Challenges in Diagnosis and Management of Takayasu Arteritis: A Case Report Highlighting Vascular Complications and Delayed Recognition.

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Introduction:

Takayasu arteritis (TA), also known as pulseless disease, is a rare systemic inflammatory condition that primarily affects the medium and large arteries, including their branches. It predominantly occurs in young Asian women, with a reported worldwide incidence of only 1 to 2 per million people[1].

Women are more frequently affected than men[2], with a varying incidence rate in different parts of the globe. Male to female ratio is 1:8 in western countries and 1:3 in Japan[3].

It is a chronic disease primarily impacting the aorta and its large branches. Early diagnosis is crucial to prevent severe end organ damage, including stroke and ischemic heart disease[4].

However, diagnosis is often challenging due to the non-specific systemic inflammatory symptoms present in the early phase, which can lead to an insidious clinical course until vascular ischemic complications emerge[5].

The disease typically progresses through two phases: an initial pre-occlusive inflammatory phase that may go unnoticed, followed by an occlusive phase characterized by ischemic vascular symptoms resulting from arterial lesions such as stenosis, occlusion, or aneurysm[6].

Extremity pain, claudication, bruits, pulselessness and unrecordable blood pressure are the common features of patient visiting health care facility. However, presentation with acute visual loss or stroke may be particularly rare[7].

18% of patients with large vessel vasculitis presents with unilateral visual loss at diagnosis, often resulting in irreversible damage. Early administration of pulsed intravenous methylprednisolone may provide some benefit to patients experiencing early onset of visual symptoms[8].

While numerous systematic reviews have explored ocular manifestations in various systemic diseases, few have focused on the eye involvement in Takayasu arteritis.

Case History/ Examination

A 30-year female weighing 59 kg presented three months back with a 4-year history of easy fatigue in the bilateral upper limbs, initially triggered by strenuous activity. She was diagnosed anemia with multivitamin deficiency and managed accordingly. However, fatigue progressively worsened over the last seven days and is now present even on general activities. Recently, she also experienced limb claudication, jaw claudication while eating, bilateral temporal headaches with orbital pain, and painful intermittent blurred vision, which worsened in the last three days. Additionally, she reported dizziness and lightheadedness for the past three days.

On examination, her systolic blood pressure was 60 mmHg with an unrecordable diastolic pressure, respiratory rate was 24 breaths per minute, pulse was 97 beats per minute(bpm), temperature was 97°F, and oxygen saturation was 98% on room air. She had a Glasgow Coma Scale (GCS) score of 15/15, and her random blood sugar was 150 mg/dL. Physical examination revealed pallor in the bilateral palpebral conjunctiva, a feeble pulse in the right radial artery with no pulse in the left radial artery, palpable bilateral dorsalis pedis, a bruit over the right carotid artery, and absent bruit over the left. Systemic examinations were otherwise normal. There was no similar history in the family.

Methods (Investigations and Treatment):

Blood investigations showed a leukocyte count of 8320/mm^3 (normal range: 4000-11000/mm^3), platelets at 288,000/mm^3 (150,000-400,000), RBC at 4.25 million/mm^3 (4-5 million/mm^3), hemoglobin at 10 mg/dL (12-16 mg/dL for women), mean cell volume at 76.2 fl (80-99 fl), mean cell hemoglobin concentration at 30.9 g/dL (32-36 g/dL), mean cell hemoglobin at 23.6 pg (26-32 pg), packed cell volume at 32.4% (36-54%), erythrocyte sedimentation rate at 66 mm/hr (0-20 mm/hour for <50 years female), and C-reactive protein at 22.9 mg/L (0-5 mg/L). Serum creatinine was 0.66 mg/dL (0.4-1.4 mg/dL), sodium was 140 mmol/L (135-150 mmol/L), and potassium was 4.11 mmol/L (3.5-5.5 mmol/L). Thyroid and liver function tests were normal. Urine examination revealed plenty of pus cells with positive (++) leukocyte esterase, but no growth in urine culture. Abdominal and pelvic ultrasound scans were normal and advised follow up.

Cardiothoracic consultation was done suspecting cardiovascular disorder which advised carotid CT angiogram. The patient was given two rapid boluses of 500 ml Ringer's Lactate (RL) over an hour. Still the blood pressure could not be recorded from upper limb, however the blood pressure was 130/80 mm of Hg in bilateral lower limb. The blood pressure fluctuation is shown below in table 1. A pint of RL was then infused at 30 ml/hour, maintaining stable vitals.

Table 1: BP fluctuations of the patient.

Day 0	At 11: 40 AM	60/-	Upper limb Blood pressure
	At 12:15 PM	130/80	Lower limb Blood pressure
	At 1 PM	170/100	
	At 2 PM	150/90	
	At 3 PM	160/90	
	At 4 PM	170/90	
	At 5 PM	120/80	
	At 6 PM	130/70	
	At 7 PM	170/70	
	At 8 PM	180/100	
Day 1	At 2 PM	110/80	
Day 2	At 1 PM	128/80	
Day 3	At 12 PM	130-120/80-90	

She was kept on tablet Aspirin 75mg per oral once a day (OD), injection methylprednisolone, nitrofurantoin 100 mg OD, pantoprazole 40 mg per oral OD and other supportive measures.

On her first day of admission (DOA), ophthalmology consultation was done. It showed the following visual acuity (Table 2) results:

Table 2: Visual acuity

Visual acuity	**Right eye**	**Left eye**
Unaided	6/9 partial	6/18 partial

Visual acuity	Right eye	Left eye
Pin hole	6/6 partial	6/9

Eyeball examination was normal, and all duction and version movements were within normal range. Posterior segment evaluation showed a cup-disc ratio of 0.3:1, arteriovenous ratio of 2:4, positive foveal reflex, bilateral microaneurysms, and flame-shaped hemorrhages more in the peripheral retina. Retinoscopy at 66cm (Fig 1) indicated a correction of -0.50D cylindrical lens at 110° for the right eye (6/6 partial) and -0.50D spherical lens with -0.50D cylindrical lens at 90° for the left eye (6/9). The patient was kept under observation for blurred vision.

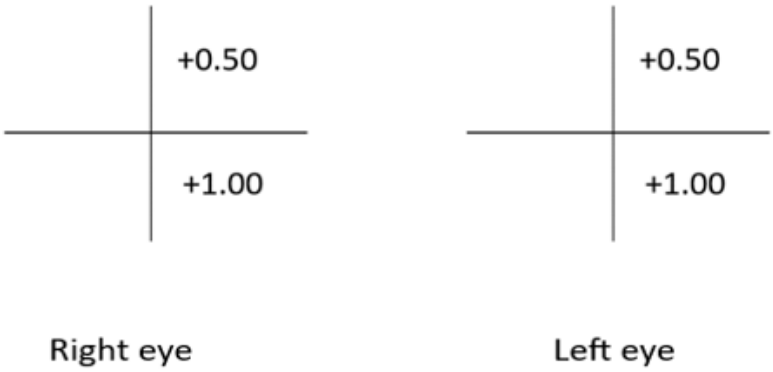


Fig 1: Retinoscopy findings of both eyes

Patient was well and alert with no fresh issues. However, she was measured hyperglycemic throughout the day as shown below in line graph (Fig 2) which prompted to manage with injection regular insulin 6 unit (indicated as *). The hyperglycemic episodes were attributed to extensive corticosteroid administration.

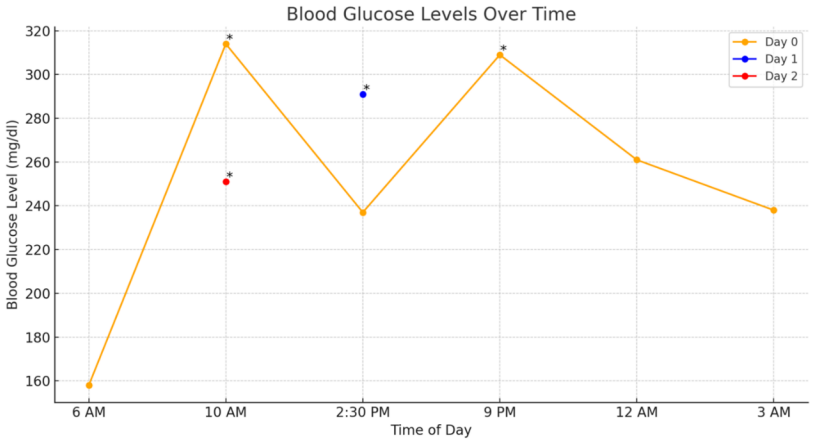


Fig 2: Line chart showing blood glucose fluctuations and regular insulin administration.

On her 2nd DOA, Carotid CT angiogram revealed features likely of type 1 Takayasu arteritis with following findings (Figure 3). There was circumferential symmetric thickening of arch of aorta and its all branches with left common carotid artery stenosis by 90% in its entire course. Patient BP was monitored and planned to

add amlodipine 2.5 mg per oral OD diagnosing reflex hypertension. CTVS recommended steroid treatment for the initial two weeks followed by bypass channel formation between right common carotid artery and right brachiocephalic trunk or arch of aorta.

She was planned to give induction with high-dose methylprednisolone (1g) for three doses in three days followed by tablet prednisolone (60 mg per oral OD) and Azathioprine (50 mg per oral OD) with a plan to increase azathioprine to 50mg twice a day (BD) and taper dose of prednisolone in next two weeks after baseline complete blood counts monitor. She was also prescribed tablet folic acid (5 mg, five times a week), tablet aspirin (75 mg), tablet rosuvastatin and tablet cefuroxime and clavulanic acid (500 mg). Regular insulin was administered as per requirement dictated by blood glucose level. The use of antibiotics was justified for focus of infection seen in routine urine examination.

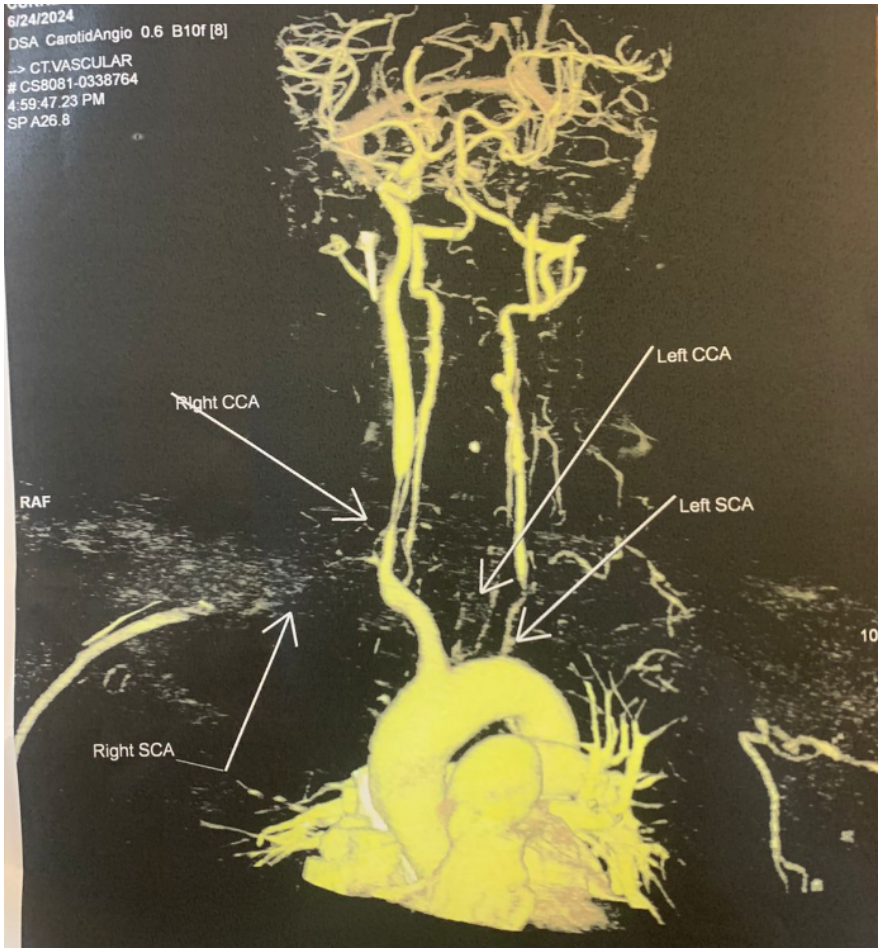


Fig 3: Carotid CT angiogram.

On the 4th DOA, the patient was discharged with hemodynamically stable vitals: pulse 78 bpm, BP 120/80 mmHg at bilateral lower limb, respiratory rate 20 breaths per minute, temperature 97.3°F, and oxygen saturation 98% on room air.

Conclusion and Results (Outcome):

The delayed diagnosis resulted in lifelong morbidity for the patient, with no procedure able to resolve the persistent fatigue experienced. However, she was counselled to undergo arterial bypass which would relief

dizziness temporarily.

Discussion:

Takayasu's arteritis is a chronic idiopathic inflammatory condition, typically beginning in the second or third decade of life. Its progression involves the gradual development of fibrotic narrowing in the aorta and its major branches. This can lead to various complications such as narrowing, clot formation, dilation, or even the formation of aneurysms. Regions like Asia, Africa, and Latin America report the highest number of cases, with Asia (2.69 cases per million per year) specifically showing an incidence rate about 100 times higher than Europe and North America[7]. It primarily affects young female during their twenties and thirties, but has been reported in children as young as 24 months of age[9].

According to Sharma et al.'s study, Indian and South Asian patients more frequently exhibit type II and III angiographic involvement compared to type I, which contrasts with the predominant type I involvement seen in Japan and Western countries. Japanese patients typically experience the disease starting in the ascending aorta and arch before progressing to the thoraco-abdominal aorta. In contrast, Indian patients commonly initially present with involvement of the abdominal aorta, which then progresses upward to affect the thoracic aorta[10]. It often presents with varied clinical manifestations. In our patient, the presenting symptoms developed lately were painful blurring of vision and orbital pain with an ocular examination finding of 2:4 arteriovenous ratio indicative of venous engorgement which align closely with recognized ophthalmic manifestations of Takayasu arteritis (TAK)[11].

It has an insidious onset which manifest as arteritis early in the course resulting in segmental stenosis, occlusion, dilatation and/or aneurysm of the vessel[7]. Vessel wall thickening, narrowing, and complete blockage can lead to reduced blood flow and tissue damage, posing significant risks to individuals with Takayasu's arteritis (TA). This condition can impair organ function due to ischemia, potentially threatening the lives of affected patients. In addition, involvement of the coronary arteries in TA is particularly concerning, as it is associated with a poor prognosis and higher mortality rates. Furthermore, performing coronary artery revascularization in patients with active TA is challenging and carries an elevated risk of major adverse cardiac events (MACE)[12].

A case of type III TA reported by Del et al in a 25 year female with 7 years of prednisolone administration resulted in disease remission, control and also improves the diameter of abdominal aorta[13].

EULAR guidelines suggested Prednisolone as the primary treatment choice with an initial dosage of 1 mg/kg/day (up to a maximum of 60 mg/day) maintaining for a month, followed by a gradual reduction in dose. In most cases, additional immunosuppressive therapy is necessary to reduce the risk of steroid-related side effects and manage disease progression. It's crucial to note that discontinuing steroid treatment can often lead to relapses. Up to 70% of Takayasu arteritis patients may require vascular surgery or bypass grafting to address aspects like renovascular hypertension. Although it has a favorable outcome, subsequent revision surgery are often necessary. Angioplasty and stent placement are associated with higher restenosis rates. It is advisable to schedule elective procedures during periods of disease remission requiring Long-term follow-up[8].

Similarly, tocilizumab (TCZ) stood better than traditional DMARDs in patient involving coronary arteries with TA in terms of reducing disease activity as a whole, improving lumen stenosis and reduction of glucocorticoid dose post- TCZ treatment for 6 months[12].

Kwon et al revealed that the administration of statins on TAK patients with active disease substantially reduces the relapse rate following remission attainment in this population[14].

In our case, four years after the onset of the disease, imaging studies revealed extensive vascular changes, including 90% stenosis of the left common carotid artery and complete occlusion of the left subclavian artery with distal reformation. The delayed diagnosis resulted in lifelong morbidity for the patient, with no procedure able to resolve the persistent fatigue experienced. However, she was counselled to undergo arterial bypass which would relief dizziness temporarily. As the disease progresses beyond the bypass's effectiveness,

the symptoms would reappear. Despite treatment initiation with high-dose steroids and immunosuppressants, the disease had progressed significantly, limiting treatment options to symptomatic relief and delay of further progression which profoundly impacted on her quality-adjusted life year. Study has shown that, it significantly impacts patients' quality of life, with both physical and mental health scores lower than those of many other chronic diseases involving peripheral vascular disease[15]. This case shows the typical natural history of type 1 Takayasu arteritis and the dreadful morbidity the patient had to suffer.

Conclusion:

Early recognition is crucial to initiate appropriate treatment promptly and mitigate the long-term morbidity and mortality associated with this rare systemic vasculitis. Takayasu arteritis (TA) can present with a range of clinical symptoms. The initial manifestation of nonspecific symptoms, such as easy fatigue in the upper limbs, can hinder the diagnosis process. This case emphasizes the importance of maintaining a high suspicion for TA, especially among females aged between the second and third decades, who experience prolonged fatigue in bilateral upper limbs.

Author Contribution:

Bindira Adhikari: Conceptualization, Writing- original draft, writing- review and editing**.**

Biraj Niraula: Validation, Writing- original draft, writing- review and editing**.**

Polina Dahal: Conceptualization, writing- review and editing**.**

Anil Suvedi: Writing- review and editing**.**

Gaurav Subedi: Writing- review and editing,

CONSENT

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review on request.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

Key Clinical Message:

Takayasu arteritis can start with vague symptoms like upper limb fatigue, complicating early diagnosis. This case highlights the critical need for suspicion in young women with such symptoms to prevent severe progression and significant impacts on quality of life.

References:

1. Trinidad B, Surmachevska N, Lala V. Takayasu Arteritis.

2. Onen F, Akkoc N. Epidemiology of Takayasu arteritis. Presse Med. 2017 Jul;46(7–8):e197–203.

3. SHARMA S, SANGAMESWARAN K, KALRA S. CLINICAL PROFILE OF TAKAYASU'S ARTERITIS. Med J Armed Forces India. 1998 Apr;54(2):140–2.

4. Somashekar A, Leung YT. Updates in the diagnosis and management of Takayasu's arteritis. Postgrad Med. 2023 Jan 2;135(sup1):14–21.

5. Zaldivar Villon MLF, de la Rocha JAL, Espinoza LR. Takayasu Arteritis: Recent Developments. Curr Rheumatol Rep. 2019 Sep 18;21(9):45.

6. Maz M, Chung SA, Abril A, Langford CA, Gorelik M, Guyatt G, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. Arthritis & Rheumatology. 2021 Aug 8;73(8):1349–65.

7. Setty N. Takayasu's arteritis - a comprehensive review. J Rare Dis Res Treat. 2017 Mar 1;2(2):63–8.

8. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2009 Mar;68(3):318–23.

9. Cakar N, Yalcinkaya F, Duzova A, Caliskan S, Sirin A, Oner A, et al. Takayasu arteritis in children. J Rheumatol. 2008 May;35(5):913–9.

10. SHARMA S, SANGAMESWARAN K, KALRA S. CLINICAL PROFILE OF TAKAYASU'S ARTERITIS. Med J Armed Forces India. 1998 Apr;54(2):140–2.

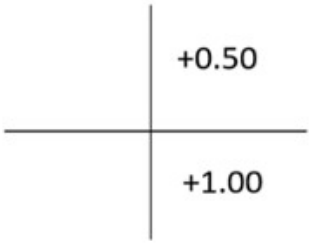
11. Mahajan S, Behera UC, Pravabati SL, Shah M, Padhy SK, Kelgaonkar A. Pulseless and blindness – An ophthalmologist's role in diagnosing Takayasu arteritis: Case series and brief review of literature. Eur J Ophthalmol. 2021 Nov 12;31(6):3525–31.

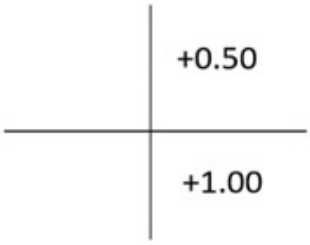
12. Pan L, Du J, Liu J, Liao H, Liu X, Guo X, et al. Tocilizumab treatment effectively improves coronary artery involvement in patients with Takayasu arteritis. Clin Rheumatol. 2020 Aug 6;39(8):2369–78.

13. Del Corso L, Moruzzo D, Agelli M, Pentimone F. Takayasu's arteritis on steroid therapy. Seven years follow-up. Panminerva Med. 1999 Dec;41(4):355–8.

14. Kwon OC, Oh JS, Park MC, Hong S, Lee CK, Yoo B, et al. Statins reduce relapse rate in Takayasu arteritis. Int J Cardiol. 2019 Jul;287:111–5.

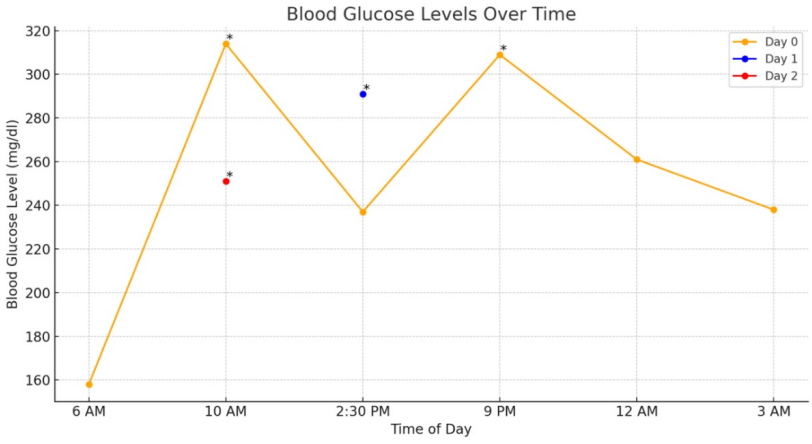
15. Abularrage CJ, Slidell MB, Sidawy AN, Kreishman P, Amdur RL, Arora S. Quality of life of patients with Takayasu's arteritis. J Vasc Surg. 2008 Jan;47(1):131–7.

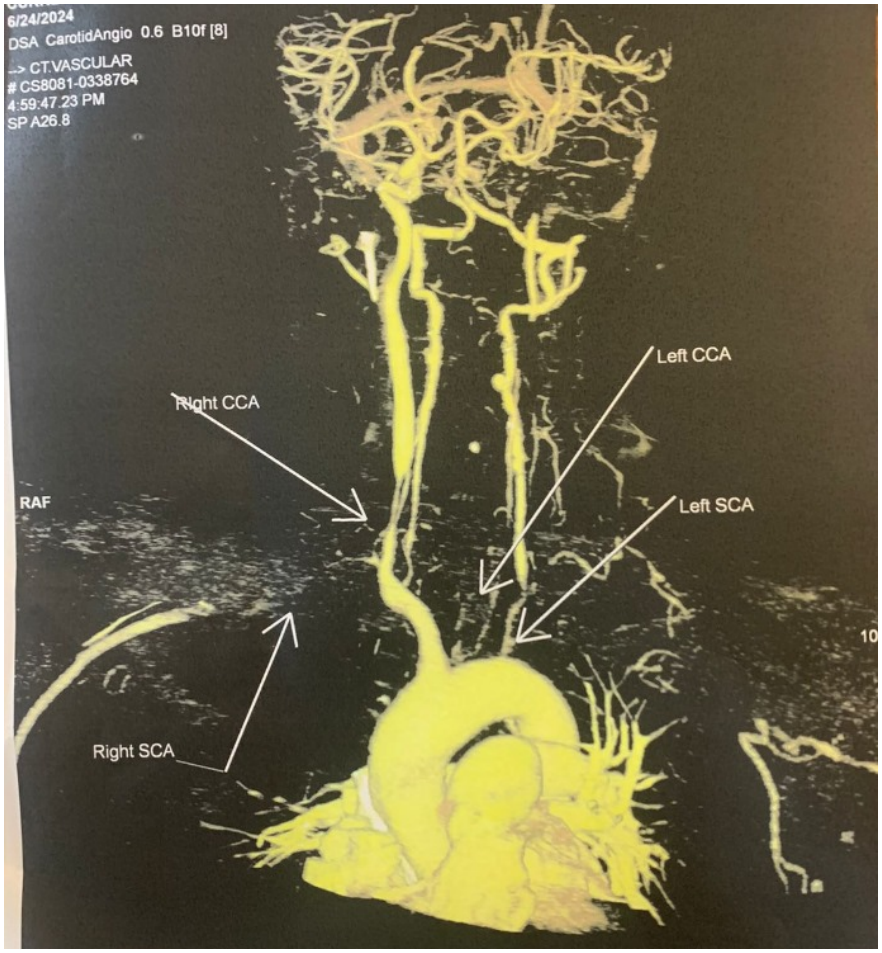




Right eye

Left eye





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