis (9, 10). Attacks of focal neurologic deficits due to fluctuating brain ischemia may be difficult to distinguish from other neurologic disorders, especially relapsing and remitting MS, considering the demographic predominance of both disorders in young women (11). Here we report a severe deterioration of TAK in a 24-year-old woman who emerged with diagnostic criteria of MS.

Case Presentation

The patient was a 24 years old married woman with a history of 18 months of gradual malaise, weight loss, fatigue, bilateral claudication in the upper extremities, and anemia, in the postpartum period. Also, she had a 2-month history of palpitations, dry cough, and paroxysmal nocturnal dyspnea. She was referred to the emergency department for abdominal pain. On physical examination, she was conscious but ill. The pulses of the left upper limb were not palpable (radial and brachial pulses), with blood pressure in the right arm of 85/60 mmHg. She had a pulse rate of 120/minute with a regular rhythm.

Laboratory investigation showed Hb:10.5 g/dl, Plt: 472 × 109/L, WBC:13× 109/L, ESR: 34 mm/hour, CRP:25 mg/L (Normal limit <6), Cr: 0.9 mg/dL, LDH: 316 IU/L, blood level of CPK, Troponin, AST.ALT, Amylase, Lipase, and urine analysis (UA), were all normal. She was visited by a rheumatologist due to aortitis that was revealed in Abdomen and pelvic computed tomography. Subsequently, echocardiography showed an EF (ejection fraction) of about 5-10%, moderate-to-severe TR (tricuspid regurgitation), PAP (pulmonary artery pressure): 35 mmHg, moderate AI (aortic insufficiency), moderate MR (mitral Regurgitation), and dilated IVC (inferior vena cava). Blood level of CPK, Troponin, were all normal. Cardiac MRI (magnetic resonance imaging) was not available in that situation. Computed tomography angiography (CTA) of the aorta showed diffuse wall thickening in the aortic arch, arch branches, and descending aorta which is associated with stenosis and obstruction of the left subclavian artery, severe stenosis in the origin of both common carotid and right brachiocephalic arteries. Furthermore, moderate to severe stenosis in the origin of the celiac and mild stenosis in the left renal arteries were detected (figure ١). Other tests were negative included PPD, wright, VDRL, ASCA, ANA, dsDNA, ANCA, RF, CCP, ACE, HLA B27, HBs Ag, HBC Ab, HCV Ab, HIV Ab, and pathergy test, but HLA B51 was positive.

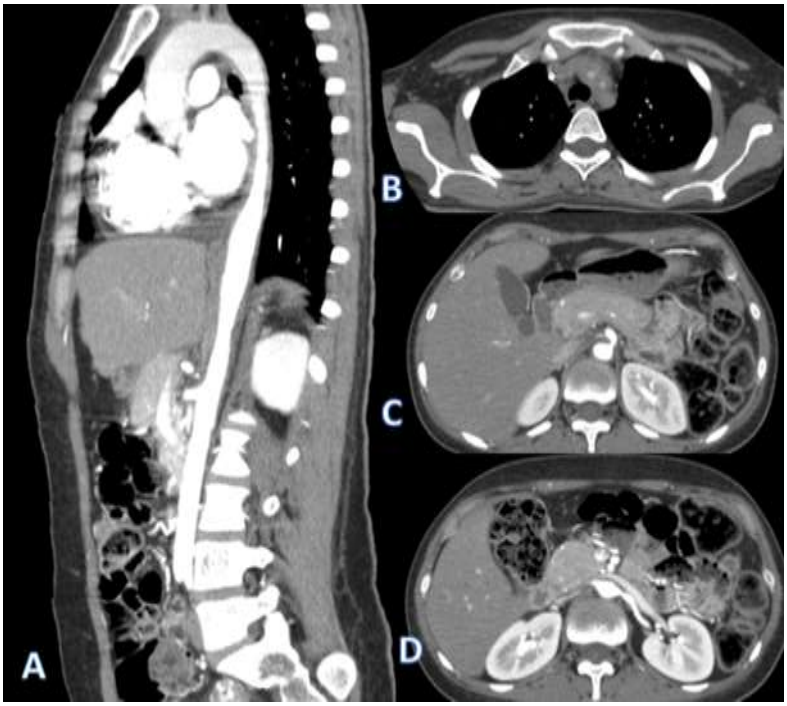

Figure 1. Thoracoabdominal CT. A of the patient showed Aortic arch, Descending Aorta, and Arch branches circumferential wall thickening (A, B) associated with narrowing of the celiac artery (C) and left Renal artery (D).

Diagnosis of TAK was confirmed based on the criteria (12) and treatment was initiated with pulse Methylprednisolone 1 g for 3 days which continued with oral Prednisolone and Cyclophosphamide 750 mg IV. Heart failure was managed by cardiologist. She complained dizziness and visual disturbance that responded to a decrease of antihypertensive and diuretic drugs by a cardiologist. Follow-up echocardiography showed no significant change in EF (EF: 10-15%). Prednisolone 50 mg daily, gradually tapered after one-month, subsequent dose of ٧٥٠mg cyclophosphamide was prescribed and, Mycophenolate Mofetil, 1500 mg daily, added because of the severity of her disease.

Two months after, when she was on Prednisolone 15 mg daily, she presented with a complaint of bilateral blurred vision .Laboratory data showed an increase in ESR (ESR:73 mm/hour, CRP:12.1 mg/L), so she received a third dose of 750 mg cyclophosphamide and a 300 mg IV infusion of infliximab due to refractory TAK. Simultaneously, ophthalmology and neurology consult were requested. Eye examination indicated a positive Marcus Gunn test and Brain MRI showed multiple T2/FLAIR high signal lesions in the white matter of cerebral and cerebellar hemispheres, some with DWI restriction and some with enhancement so vasculitis, demyelinating process, and microvascular ischemic changes are in the differential diagnosis (figure٢).

These results suggested possible MS; therefore, the neurologist administered another pulse of methylprednisolone 1g for five days. Unexpectedly, the lumber puncture result showed seven bands of IgG in the cerebrospinal fluid (CSF), also the IgG index was 0.71. Since more than two CSF IgG bands and no serum IgG bands were detected, concomitant MS was diagnosed in the patient based on McDonald's criteria (13). The neurologist recommended continuing the identical immunosuppressive agents that use in TAK. As regards Tumor necrosis factor (TNF), inhibitors are contraindicated in demyelinated disease, the patient did not take a second dose of infliximab.
Two weeks later she returned with syncope and headache. Her general conditions changed dramatically. Her consciousness was disrupted by head elevation from the bed. Lab test showed ESR:37 mm/hour, CRP:0.9 mg/L. The interventional neurologists discouraged us from possible interventions to decrease the patient's symptoms.

Unfortunately, she lost consciousness. There were multiple hypodense lesions in the frontoparietal and parietooccipital lobes probably due to watershed infarction in the patient's new brain computed tomography, which was also confirmed by Magnetic Resonance Imaging (MRI) (figure ٣). Therefore, Tocilizumab 400 mg IV infusion was started for the patient but she died after 15 days due to a severe bilateral ischemic stroke.

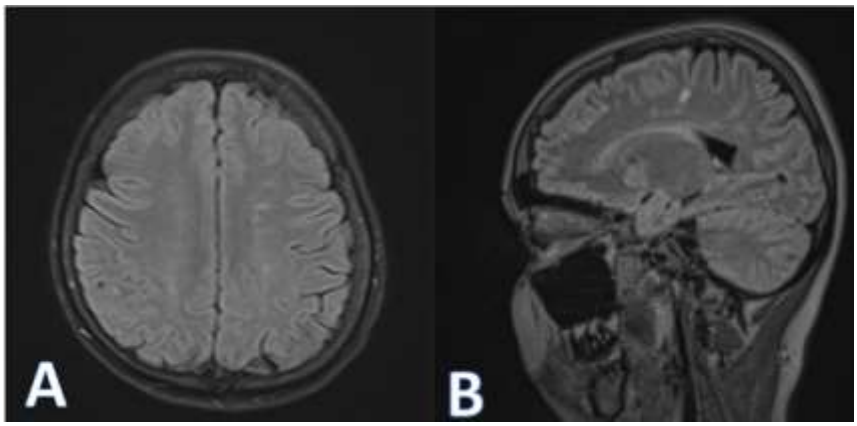

Figure 2. Axial (A) and Sagittal (B) FLAIR depicted high signal peri ventricular lesions with Dawson's finger appearance suggestive of demyelination.

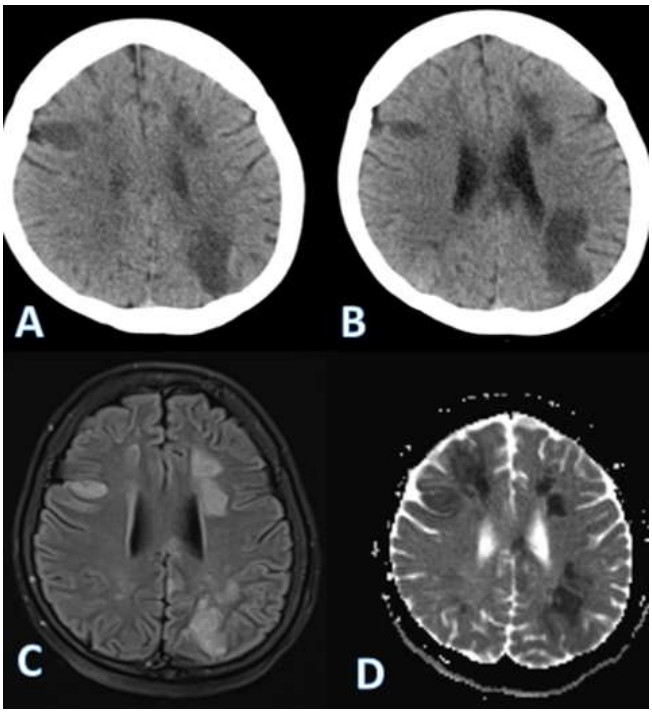

Figure 3. Axial Brain CT scan (A, B) showed hypodense cortical and subcortical wedge shape lesions suggestive of watershed infarctions. These findings are confirmed in DWI (C) and ADC (D) sequences.

Discussion

Neurologic complications as initial manifestations of TAK are uncommon (14, 15). Major neurological events that occurred in about one-half of the patients with TAK are TIA (transient ischemic attack), cerebral infarction, hypertensive encephalopathy, seizure, paraplegia, and even Moya-Moya phenomenon which could happen even with normal acute-phase reactants (16-19).

New data showed that nearly 48% with vertebral artery involvement, experience visual disturbance manifested as a problem in the anterior or the posterior segment of the eye. Ocular manifestations were categorized as disease-related or treatment-related, including complications of steroid therapy like cataract, hypertensive retinopathy, ocular ischemic syndrome, iris neovascularization, anterior ischemic optic neuropathy, and uveitis, in descending order of frequency (20). As we know, an association between TAK and MS is not reported in the literature. MS is a chronic T-cell immune-mediated inflammatory disease associated with uncontrolled inflammation, autoimmunity, and secondary neurodegeneration that causes significant disability in patients over time. It is characterized by the formation of multiple plaques in the brain and spinal cord . The diagnostic criteria for MS are based on a combination of clinical, imaging, and laboratory evidence for disease in the CNS (13, 21-25).

CSF elevated protein, lymphocytic pleocytosis, increased IgG synthesis, and the presence of oligoclonal bands in primary angiitis of CNS are described (26) but there is no evidence of these changes in TAK. CSF-restricted oligoclonal bands (OCB) are indicative of intrathecal immunoglobulin synthesis and frequently found in various inflammatory CNS diseases such as bacterial meningitis, viral encephalitis, neurosyphilis, lupus, sarcoid, and attain almost 100% in multiple sclerosis (27-29). The diagnostic significance of OCB as a biomarker has been emphasized by the implementation in the latest revision of the McDonald criteria for multiple sclerosis as a substitute for dissemination in time (13).

As mentioned, our patient was on an immunosuppressive agent caused by the TAK diagnosis. Nevertheless, she developed optic neuritis, in which the presence of brain plaque and CSF OCB suggested MS. Diagnostic confusion in this situation was a differentiation of CNS vasculitis related to TAK from the concomitant of two autoimmune diseases that affect CNS. However, steroids are the mainstay the treatment for both diseases. Acute flares of MS are treated with steroids (30) and high-dose oral Glucocorticoids in combination with csDMARDs (Conventional synthetic disease-modifying antirheumatic drugs) or TNFis (Tumor necrosis factor inhibitors), which are recommended in TAK (31). What caused concern in this situation was the continuation of treatment with infliximab. Many CNS demyelination events in patients receiving anti-TNF drugs have been reported (32-34). As a result, TNFis are contraindicated in pre-existing demyelinating diseases (34, 35). Therefore, we switched the treatment to tocilizumab.

Although the presence of brain plaque and OCB is not reported in TAK. Some cases have been reported of patients who were first treated as MS and later diagnosed with TAK. One study reported development of TAK in the woman with relapsing-remitting MS, being treated with Interferon (IFN) beta-1a, who her vasculitis improved after withdrawal of IFN beta (36). Another study introduced a woman who initially received interferon beta, being diagnosed with MS because of focal neurological deficits with bilateral white matter lesions, when a few months later, a second attack with left-sided weakness and bilateral blurred vision occurred that fundoscopy examination was normal and CSF analysis showed a normal pattern without the oligoclonal band and further investigation led to confirm of TAK diagnosis (11).

Classical ophthalmic features of TAK are because of the reduced ocular perfusion, also dizziness and falling episodes are secondary to hypoperfusion of brain stem structures as Ashjazadeh et.al reported a clinical presentation of TAK in a girl, at first presenting itself as a loss of vision that had been misdiagnosed as Optic neuritis (ON) caused by MS due to the presence of bilateral abnormal T2 signals in the white matter whereas these were ischemia in watershed zones secondary to severe hypoperfusion in carotids and vertebral arteries circulation; finally, CTA and conventional angiography of the thoracic and cervical arteries were the most helpful in diagnosing TAK (17).

Although ON may be a rare neurologic manifestation of TAK. In mentioned case reports, the initial misdiagnosis of MS was given due to visual symptoms and brain lesions without the presence of CSF OCB. While, fundoscopic exam, imaging, and CSF fluid finding in our patient were seen along with the findings confirming optic neuritis caused by MS. We reported a very rare co-existence of TAK and MS. Our report highlights the complexity and unknown nature of TAK and its related complications. Appropriate management of TAK with neurologic manifestation is complex. Selection of appropriate approach and immunosuppressive agents and ongoing disease monitoring is often challenging and a good partnership between a rheumatologist and neurologist is critical. The development

of Multiple sclerosis may be concurrent with Takayasu's arteritis, or MS-like symptoms may be another unusual neurological manifestation in TAK, that sometimes it is not possible to differentiate between these two conditions and what is important is to avoid giving a TNF inhibitor.

Acknowledgments

The authors would like to thank the Clinical Research Development Unit (CRDU) of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences Tehran, Iran, for their support throughout the study.

Funding: No grant numbers

Ethics approval: No ethics approval is needed for this manuscript

Consent for publication: We declare no conflicts of interest.

Authors' contribution: Mohammad Mehdi Emam and Mahdiye Abiyarghamsari: contributed equally; Resources, Writing - Original Draft. Muhanna Kazempour: Conceptualization, Investigation, Data Curation, Writing - Original Draft, Writing - Review & Editing. Maryam Haghighi-Morad: Data Curation, interpretation of imaging. Farane Farsad: Resources.

References

1. Maffei S, Di Renzo M, Bova G, Auteri A, Pasqui AL. Takayasu's arteritis: a review of the literature. Intern Emerg Med 2006; 1: 105-12.
2. Manfrini O, Bugiardini R. Takayasu's arteritis: A case report and a brief review of the literature. Heart Int 2006; 2: 66.
3. Johnston S, Lock R, Gompels M. Takayasu arteritis: a review. J Clin Pathol 2002; 55: 481-6.
4. Onen F, Akkoc N. Epidemiology of Takayasu arteritis. Presse Med 2017; 46: e197-203.
5. Saritas F, Donmez S, Direskeneli H, Pamuk ON. The epidemiology of Takayasu arteritis: a hospital-based study from northwestern part of Turkey. Rheumatol Int 2016; 36: 911-6.
6. Roy AT, Singhal AB. Pulse on Stroke in Pulseless Disease (Takayasu Arteritis). Stroke 2022; 53: 1558-9.
7. Rutter M, Bowley J, Lanyon PC, Grainge MJ, Pearce FA. A systematic review and meta-analysis of the incidence rate of Takayasu arteritis. Rheumatology (Oxford) 2021; 60: 4982-90.
8. Russo RA, Katsicas MM. Takayasu arteritis. Front Pediatr 2018; 6: 265.
9. Sun Y, Yip PK, Jeng JS, Hwang BS, Lin WH. Ultrasonographic study and long-term follow-up of Takayasu's arteritis. Stroke 1996; 27: 2178-82.
10. Hatri A, Guermaz R, Laroche J, Zekri S, Brouri M. Takayasu's arteritis and atherosclerosis. J Med Vasc 2019; 44: 311-7. [in French]
11. Sasannejad P, Verdipour M, Asadi M, Ahmadi H. Recurrent ischemic stroke in a case of Takayasu's arteritis, mimicking multiple sclerosis. Iran J Neurol 2019; 18: 145.
12. Ruperto N, Ozen S, Pistorio A, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: Overall methodology and clinical characterisation. Ann Rheum Dis 2010; 69: 790-7.
13. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018; 17: 162-73.
14. Gouda W, Alsaqabi F, Alkadi A, et al. Ischemic stroke as the first presentation of takayasu's arteritis in young male. Clin Case Rep 2020; 8: 258-61.
15. Gao P, Dmytriw AA, Wang T, et al. Contemporary challenges of acute ischemic stroke in Takayasu arteritis. Stroke 2020; 51: e280-e284.
16. Pugh D, Grayson P, Basu N, Dhaun N. Aortitis: recent advances, current concepts and future possibilities. Heart 2021; 107: 1620-9.
17. Ashjazadeh N, Shokouhyar S, Ostovan MA. Takayasu arteritis presenting as sudden onset vision loss simulates multiple sclerosis: a case report. J Res Med Sci 2011; 16 Suppl 1: S442-6.
18. Misra DP, Rathore U, Mishra P, et al. Comparison of presentation and prognosis of Takayasu arteritis with or without stroke or transient ischemic attack—A retrospective cohort study. Life 2022; 12: 1904.
19. Dai Y, Zhong Y, Jian B, et al. Bridging therapy for acute stroke as the initial manifestation of takayasu arteritis: A case report and review of literature. Front Immunol 2021; 12: 630619.
20. Peter J, David S, Danda D, et al. Ocular manifestations of Takayasu arteritis: a cross-sectional study. Retina 2011; 31: 1170-8.
21. Trapp BD, Nave KA. Multiple sclerosis: an immune or neurodegenerative disorder? Annu Rev Neurosci 2008; 31: 247-69.
22. Kirstein-Grossman I, Beckmann JS, Lancet D, Miller A. Pharmacogenetic development of personalized

medicine: Multiple sclerosis treatment as a model. Drug News Perspect 2002; 15: 558-67.
23. Smets I, Fiddes B, Garcia-Perez JE, et al. Multiple sclerosis risk variants alter expression of co-stimulatory genes in B cells. Brain 2018; 141: 786-96.
24. Longo DL. Reich DS, Lucchinetti CF, Calabresi PA. Multiple Sclerosis. N Engl J Med 2018; 378: 169-80.
25. Fresegna D, Bullitta S, Musella A, et al. Re-examining the role of TNF in MS pathogenesis and therapy. Cells 2020; 9: 2290.
26. Minagar A, Alezander JS. Inflammatory disorders of the nervous system: pathogenesis, immunology, and clinical management. Humana Press; 2005th edition, Springer 2005; pp: ٢٥٧-٦٧.
27. Petzold A. Intrathecal oligoclonal IgG synthesis in multiple sclerosis. J Neuroimmunol 2013; 262: 1-10.
28. Schwenkenbecher P, Sarikidi A, Wurster U, et al. McDonald criteria 2010 and 2005 compared: persistence of high oligoclonal band prevalence despite almost doubled diagnostic sensitivity. Int J Mol Sci 2016; 17: 1592.
29. Sorensen PS, Sellebjerg F. Pulsed immune reconstitution therapy in multiple sclerosis. Ther Adv Neurol Disord 2019; 12: 1756286419836913.
30. Hecker C, Welponer T, Herold M, et al. Update on treatment strategies for vasculitis affecting the central nervous system. Drug Discov Today 2021; 27: 1142-55.
31. Chey SY, Kermode AG. Central nervous system demyelination related to tumour necrosis factor alpha inhibitor. Mult Scler J Exp Transl Clin 2022; 8: 20552173211070750.
32. Kumar N, Abboud H. Iatrogenic CNS demyelination in the era of modern biologics. Mult Scler 2019; 25: 1079-85.
33. Kaltsonoudis E, Voulgari PV, Konitsiotis S, Drosos AA. Demyelination and other neurological adverse events after anti-TNF therapy. Autoimmun Rev 2014; 13: 54-8.
34. Mansouri B, Horner ME, Menter A. Tumor necrosis factor-α inhibitor use in psoriasis patients with a first-degree relative with multiple sclerosis. J Drugs Dermatol 2015; 14: 876-8.
35. Zahid M, Busmail A, Penumetcha SS, Ahluwalia S, et al. Tumor necrosis factor alpha blockade and multiple sclerosis: Exploring new avenues. Cureus 2021; 13: e18847.
36. Diamantopoulos AP, Hetland H, Hansen AE, Myklebust G. Severe deterioration of newly diagnosed Takayasu arteritis in a patient re-treated with interferon beta-1α for concomitant longstanding multiple sclerosis. Mod Rheumatol 2012; 22: 474-8.