EJR European Journal of Rheumatology

DOI:10.5152/eurjrheum.2023.22043

Case-Based Review

Behcet's Syndrome Resembling Takayasu's Arteritis with the Distribution of Arterial Involvement: A Case Report and Literature Review

Gamze Akkuzu, Duygu Sevinç Özgür, Bilgin Karaalioğlu, Melek Yalçın Mutlu, Fatih Yıldırım, Mustafa Erdoğan, Burak İnce, Cemal Bes

Abstract

Behcet's syndrome is a variable vessel vasculitis characterized by recurrent oral and genital ulcers with concomitant skin, ocular, neurologic, gastrointestinal, and joint involvement. Herein, we present a patient who was diagnosed with Behcet's syndrome, which with magnetic resonance angiography showed occlusion of the right subclavian artery at the level of the thoracic outlet and reverse flow in the right vertebral artery consistent with subclavian steal syndrome. In addition, partial narrowing was noted in the left renal artery. The distribution of arterial involvement resembled Takayasu's arteritis, although the presence of mucocutaneous lesions, male gender, history of deep vein thrombosis, and HLA-B51 positivity favored a diagnosis of vasculo-Behçet's syndrome. We treated the patient with methylprednisolone and cyclophosphamide. After the regression of vascular inflammation with immunosuppressive therapy, stenting was performed in the left renal artery.

Keywords: Behçet's syndrome, subclavian artery occlusion, Takayasu's arteritis

ORCID iDS of the authors:
G.A. 0000-0002-2133-0282;
D.S.O 0000-0002-1294-926X;
B.K. 0000-0001-7584-8549;
M.Y.M 0000-0003-0598-5737;
F.Y. 0000-0003-3909-7500;
M.E. 0000-0003-4087-6667;
B.I. 0000-0001-9813-2228;
C.B. 0000-0002-1730-2991.

Cite this article as: Akkuzu G, Özgür DS, Karaalioğlu B, et al. Behcet's syndrome resembling takayasu's arteritis with the distribution of arterial involvement: A case report and literature review. *Eur J Rheumatol.* 2023;10(2):62-66.

Department of Rheumatology, University of Health Sciences, Başakşehir Çam and Sakura City Hospital, Istanbul, Turkey

Corresponding author:
Cemal Bes
E-mail: cemalbes@hotmail.com

Received: March 11, 2022
Accepted: May 04, 2023
Publication Date: July 13, 2023

Introduction

Behçet's syndrome (BS) is an inflammatory disease characterized by recurrent oral and/or genital aphthous ulcers and multiple systemic manifestations. Vasculitis is considered to be the main pathological finding in BS. Vessels of any size can be affected on both the venous and arterial sides of the circulatory system. Vascular involvement in BS is observed at rates of up to 40%, especially in young men, and is one of the most important causes of morbidity and mortality.[1] Venous involvement is reported to be more common than arterial involvement (up to 80%).[2] Arterial involvement is a late event, averaging 5-10 years after the onset of the disease.[3] Its frequency is less than 5%.[4] Infrarenal abdominal aortic and iliac, femoral, popliteal, and pulmonary carotid arteries are the more commonly affected arterial sites. Clinical manifestations vary according to the affected arterial area.[4,5]

Takayasu arteritis (TAK) is a rare, idiopathic, chronic inflammatory disease characterized by granulomatous panarteritis of the aorta and its major branches, typically presenting before the age of 40. The entire length or branches of the aorta may be affected. The most commonly affected branches are the subclavian and common carotid arteries. Although the disease pattern varies geographically, the most common pattern is stenotic lesions found in >90% of patients. However, aneurysms are reported at a rate of approximately 25%.[6] Sometimes these 2 diseases, BS and TAK, can coexist or mimic each other. Herein, we report a case of BS with multiple arterial involvements.

Case Presentation

A 44-year-old male patient was first admitted to the emergency department of our hospital in July 2020 with complaints of weakness, dizziness, and nausea. On admission, he was afebrile with a pulse rate of 82 beats/min, arterial blood pressure measured 130/80 mmHg, and inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, were found to be elevated. Despite the high CRP/ESR levels, there was no fever or other signs of infection. In addition, neurological examination or cranial imaging did not give any clue as to the cause of the dizziness. Unexplained causes of dizziness and elevated CRP/ESR levels were referred to rheumatology when it was understood that he had a previous deep vein thrombosis (DVT) and recurrent oral aphthous lesions. He had acute DVT in the right lower extremity in 2019 and had painful oral aphthous lesions recurring 2-3 times a month. There was no genital ulcer or scar

was observed on examination. Pathergy test and HLA-B51 were positive. Although we consulted an ophthalmologist, there were no signs of uveitis. No pathology was detected in brain magnetic resonance imaging and magnetic resonance venography examinations, lower extremity arterial and venous Doppler ultrasound examinations, or computed tomography angiography (thorax and abdomen). There was no occlusion or aneurysm in the vascular areas examined. (Thoracic aorta, abdominal aorta, and pulmonary arteries were scanned, but subclavian and carotid arteries were not included in the scan area.) No pathological finding was detected in the echocardiography. The patient's thrombophilia screening was negative. The patient did not fulfill the criteria according to the International Study Group for Behçet's Disease with a history of DVT, recurrent oral aphthous lesions, pathergy positivity, but scored 4 points according to The International Criteria for Behçet's Disease and diagnosed BS.[7,8] Then colchicine treatment was started. Inflammatory markers remained high in the follow-up of the patient (Figure 1). The patient described pain and fatigue in the arms and loss of appetite during his last outpatient visit. On physical examination, no radial pulse was palpable in the right arm. While the blood pressure measured in the right arm was 95/65 mmHg, it was 154/75 mmHg in the left arm. Magnetic resonance angiographic (MRA) examination revealed occlusion of the right subclavian artery at the level of the thoracic outlet and reverse flow in the right vertebral artery consistent with subclavian steal syndrome. In addition, there was a narrowing in the left renal artery (Figure 2). These findings suggested TAK or vascular BS. The diagnosis of vascular BS was made based on the patient's gender, presence of oral aphthous ulceration, and previous vein thrombosis. Intravenous pulse 1000 mg/day methylprednisolone (for 3 days, then continue with 1 mg/kg/day dose with prednisolone) and monthly pulse intravenous 1000 mg cyclophosphamide treatment was started for control of vascular inflammation. Consent was obtained from the patient.

Search Strategy

A literature review on subclavian artery involvement in BS was performed in the MEDLINE/PubMed database. The search was limited to English and full-text publications from February 1980 to July 2022. The keywords "Behcet" and "subclavian artery" were used in the search.

Discussion

We found 22 articles reporting BS patients with subclavian artery involvement and meeting the criteria.[5,9-29] (Table 1). Arterial involvement is a late event, averaging 5-10 years after the onset of the BS.[3] Its frequency is less than 5%. Male predominance is evident. The main locations of arterial lesions in BS are the aorta, lower extremity arteries, and pulmonary arteries. Subclavian artery involvement has been reported very rarely.[4,5] The tendency to affect the venous rather than the arterial side is the distinguishing feature of BS from other vasculitides. Lower extremity vein thrombosis can be considered as its hallmark. Arterial involvement, differently from TAK, is manifested commonly in the form of aneurysms and rarely in the form of thrombotic occlusions.[4] According to the European League Against Rheumatism (EULAR) recommendations for the management of BS, treatment of pulmonary artery aneurysms and thrombosis, and peripheral artery aneurysms is with high-dose glucocorticoids and cyclophosphamide.[30] We preferred intravenous pulse 1000 mg/day methylprednisolone (for 3 days, then continue with 1 mg/kg/day dose with prednisolone) and monthly pulse intravenous 1000 mg cyclophosphamide treatment for this case. Inflammatory markers regressed to normal levels after immunosuppressive therapy (Figure 1). An essential discussion topic regarding the diagnosis is the co-existence of TAK and other inflammatory diseases. In a study investigating the frequency of such chronic inflammato ry/autoimmune disorders in a large cohort of patients with TAK, it was reported that BS was detected in 10 (5%) of 198 patients with TAK. The fact that 70% of these patients were women and only one had previous venous thrombosis was emphasized as the distinguishing feature of the patients from vascular BS.[31] As we have mentioned before in our case, the fact that the case was male, and the history of oral aphthous ulcers and venous thrombosis were the reasons why we approached vascular BS in the diagnosis.

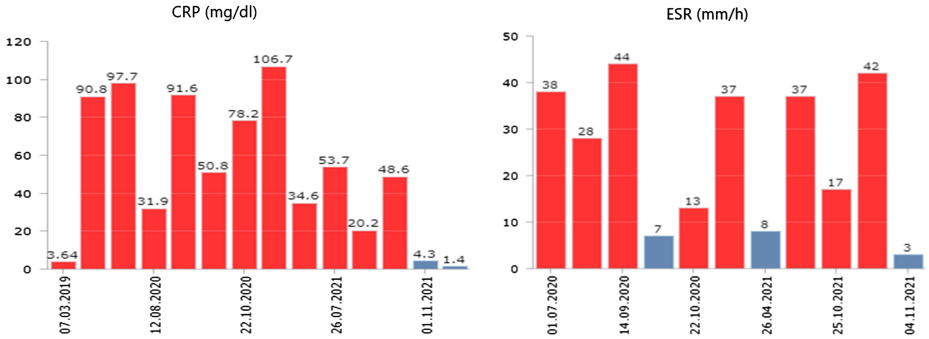

Figure 1. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated from the first admission of the patient and decreased to normal levels 3 days after intravenous pulse methylprednisolone treatment.

The utility of ultrasound (US), MRA, and computed tomographic angiography (CTA) for the evaluation of vascular lesions is already known. These examinations are noninvasive and can be easily repeated as needed. On the other hand, conventional angiography requires special conditions and techniques and has risks such as unexpected vascular injury and bleeding. Magnetic resonance angiography, US, and CTA may be appropriate for the detection and follow-up examination of vascular lesions due to the low risk of iatrogenic complications. In this case report, it was reported that in a young patient with acute phase reactants elevation, prominent arterial lesions were detected while the patient was still asymptomatic with early vascular investigations, and a diagnosis

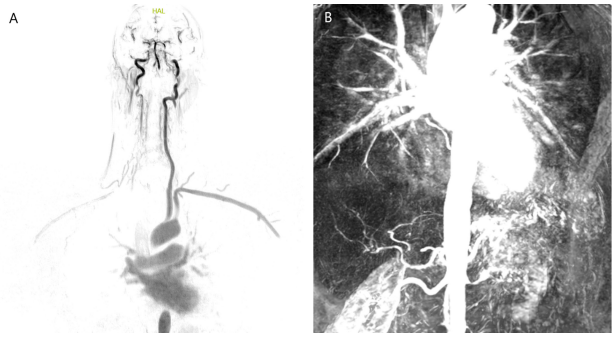

Figure 2. Magnetic resonance angiography of the aortic arch and abdominal aorta. (A) Occlusion of the right subclavian artery and right vertebral artery. (B) Narrowing of the left renal artery.

Table 1. Characteristics of Patients Diagnosed with BS with Subclavian Artery Involvement

Study	Origin	Age/Gender	Symptom	Finding	CRP/ESR	Treatment
Li et al	China	32/male	Pain in the left neck and shoulder	Pseudoaneurysm of the left subclavian artery	6/18	Endovascular repair and high-dose anti-inflammatory therapy
Abe et al	Japan	42/male	Pain in the left clavicle and a pulsatile mass	Rupture of a 6.5 × 4.5 cm pseudoaneurysm with thrombus in the left subclavian artery	15/–	Endovascular treatment and immunosuppressive therapy
Ocon et al	USA	42/male	Acute severe abdominal pain	Acute dissection of the coeliac artery trunk, common hepatic artery, and proper hepatic arteries, with the right hepatic artery and the splenic artery demonstrating hypoattenuated filling. Additionally, there was asymmetric wall thickening of the proximal left subclavian artery and circumferential wall thickening of the abdominal infrarenal aorta	216/50	Methylprednisolone and canakinumab
So et al	China	41/female	Collapse (semiconscious and hypotensive)	Anterior wall acute myocardial infarction; a critical ostial left anterior descending artery stenosis, and a blocked left subclavian artery from the ostium and a tight ostial left carotid artery stenosis	Elevated	Prednisolone, colchicine, and azathioprine
Yildirim et al	Turkey	29/male	Pain and a pulsatile mass in the right neck area	Thrombosed aneurysm in the right subclavian artery, thrombosis in the left iliac vein and hepatic vein	32/102	Prednisolone and cyclophosphamide
Nishimura et al	Japan	70/male	Left subclavian pulsatile mass	A left subclavian artery pseudoaneurysm	—	Endovascular treatment (continued to be administered prednisolone (5 mg/day), colchicine (1 mg/day), and methotrexate (4 mg/day); also had a medical history of rheumatoid arthritis)
Park et al	Korea			Aortic and arterial aneurysms in Behçet disease: management with stent-grafts—initial experience [subclavian (n = 2)]	—	Stent-graft
Yoo et al	Korea	39/male	Weakness and hypoesthesia of the right upper arm	Right subclavian artery aneurysm	32/67	Prednisolone and azathioprine
Lee et al	Korea	38/male	Pain and weakness in the right arm	Round aneurysm of the right subclavian artery at the level of the clavicle with partial thrombosis	—	Transluminal stent-graft and steroid and azathioprine medication
Cingoz et al	Turkey	44/Female	Dizziness, paresthesia, and angina pectoris, which increased in severity with the movement of her left arm	The left subclavian artery is totally occluded The left basilar artery is filled by Willis polygon. The left subclavian artery and LITA are retrogradely filled by the vertebral artery	–/–	Vascular graft (azathioprine, colchicum, and corticosteroid therapy)
Nair et al	India	25/Male	Low-grade fever followed by gradually increasing swelling of neck and face	large saccular aneurysm with thrombosis of bilateral subclavian arteries of which the right one caused external compression of the right innominate vein draining into the SVC	—	Steroids and azathioprine
Kalko et al	Turkey			The surgical treatment of arterial aneurysms in Behçet disease: a report of 16 patients [subclavian artery (n = 1)]	—	Vascular surgery

(Continued)

Table 1. Characteristics of Patients Diagnosed with BS with Subclavian Artery Involvement (Continued)

Study	Origin	Age/Gender	Symptom	Finding	CRP/ESR	Treatment
Kim et al	Korea			Endovascular treatment for aortic pseudoaneurysm in Behcet's disease (n = 10) [subclavian artery (n = 1)]		Stent-graft
Fei et al	China			Major vascular involvement in Behçet's disease: a retrospective study of 796 patients 102 vasculo-BD 56 BD patients developed arterial lesions with the majority (24 cases) of aneurysms subclavian (n = 5) arteries		
Tuzun et al	Turkey	20 to 53 years/all patients were male		Management of aneurysms in Behçet's syndrome: an analysis of 24 patients [subclavian artery (n = 1)]		
Nakamura et al	Japan	18/female	Attacks of dizziness, no pulse in her left arm	Widespread arterial narrowing was noted, including the bilateral carotid arteries, the left vertebral artery, and the left subclavian artery (all branches of the aortic arch). The most severely affected vessel was the left subclavian artery	25/64	Prednisolone and warfarin potassium
Kwon Koo et al	Korea	31/male 33/male 38/male		Endovascular therapy combined with immunosuppressive treatment for pseudoaneurysms in patients with Behcet's disease Left subclavian artery Left subclavian artery Right subclavian artery		Pre-endograft drug/current drug None/prednisolone prednisolone and azathioprine/prednisolone Prednisolone/ prednisolone and azathioprine
Vignesh et al	India	20/female	Feeble bilateral radial pulses	Bilateral occlusion of subclavian arteries beyond the origin of vertebral arteries	—	Azathioprine
Cakir et al	Turkey	35/male	A massive, painful, pulsatile, mass on the clavicle on the right side of the neck	A lobular giant saccular aneurysm on the proximal side of the right subclavian artery, giant aneurysm on the left subclavian artery, and occlusion on the distal side of the left subclavian and axillary artery	118/40	Vascular graft
Okita et al.	Japan	38/male	Hoarseness, dysphagia	Saccular-type aneurysms of the aortic arch, right subclavian artery, and infrarenal abdominal aorta	79/45	Prednisolone and vascular surgery
Park et al	Korea			Aortic and arterial aneurysms in Behcet disease: management with stent-grafts—initial experience [right and left subclavian (n = 2)]		Stent-graft
Sugisaki et al	Japan	24/female	High fever	From the aortic arch to the common carotid and vertebral arteries also revealed irregular thickness and stenosis in the bilateral common carotid arteries, and partial narrowing in the left subclavian artery	120/97	Prednisolone, mesalazine, and colchicine

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

of vasculo-BS was made.[14] In summary, it is obvious that there is no doubt in the diagnosis of BS with recurrent oral aphthous lesions, previous DVT, positive pathergy, and HLA-B51 tests in our patient. Of course, the coexistence of the diagnoses of BS and TAK may come to mind in this patient. However, such high levels of acute phase reactants for such a long period of time are not common in TAK. In fact, CRP>25 mg/L has been associated with a high risk of resistance to treatment in TAK.[32] On the other hand, severe systemic inflammation and high acute phase reactant levels in serum as an indicator of vasculo-BS are much more likely. This situation also includes the message that the authors want to give. In this case report of arterial involvement resembling TAK, which is rarely seen in BS, we wanted to emphasize the importance of persistently investigating vascular involvement when acute phase reactant elevation in BS cannot be explained by any other reason.

Informed Consent: Informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.B.; Design – G.A.; Supervision – C.B.; Resources – G.A., C.B.; Materials – G.A.; Data Collection and/or Processing – M.E., D.S.Ö.; Analysis and/or Interpretation – B.İ., B.K.; Literature Search – G.A., M.Y.M., F.Y.; Writing – G.A., X.X.; Critical Review – C.B.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

References

1. Alibaz-Oner F, Direskeneli H. Management of vascular Behcet's disease. *Int J Rheum Dis*. 2019;22(suppl 1):105-108. [CrossRef]
2. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. *N Engl J Med*. 1999;341(17):1284-1291. [CrossRef]
3. Tascilar K, Melikoglu M, Ugurlu S, Sut N, Caglar E, Yazici H. Vascular involvement in Behçet's syndrome: a retrospective analysis of associations and the time course. *Rheumatology (Oxford)*. 2014;53(11):2018-2022. [CrossRef]
4. Seyahi E. Behçet's disease: how to diagnose and treat vascular involvement. *Best Pract Res Clin Rheumatol*. 2016;30(2):279-295. [CrossRef]
5. Fei Y, Li X, Lin S, et al. Major vascular involvement in Behçet's disease: a retrospective study of 796 patients. *Clin Rheumatol*. 2013;32(6):845-852. [CrossRef]
6. Mason JC. Takayasu arteritis--advances in diagnosis and management. *Nat Rev Rheumatol*. 2010;6(7):406-415. [CrossRef]
7. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's disease. *Lancet*. 1990;335(8697):1078-1080.
8. ITR-ICBD. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. *J Eur Acad Dermatol Venereol*. 2014;28(3):338-347. [CrossRef]
9. Li L, Gu Y, Qi L. Endovascular repair of a subclavian artery aneurysm in Behçet's disease. *Interact Cardiovasc Thorac Surg*. 2018;27(3):461-462. [CrossRef]
10. Abe K, Uchida K, Sugano T, Ishigami T, Ishikawa T. Subclavian artery pseudoaneurysm in vascular Behcet's disease repaired using endovascular treatment: a case report of the clinical course over 10 years. *J Cardiol Cases*. 2021;24(1):1-5. [CrossRef]
11. Ocon AJ, Mehta VR, Peredo-Wende R. Coeliac artery dissection as a rare manifestation of Behcet's disease. *BMJ Case Rep*. 2018;2018:bcr2018226039. [CrossRef]
12. So H, Yip ML. Acute myocardial infarction and subclavian artery occlusion in a 41-year-old woman with Behçet's disease: coronary and large vessel arteritis. *Singapore Med J*. 2014;55(9):e145-e147. [CrossRef]
13. Yildirim A, Isik A, Koca S. Subclavian artery pseudoaneurysm in Behcet's disease. *Clin Rheumatol*. 2007;26(7):1151-1154. [CrossRef]
14. Sugisaki K, Saito R, Takagi T, et al. HLA-B52-positive vasculo-Behçet disease: usefulness of magnetic resonance angiography, ultrasound study, and computed tomographic angiography for the early evaluation of multiarterial lesions. *Mod Rheumatol*. 2005;15(1):56-61. [CrossRef]
15. Park JH, Chung JW, Joh JH, et al. Aortic and arterial aneurysms in Behçet disease: management with stent-grafts--initial experience. *Radiology*. 2001;220(3):745-750. [CrossRef]
16. Yoo WH, Kim HK, Park JH, Park TS, Baek HS. Mediastinal mass and brachial plexopathy caused by subclavian arterial aneurysm in Behçet's disease. *Rheumatol Int*. 2000;19(6):227-230. [CrossRef]
17. Lee KY, Sunwoo IN, Oh WS, Kim SM, Choi BO. Brachial plexopathy caused by subclavian artery aneurysm in Behçet's disease. *Muscle Nerve*. 1999;22(12):1721-1723. [CrossRef]
18. Cingoz F, Bingol H, Ozal E, Tatar H. Coronary subclavian steal syndrome in a patient with Behçet's disease. *Thorac Cardiovasc Surg*. 2010;58(4):244-246. [CrossRef]
19. Nair AA, Christopher DJ, Moidu F, Chandran D. Superior vena caval obstruction: a rare presentation of Behcet's disease. *BMJ Case Rep*. 2020;13(12):e236658. [CrossRef]
20. Kalko Y, Basaran M, Aydin U, Kafa U, Basaranoglu G, Yasar T. The surgical treatment of arterial aneurysms in Behçet disease: a report of 16 patients. *J Vasc Surg*. 2005;42(4):673-677. [CrossRef]
21. Kim SW, Lee DY, Kim MD, et al. Outcomes of endovascular treatment for aortic pseudoaneurysm in Behcet's disease. *J Vasc Surg*. 2014;59(3):608-614. [CrossRef]
22. Tüzün H, Beşirli K, Sayin A, et al. Management of aneurysms in Behçet's syndrome: an analysis of 24 patients. *Surgery*. 1997;121(2):150-156. [CrossRef]
23. Nakamura H, Ueki Y, Horikami K, et al. Vasculo-Behçet's syndrome with widespread arterial involvement. *Mod Rheumatol*. 2001;11(4):332-335. [CrossRef]
24. Kwon Koo B, Shim WH, Yoon YS, et al. Endovascular therapy combined with immunosuppressive treatment for pseudoaneurysms in patients with Behçet's disease. *J Endovasc Ther*. 2003;10(1):75-80. [CrossRef]
25. Vignesh P, Singhal M, Suri D, et al. Extensive oral scarring and bilateral subclavian artery stenosis in pediatric-onset Behçet's disease. *J Clin Rheumatol*. 2020;26(5):e91-e92. [CrossRef]
26. Cakir O, Eren N, Ulkü R, Nazaroğlu H. Bilateral subclavian arterial aneurysm and ruptured abdominal aorta pseudoaneurysm in Behçet's disease. *Ann Vasc Surg*. 2002;16(4):516-520. [CrossRef]
27. Okita Y, Ando M, Minatoya K, Kitamura S, Matsuo H. Multiple pseudoaneurysms of the aortic arch, right subclavian artery, and abdominal aorta in a patient with Behçet's disease. *J Vasc Surg*. 1998;28(4):723-726. [CrossRef]
28. Park JH, Chung JW, Joh JH, et al. Aortic and arterial aneurysms in Behçet disease: management with stent-grafts--initial experience. *Radiology*. 2001;220(3):745-750. [CrossRef]
29. Nishimura K, Hamasaki T, Yamamoto S, Kawai T, Sugiura K. Endovascular treatment of left subclavian artery pseudoaneurysm after clavicle fracture in an elderly adult with a 40-year history of Behçet's disease. *Ann Vasc Dis*. 2015;8(4):328-330. [CrossRef]
30. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Ann Rheum Dis*. 2018;77(6):808-818. [CrossRef]
31. Esatoglu SN, Ok AM, Ucar D, et al. Takayasu's arteritis: associated inflammatory diseases. *Clin Exp Rheumatol*. 2020;124(2):61-68.
32. Sun Y, Ma L, Chen H, et al. Analysis of predictive factors for treatment resistance and disease relapse in Takayasu's arteritis. *Clin Rheumatol*. 2018;37(10):2789-2795. [CrossRef]