Vascular Specialist International
Vol. 36, No. 3, September 2020
pISSN 2288-7970 • eISSN 2288-7989

Case Report

Takayasu Arteritis Presenting as Bilateral Ocular Ischemic Syndrome

Ramon B. Larrazabal Jr.[1], Harold Henrison C. Chiu[2], and Angeline Therese Magbitang-Santiago[3]

[1]Department of Medicine, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines, [2]Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines, [3]Division of Rheumatology, Department of Medicine, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines

A 26-year-old female came in with progressive blurring of vision. She had developed memory loss and complained of headache, significant weight loss, and exertional left calf pain after prolonged walking. Pertinent physical findings included light perception on visual acuity examination, and the brachial and radial pulses of both arms were not appreciable. Thoracic and abdominal aortic imaging by computed tomography with contrast revealed narrowing along the thoracic aorta and its branches. Carotid Doppler showed bilaterally thickened walls in the common carotid arteries, with near total occlusion of the left carotid artery. These findings were consistent with bilateral ocular ischemic syndrome in Takayasu arteritis. She was given methylprednisolone 500 mg intravenously daily for 3 days with noted improvement in vision. She was discharged and showed improvement on prednisone 35 mg/day and aspirin 80 mg/day. On follow-up two weeks post-discharge, she reported being able to see silhouettes of persons and objects.

Key Words: Takayasu arteritis, Vasculitis, Retinopathy

Received May 14, 2020
Revised July 17, 2020
Accepted August 2, 2020
Published online September 1, 2020

Corresponding author: Ramon B. Larrazabal Jr.
Department of Medicine, Philippine General Hospital, University of the Philippines Manila, 1000 Taft Avenue, Ermita, Manila, Philippines
Tel: 63-2-554-8400
Fax: 63-2-554-8400
E-mail: ramonlarrazabaljr@gmail.com
https://orcid.org/0000-0003-4538-416X

Vasc Specialist Int 2020;36(3):163-169 • https://doi.org/10.5758/vsi.200031

INTRODUCTION

Takayasu arteritis (TA) is an autoimmune, inflammatory, granulomatous large vessel vasculitis mainly affecting the aorta and its major branches. It is characterized by stenosis, occlusion, dilatation, or aneurysm formation [1]. Data on the epidemiology of the disease are lacking due to it being extremely rare, but some studies have noted that the prevalence was as high as 40 per million in Japan and as low as 0.9 per million in the United States [2] with a female predominance, especially in cases under 40 years old and among Southeast Asians [3].

The initial stage (pre-vasculitic phase) is characterized by the presence of nonspecific symptoms. During the late stages of the disease, symptoms of arterial occlusion, aneurysm formation, and vascular pain start to manifest. Patients often present with pulseless extremities, claudication, vascular bruits, hypertension, Raynaud syndrome, pericarditis, aortic regurgitation, congestive heart failure, stroke, and myocardial infarction [4]. Neurological manifestations are not uncommon and may include seizures, which can also be the initial presentation of the disease [5].

Ocular ischemic syndrome (OIS) is a spectrum of ocular manifestations of arterial hypoperfusion of the affected eye, caused mainly due to carotid artery stenosis [6]. It manifests as decline in visual acuity and as ocular pain, indicating the involvement of the anterior and the posterior segments. OIS is a rare initial presentation of TA and its prevalence is unknown. Currently, we have found and retrieved eight case reports recently published to provide context regarding the different management techniques and outcomes of these patients (Table 1) [7-14]. Here, we

Table 1. Summary of similar published studies

Reference	Age (y)	Sex	Ethnicity	Chief complaint/s	Therapy	Outcome
Kannan et al. [7] (2019)	13	Male	Indian	Sudden vision loss	- Oral steroids at 1 mkd - Oral methotrexate 10 mg/week - Bevacizumab for 3 doses	Loss of vision
Anguita et al. [8] (2019)	12	Female	Peruvian	Headache Amaurosis fugax, oculus sinister Right hemiparesis Bradylalia	- Steroids - Mycophenolate mofetil	Partial reperfusion of carotids and good perfusion of both eyes
Malik et al. [9] (2015)	35	Female	Pakistani	Gradual loss of vision in both eyes	- Oral dexamethasone 60 mg daily	Loss of vision
Shailaja et al. [10] (2013)	22	Female	Indian	Gradual loss of vision in both eyes and chronic pain in both eyes	- Systemic steroids at 1 mkd	Sudden cardiac death
Sakthiswary et al. [11] (2012)	20	Female	Malaysian	Loss of vision in both eyes, fatigue, and headache	- Methylprednisolone 1 gram daily for 3 days - Followed by prednisolone 1 mkd - Oral methotrexate 15 mg weekly - Oral warfarin - Panretinal photocoagulation	No improvement in visual acuity
Pelegrín et al. [12] (2012)	42	Male	Pakistani	Gradual loss of vision	- Prednisolone 60 mg/day - Aspirin 100 mg/day - Oral methotrexate 20 mg/week - Cataract surgery and pars plana vitrectomy - Panretinal endophotocoagulation - Intracameral and intravitreal injection of 1.25 µg/0.05 mL of bevacizumab	Stromal iris neovascularization was improved
Demir et al. [13] (2010)	14	Female	Turkish	Gradual visual loss in both eyes	- Intravenous methylprednisolone 1 g/day for 3 days - Followed by oral methotrexate 10 mg/day with oral steroids on a tapered basis - Panretinal photocoagulation for four sessions	Developed cataracts and eventually phthisis bulbi
Koz et al. [14] (2007)	45	Male	Turkish	Fatigue, both upper extremity weakness, and blurring of vision	- Methylprednisolone 1 mkd - Oral methotrexate 15 mg/week - Cyclophosphamide therapy	Died during bypass graft surgery

mkd, mg/kg of body weight per day.

report a case of worsening vision in a 26-year-old female with OIS in TA and discuss our approach for diagnosis and treatment. This is the first documented report of OIS in TA from the Philippines.

CASE

A 26-year-old female presented with an 11-month duration of progressive blurring of vision, beginning with the left eye and eventually involving both eyes. She also complained of headache, left facial asymmetry, weight loss, and exertional left calf pain after prolonged walking, and had developed memory loss. Other pertinent medical history included treatment for pulmonary tuberculosis and an incidental finding of weak pulses on her upper extremities during her admission for childbirth 2 years prior.

Pertinent physical examination findings included: light perception on visual acuity testing and whitish opacities in the pupil of the left eye. Fundoscopic examination revealed: mature cataracts; punctate uptake of fluorescein dye on both eyes; disconjugate gaze; nystagmus on both eyes; and left facial palsy. Both brachial and radial pulses were unappreciable, while both the carotid pulses, and the popliteal and dorsalis pedis pulses, were weak. Blood pressure was 120/80 mmHg in the right and 100/90 mmHg in the left popliteal areas, respectively. There were no other signs or symptoms of ischemia or claudication noted.

Work-up done on admission revealed: protein S: 113% (normal value [NV]: 72% to 106%); C-reactive protein: >1.2 mg/dL (NV: <0.6 mg/dL); and antithrombin III: 131.5% (NV: 83% to 128%). Complete blood count revealed microcytic and hypochromic anemia. Thyroid function tests, chemical profile, protein C, erythrocyte sedimentation rate, antinuclear antibodies titer, cytoplasmic antineutrophilic cytoplasmic autoantibody, and perinuclear antineutrophilic cytoplasmic autoantibody were all within normal limits.

Computed tomography (CT) and angiogram of the cranium and the neck revealed arterial wall thickening with associated luminal stenosis involving the proximal branches of the aortic arch, and multiple small chronic infarcts in the left frontal lobe (Fig. 1). CT of the thoracic and abdominal aorta and its branches, with intravenous contrast, revealed segmental areas of wall thickening along the thoracic aorta and its branches, with narrowing of the latter with minimal plaque formation in the following (with length of involvement): aortic arch (62 mm); innominate artery (36 mm); right subclavian artery (12 mm); left subclavian artery (22 mm); and descending thoracic aorta (72 mm). There was good opacification of the celiac artery, the superior mesenteric artery, the inferior mesenteric artery, and their branches (Fig. 2). Fluorescein angiography of the eyes revealed diffuse retinal occlusive vasculopathy (more of the veins) with secondary neovascularization and macular edema in the right eye and cataract in the left eye (Fig. 3); Optical coherence tomography revealed neuropathy of the right eye and media opacity of the left eye. Carotid Doppler studies revealed diffusely and circumferentially thickened common carotid arteries with smooth, homogenous, and mildly echogenic walls; the left proximal common carotid artery was noted to have near-total occlusion and absent flow on color flow study. The mid to distal left common carotid artery exhibited flow on color flow study; however, its di-

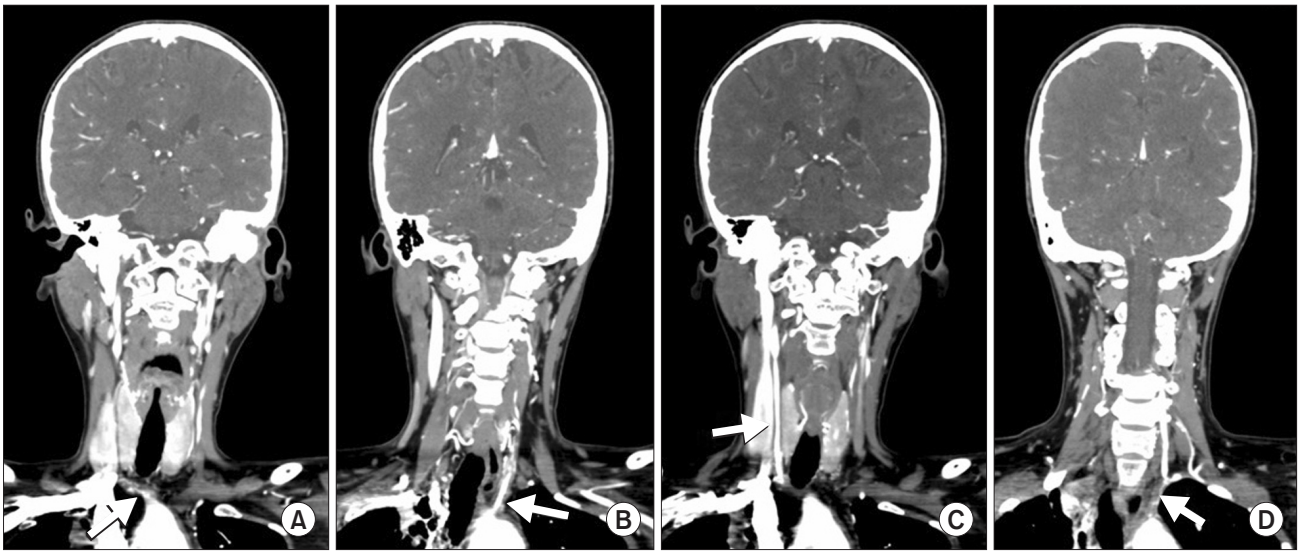

Fig. 1. Computed tomography of the cranium and the neck showed narrowing of the following vessels. (A) Innominate artery (arrow). (B) Left common carotid artery (arrow). (C) Right common carotid artery (arrow). (D) Left subclavian artery (arrow).

https://doi.org/10.5758/vsi.200031

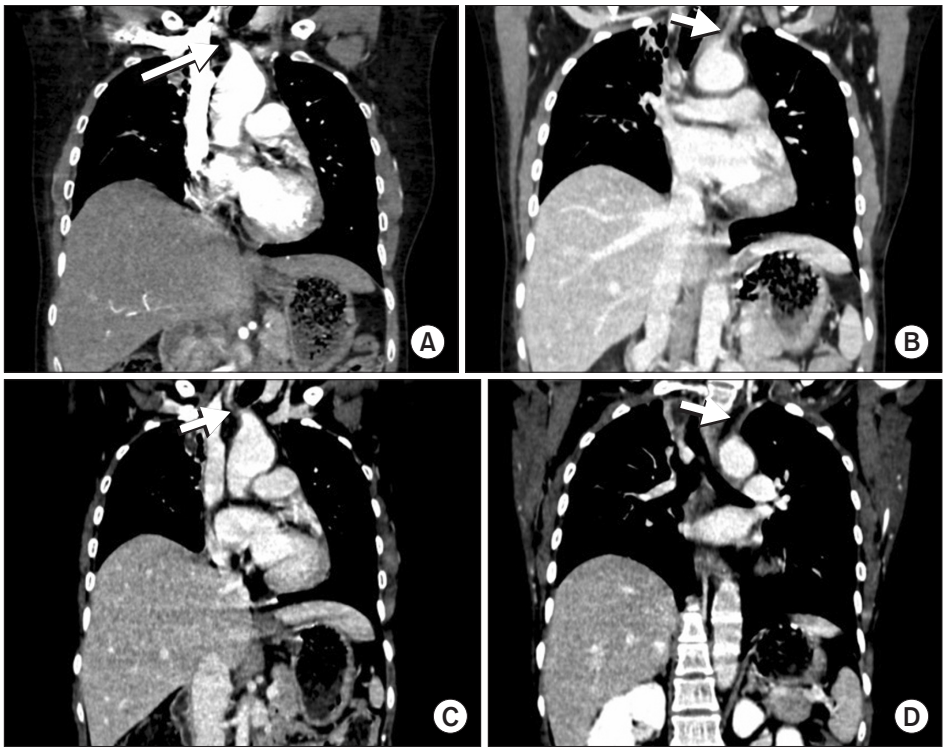

Fig. 2. Computed tomography of the thoracic and abdominal aorta showed narrowing of the following vessels as pointed by the arrows. (A) Innominate artery. (B) Left common carotid artery. (C) Right common carotid artery. (D) Left subclavian artery. No lesion was noted in the aortic bifurcation.

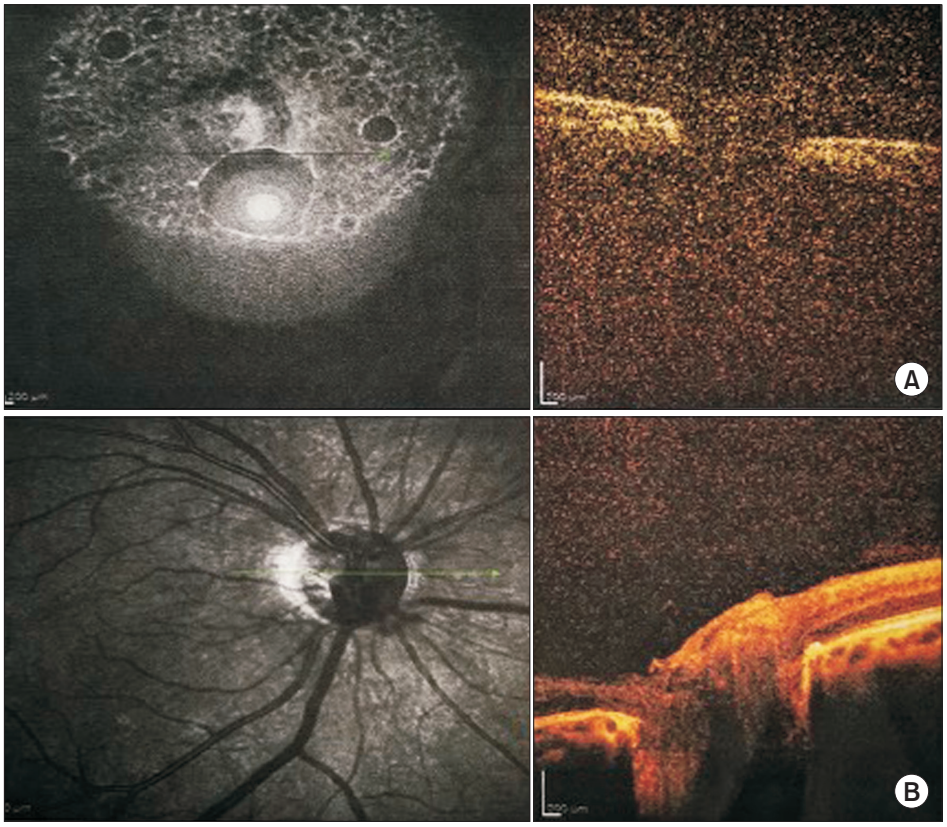

Fig. 3. Fluorescein angiography. (A) Oculus sinister mature cataract. (B) Oculus dexter vasculopathy with neovascularization.

ameter was narrowed to 0.9 mm. On the right, the luminal diameter measured 1.0 mm. The maximum thickness of the intima and media on the right was 2.0 mm as seen along its proximal aspect (Fig. 4). The resultant irregular narrowing of the lumina (of the common carotid arteries) resembled a "beaded" pattern in appearance.

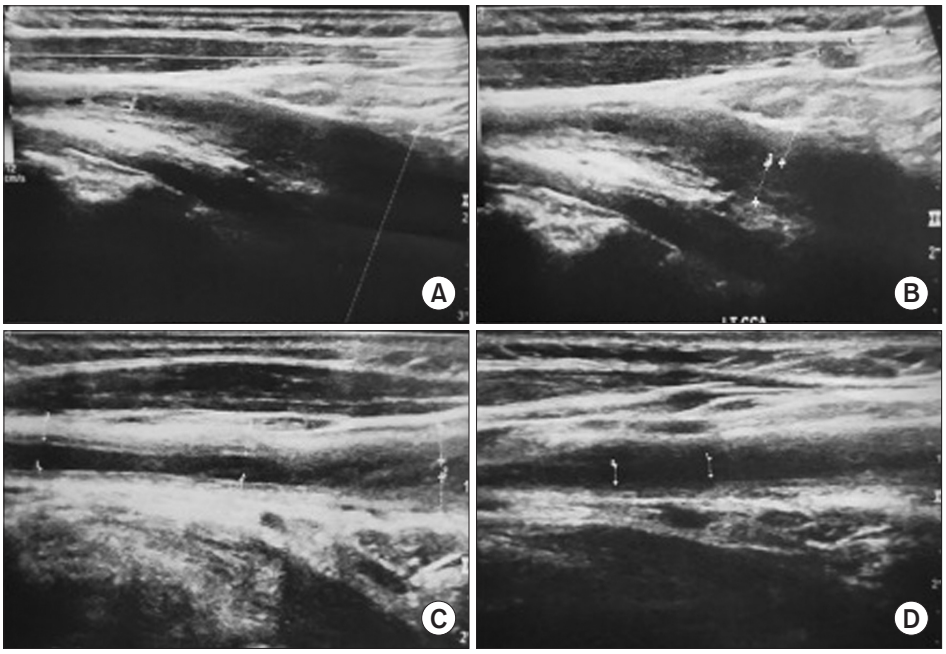

Fig. 4. Carotid ultrasound. (A) Near total occlusion at the left common carotid artery (CCA). (B) Thickened walls of the left CCA. (C) Narrowest luminal diameter of the right CCA. (D) Thickened walls of the right CCA.

Further work-up included two-dimensional echocardiography that revealed an ejection fraction of 62% (NV: >55%) and concentric remodeling of the left ventricle with hypokinesia of the anterior and basal inferior interventricular segments, which was attributed to TA activity. Magnetic resonance imaging of the brain with contrast revealed prominent (5.0 mm) perivascular spaces in the basal ganglia, frontal white matter, and semioval center.

Our patient's medical profile, physical findings, and imaging results were consistent with the diagnosis of OIS in TA based on the American College of Rheumatology (ACR) guidelines. We managed our patient as a case of bilateral OIS in TA with stage 4 retinopathy. We started her on high dose steroids (methylprednisolone 500 mg intravenously) given daily for 3 days. She reported subjective improvement in vision, described as being able to see silhouettes compared with just light perception prior to treatment. Follow-up fundoscopy 5 days after methylprednisolone therapy did not reveal any improvement. However, more invasive surgical management was deferred at that time due to the high TA activity. A carotid stent placement procedure was offered and explained to the patient, but she did not give consent to go through with the procedure. She was discharged and showed improvement on prednisone 35 mg/day and aspirin 80 mg/day. On outpatient follow-up 2 weeks post-discharge, she reported an improvement in her overall well-being as well as being able to see silhouettes of persons and objects. She had no further episodes of behavioral changes, memory loss, headache, or neurologic deficits.

The patient was able to follow-up for two months post-discharge at our out-patient clinic and she reported being able to see better (i.e., being able to see objects and faces better). On physical examination, she had a blood pressure of 90/60 mmHg (which was previously unappreciable during her admission) on both right and left upper extremities. Furthermore, she had a carotid ultrasound done which revealed: a) narrowed left common carotid artery (from near total occlusion) and b) thickened walls of the right common carotid artery.

We then explained to the patient that we planned to control the inflammation prior to any form of surgical management. Our long-term plan is to perform a percutaneous angioplasty or a carotid stent placement.

DISCUSSION

TA begins in the adventitia of the vessels and progresses inward to the intima with significant proliferation and fibrosis. This eventually causes narrowing, occlusion, and/or thrombus formation. There is a consequential compromise in the blood flow of the affected vessels, with a possibility of aneurysm formation [15]. Clinical manifestations between pediatric and adult populations vary: hypertension is the most common (73%), followed by headache (53%), nonspecific constitutional symptoms (53%), and fever (45%) [3]. The clinical manifestations in TA are classified into either hypertensive or hypoperfusive. In the hypertensive subgroup, the manifestations occur due to the involvement of the renal artery or the suprarenal aorta, leading to severe and uncontrolled hypertension. In contrast, in the hypoperfusive subgroup, the manifestations are mainly due to

https://doi.org/10.5758/vsi.200031

an occlusive arteritis of the aortic arch and/or its branches (occluded or severely stenosed carotid arteries), which leads to ischemic ocular manifestations [16]. OIS is a hypotensive from of retinopathy due to chronic hypoperfusion of the ophthalmic artery secondary to carotid artery stenosis from large vessel vasculitis.

Our case was more consistent with the hypoperfusive subgroup, thus the symptoms were mainly ocular and ophthalmologic from the carotid artery occlusion [1]. The best described ischemic ocular manifestation among patients with TA is called Takayasu retinopathy, which has four stages, as described by Uyama and Asayma: stage 1: distension of veins; stage 2: micro-aneurysm formation; stage 3: formation of arterio-venous anastomoses; and stage 4: presence of cataract, rubeosis iridis, retinal ischemia, neovascularization, and vitreous hemorrhage [17]. Its pathogenesis is described as: 1) patients develop generalized tortuosity and vasodilatation of the retinal veins with formation of arteriovenous anastomosis, capillary drop-out, and micro-aneurysmal formation; 2) this leads to vitreous hemorrhage, retinal detachment, neovascular glaucoma, and optic atrophy, which ultimately leads to blindness [1]. More often than not, eye changes are hardly noticeable and the conditions are often asymptomatic. Therefore, all patients diagnosed with TA should undergo ophthalmologic evaluation to rule out eye abnormalities [16].

We based our diagnosis on the ACR guidelines for TA, defined as the presence of any 3 or more of the following criteria (sensitivity of 90.5% and specificity of 97.8%): 1) age of 40 years or younger at disease onset; 2) claudication of the extremities; 3) decreased pulsation of one or both brachial arteries; 4) difference of at least 10 mmHg in systolic blood pressure between arms; 5) bruit over one or both subclavian arteries or the abdominal aorta; and 6) arteriographic narrowing or occlusion of the entire aorta, its primary branches, or the large arteries in the upper or lower extremities that is not due to arteriosclerosis, fibromuscuar dysplasia, or other causes. Our patient fulfilled criteria 1), 3), 4), and 6), consistent with the diagnosis of TA [18].

The primary goals in the management of active disease flares are 1) suppressing inflammation and 2) preserving the vasculature. The treatment of TA is based on the use of immunosuppressants such as steroids. Methotrexate and low-dose aspirin are among the mainstay therapies used to control inflammation [18]. Anti-inflammatory therapy can lead to a dramatic improvement in the disease. The 5-year survival rate in adults can be as high as 94%. Invasive treatment procedures, including stent placement, endarterectomy, bypass grafts, and angioplasty, are often reserved for cases of severe and symptomatic stenosis or occlusion of the arteries. These invasive interventions have potential short-term benefits; however, they have been associated with device failure and poorer outcomes when performed during the active inflammatory phase of the disease [19].

Our case illustrated the protean features of TA. It emphasized the significance of a high index of suspicion, a thorough medical history, a complete physical and ophthalmologic examination, and a judicious use of imaging modalities to arrive at the correct diagnosis. This translated to prompt institution of treatment to prevent further ophthalmologic complications and visual deterioration. Lastly, early detection of the disease allows for closer monitoring as the complications of TA are largely preventable.

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to Dr. Kirky Maramara for guiding us in the management of this patient. We would also like to thank Dr. Sandra Sanidad for her opinions and insights when writing this case report.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ORCID

Ramon B. Larrazabal Jr.
https://orcid.org/0000-0003-4538-416X
Harold Henrison C. Chiu
https://orcid.org/0000-0002-2021-7843
Angeline Therese Magbitang-Santiago
https://orcid.org/0000-0003-1152-331X

AUTHOR CONTRIBUTIONS

Concept and design: RBL, HHCC. Analysis and interpretation: RBL, HHCC. Data collection: RBL. Writing the article: RBL. Critical revision of the article: RBL, HHCC, ATMS. Final approval of the article: all authors. Statistical analysis: none. Obtained funding: none. Overall responsibility: RBL.

REFERENCES

1) Karam EZ, Muci-Mendoza R, Hedges TR 3rd. Retinal findings in Takayasu's arteritis. Acta Ophthalmol Scand 1999;77:209-213.
2) Onen F, Akkoc N. Epidemiology of Takayasu arteritis. Presse Med 2017;46(7-8 Pt 2):e197-e203.
3) Mathew AJ, Goel R, Kumar S, Danda D. Childhood-onset Takayasu arteritis: an update. Int J Rheum Dis 2016;19:116-126.
4) 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-S446.
5) Vidhate M, Garg RK, Yadav R, Kohli N, Naphade P, Anuradha HK. An unusual case of Takayasu's arteritis: evaluation by CT angiography. Ann Indian Acad Neurol 2011;14:304-306.
6) Gavrilenko AV, Kuklin AV, Kiseleva TN. [Efficacy of carotid endarterectomy in patients with stenosis of carotid arteries and acute vision impairment]. Angiol Sosud Khir 2013;19:106-112. Russian.
7) Kannan NB, Kohli P, Ramachandran N O. Abnormal retinal vasculature in a young child: a diagnostic dilemma. Ocul Immunol Inflamm 2019. doi: 10.1080/09273948.2019.1672199. [Epub ahead of print]
8) Anguita R, Nazar C, Kobus R, Salinas A, Astete M. Bilateral ocular ischemic syndrome as a manifestation of Takayasu arteritis in children. Can J Ophthalmol 2019;54:e105-e108.
9) Malik TG, Khalil M, Ijaz AU, Bhatti MM. Ocular ischemic syndrome and ischemic optic neuropathy in Takayasu arteritis. J Coll Physicians Surg Pak 2015;25 Suppl 1:S47-S49.
10) Shailaja S, Vivek G, Shetty R, Kamath Y. 'Eye is a window to the pulse': bilateral ocular ischaemic syndrome as a presenting manifestation of Takayasu arteritis. BMJ Case Rep 2013;2013:bcr2013009461.
11) Sakthiswary R, Syazarina SO, Shaharir SS, Said MS, Hanom F. Blindness in a pulseless young woman: lessons learned. Ocul Immunol Inflamm 2012;20:309-311.
12) Pelegrín L, Mesquida M, Rey A, Sánchez-Dalmau B, Frohman L. Blind runner. Surv Ophthalmol 2012;57:486-494.
13) Demir MN, Hazirolan D, Altiparmak UE, Acar MA, Unlü N, Ornek F. Takayasu's disease and secondary ocular ischemic syndrome. J Pediatr Ophthalmol Strabismus 2010;47:54-57.
14) Koz OG, Ates A, Numan Alp M, Gultan E, Karaaslan Y, Kural G. Bilateral ocular ischemic syndrome as an initial manifestation of Takayasu's arteritis associated with carotid steal syndrome. Rheumatol Int 2007;27:299-302.
15) Szugye HS, Zeft AS, Spalding SJ. Takayasu arteritis in the pediatric population: a contemporary United States-based single center cohort. Pediatr Rheumatol Online J 2014;12:21.
16) Peter J, David S, Joseph G, Horo S, Danda D. Hypoperfusive and hypertensive ocular manifestations in Takayasu arteritis. Clin Ophthalmol 2010;4:1173-1176.
17) Uyama M, Asayama K. Retinal vascular changes in Takayasu's disease (Pulseless disease), occurrence and evolution of the lesion. In: Laey JJ, editor. International symposium on fluorescein angiography Ghent 28 March-1 April 1976. Dordrecht: Springer Netherlands; 1976. p. 549-554.
18) Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lie JT, Lightfoot RW Jr, Masi AT, McShane DJ, Mills JA, Stevens MB, Wallace SL, Zvaifler NJ. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990;33:1129-1134.
19) Khan MAM, Banoo H. A case report of Takayasu's arteritis. Med Today 2012;24:79-81.

https://doi.org/10.5758/vsi.200031