

Radiological Imaging In Pediatric Patients with Takayasu Arteritis

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Abstract

Takayasu Arteritis (TA) is a rare chronic inflammatory large-vessel vasculitis that predominantly affects the aorta and its main branches, leading to significant morbidity and mortality. This condition is most observed in Asian women, though pediatric cases remain exceptionally rare and challenging to diagnose due to varied clinical presentations. We report a case of a 10-year-old girl presenting with bilateral lower extremity weakness, tremors, and constitutional symptoms. Physical examination revealed absent pulsations in the bilateral radial arteries, brachial arteries, and left dorsalis pedis artery. Laboratory findings showed elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). CT angiography of the thoracic-abdominal region demonstrated diffuse wall thickening of the left common carotid artery, left subclavian artery, and brachiocephalic artery with near-complete occlusion, consistent with Takayasu Arteritis type I. Duplex sonography vascular examination of the upper extremities revealed findings suggestive of peripheral arterial disease with suspected Takayasu Arteritis. The patient met the 2022 ACR/EULAR classification criteria with a total score of 5 points, confirming the diagnosis. This case emphasizes the critical role of multimodal imaging approaches, including CT angiography and duplex sonography, in the early diagnosis and classification of pediatric Takayasu Arteritis. Prompt radiological evaluation is essential for appropriate management and prevention of severe vascular complications in this rare pediatric population.

Keywords: Takayasu Arteritis, pediatric vasculitis, large vessel vasculitis, CT angiography, Duplex Sonography

INTRODUCTION

Takayasu Arteritis (TA) is a disease characterized by the presence of an inflammatory, chronic, and rare condition of vasculitis that mainly affects large arteries. This disease can cause significant morbidity and mortality. TA is characterized by autoimmune-mediated inflammation, vascular remodeling, and endothelial dysfunction (Bhandari *et al.*, 2023). TA predominantly affects Asian women, involving the aorta and its main branches, including the renal artery, carotid artery, and subclavian artery, subsequently causing stenosis, occlusion, or degenerative aneurysms of these major vessels (Alnabwani *et al.*, 2021). The disease has a reported annual incidence of approximately 2 per million population globally, with significant geographic variation and a marked female predominance with a male-to-female ratio of 1:8.

Abnormalities of immune cells are the main pathogenesis of TA, but until now the etiology is still not clearly known. The disease progresses through three stages (active, chronic, and healing phases) which in each phase will give different clinical characteristics. Previous studies have documented the challenges in diagnosing pediatric TA, with diagnostic delays averaging 6-24 months from symptom onset due to nonspecific presentations (Aeschlimann *et al.*, 2022). Early studies by Johnston *et al.* (2002) highlighted the diagnostic difficulties posed by the variable clinical manifestations of TA, particularly in children where constitutional symptoms may dominate the early disease course. Because there are various clinical manifestations that this disease can present, the enforcement of the diagnosis of TA is a

challenge and until now there are not many specific examinations available. The evolution of imaging techniques, particularly multimodal approaches combining CT angiography, MR angiography, and Duplex ultrasonography, has significantly improved diagnostic accuracy in recent years (Nienhuis et al., 2022; Slart et al., 2018). Various imaging modalities, such as angiography, ultrasound, and Doppler techniques, play an important role in the diagnosis of TA by visualizing arterial involvement and assessing the extent of the disease (Bhandari et al., 2023).

Treatment of TA generally begins with pharmacology, but invasive management is now more popular because the use of drugs is found to be less able to produce disease regression and high recurrence rates (Saadoun *et al.*, 2021). The management of TA will involve multidisciplinary approaches, with disease-modifying anti-rheumatic drugs (DMARD) as a first-line therapy. DMARD is used to induce remission, control inflammation, and prevent complications from occurring. Non-pharmacological therapies, such as resistance training and curcumin supplementation, show potential benefits. Invasive interventions, including endovascular therapy and open surgery, are used to manage vascular lesions (Bhandari et al., 2023).

However, there are still challenges in understanding and managing the disease, including heterogeneity of disease presentation and the lack of standardized treatment guidelines. This case report is particularly significant given the rarity of pediatric TA and demonstrates the critical value of multimodal imaging in establishing early diagnosis. The novelty of this case lies in the comprehensive radiological documentation of Type I TA in a pediatric patient, utilizing both CT angiography and Duplex Sonography to characterize the extent of vascular involvement. Furthermore, this case illustrates the application of the newly updated 2022 ACR/EULAR classification criteria in a pediatric context, contributing to the limited body of literature on diagnostic approaches in childhood-onset TA. The future of TA management relies on precision medicine, which utilizes biomarkers and molecular profiles to be able to determine treatment regimens and improve patient outcomes. More research is needed to uncover the underlying mechanisms of TA and develop targeted therapies (Bhandari et al., 2023).

CASE REPORT

The patient was a girl, 10 years old, came with complaints of weakness in both legs and the whole body. The patient was a referral patient from another hospital with complaints of weakness in both legs since 2 months ago. Tremors were also found since 1 month ago, felt on the tips of the hands, with a duration of 30 seconds, and appeared 2-3 times every day, especially when the patient felt tired. Other complaints in the form of cough and fever for approximately 2 weeks, felt to disappear. A history of weight loss, decreased appetite, night sweats, or coughing with bloody sputum is denied.

The patient has 2 siblings, the patient was born spontaneously with the patient's mother's birth weight, it was said that at birth the patient immediately cried. Currently, the patient lives in the same house with both parents, two siblings, and the patient's grandmother. Patients can still do activities according to their age. The history of shortness of breath disease in the family is denied. The history of TB treatment in families in the same house with the patient is denied. The patient's immunization history is unclear (the patient's mother forgets).

Physical examination found no pulsation in both radial arteries, brachialist arteries, and left dorsalis pedis arteries. On eye examination, no anemic conjunctiva was found and no icteric sclera. On the examination of the neck, no enlarged lymph nodes were found. Thoracic inspection was found to be symmetrical and there was no retraction. Heart and lung examination within normal limits. Abdominal examination there is no distension, normal intestinal noise. On the examination of the esctrema, it was found that the acral digin, the CRT was elongated >3 seconds, there was no palpated swelling in the bones and joints.

Echocardiography examination showed that it was within normal limits. Other supporting examinations were carried out *CT angiography* in the thoracic-abdominal region and diffuse thickening of the walls of the left communist carotid artery, left subclavian artery, and brachiocephalic artery which caused almost complete occlusion with Takayasu Arteritis type I Conclusion. Hepatomegali. Non-specific multiple lymphadenopathy in the prevascular, supraclaviular, left and right axile, para-aorta, superior-inferior mecentric, iliac, right and left inguinals.

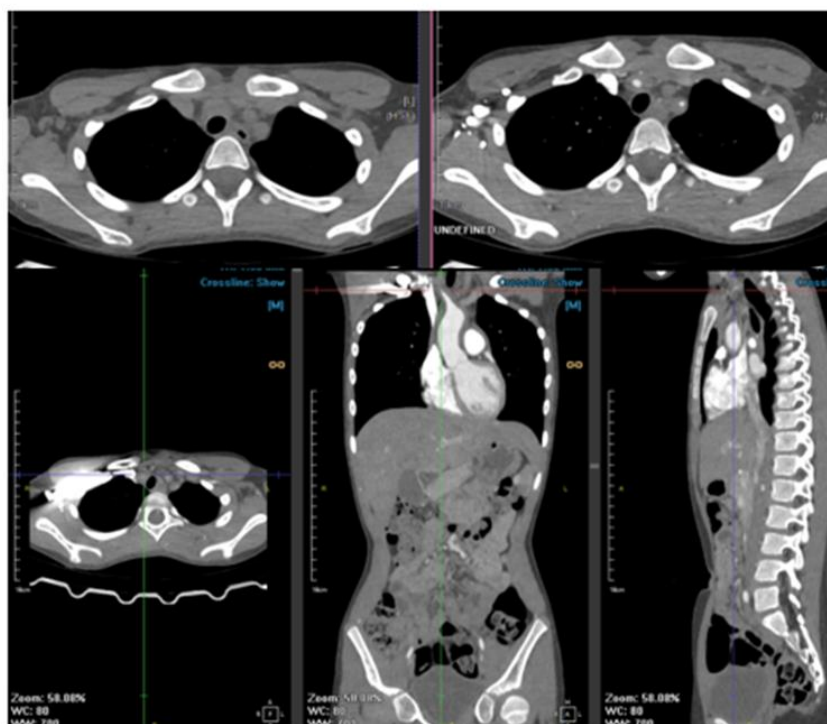


Figure 1. CT-scan Angiography Examination

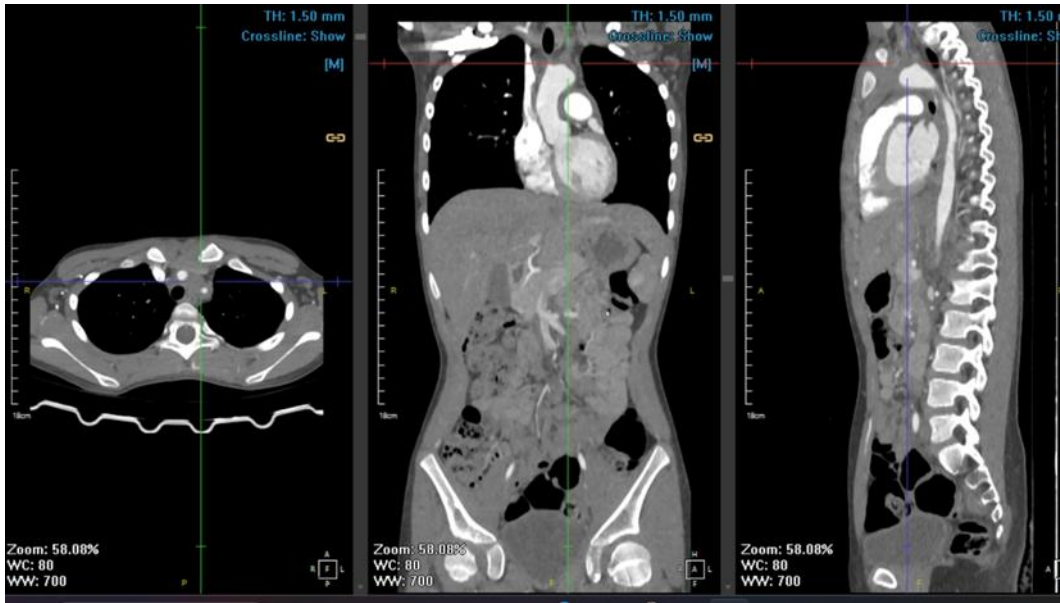


Figure 2. CT-scan Angiography Examination

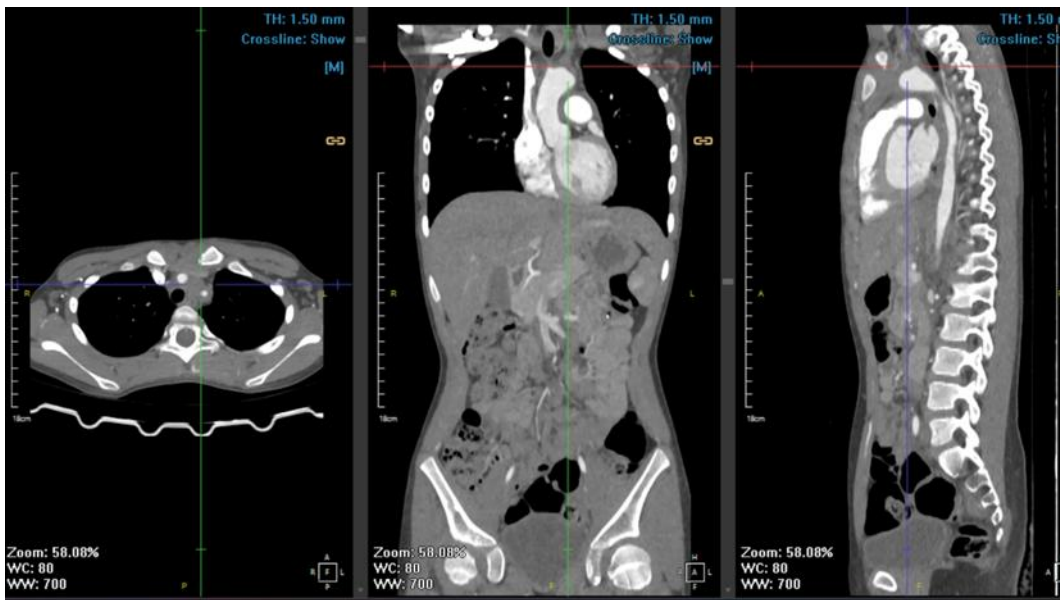


Figure 3. CT-scan Angiography Examination

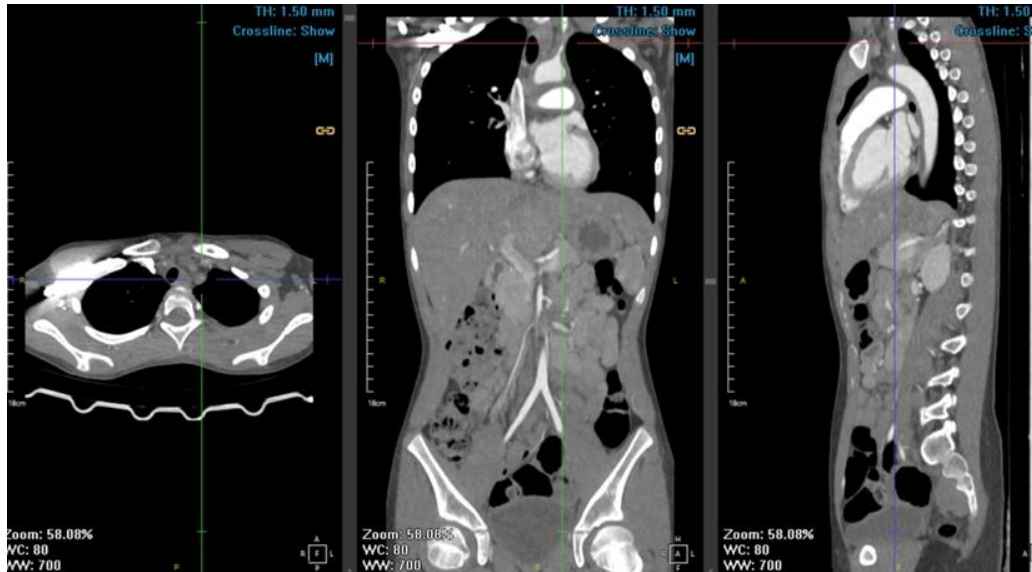


Figure 4. CT-scan Angiography Examination

The patient also performed a *Duplex Sonography Vascular examination* on the interior extremity with results on the inferior extremities of the dextra and sinistra no PAD, DVT, and CVI were found. On the right and left superior extremities, an image of PAD with the suspect Takayasu Arthritis was found.

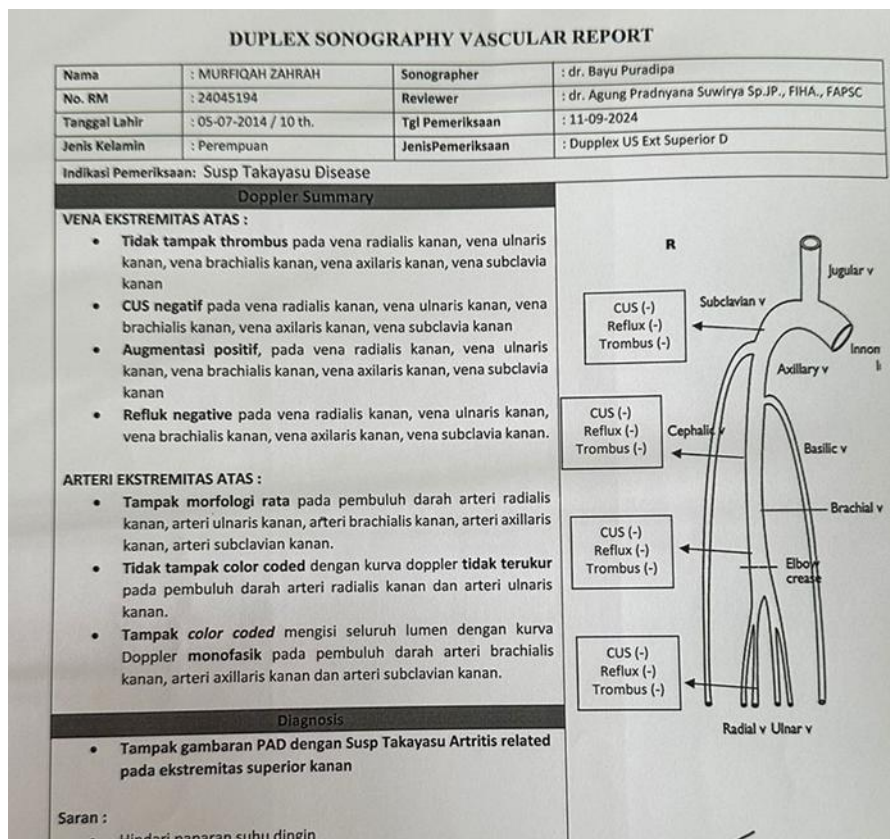


Figure 5. Results of Duplex Sonography Vascular Right Superior Extremita

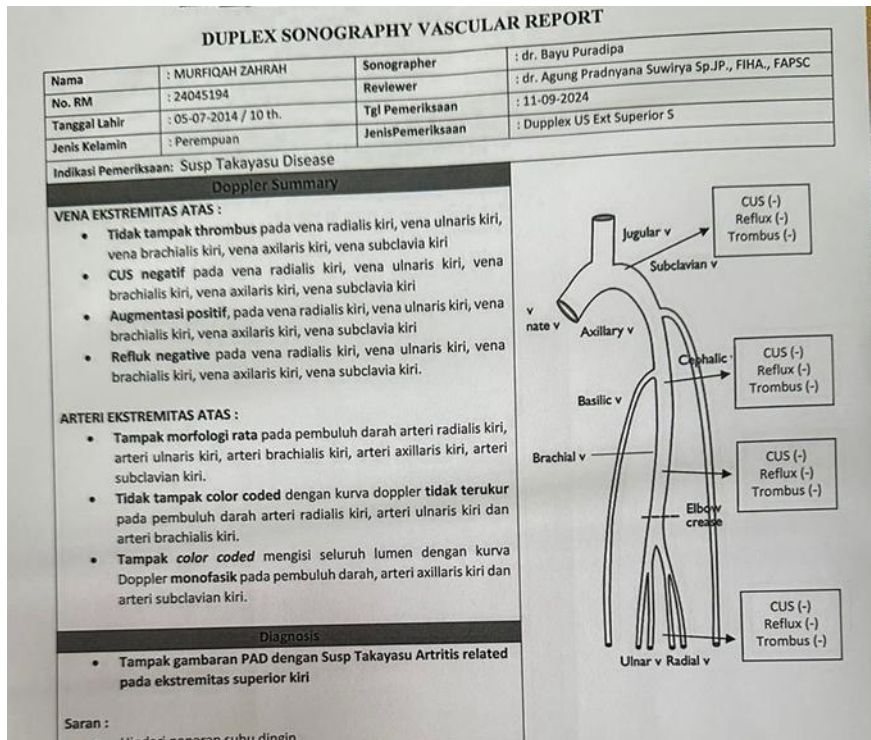


Figure 6. Results of the left superior superior vascular Sonography examination

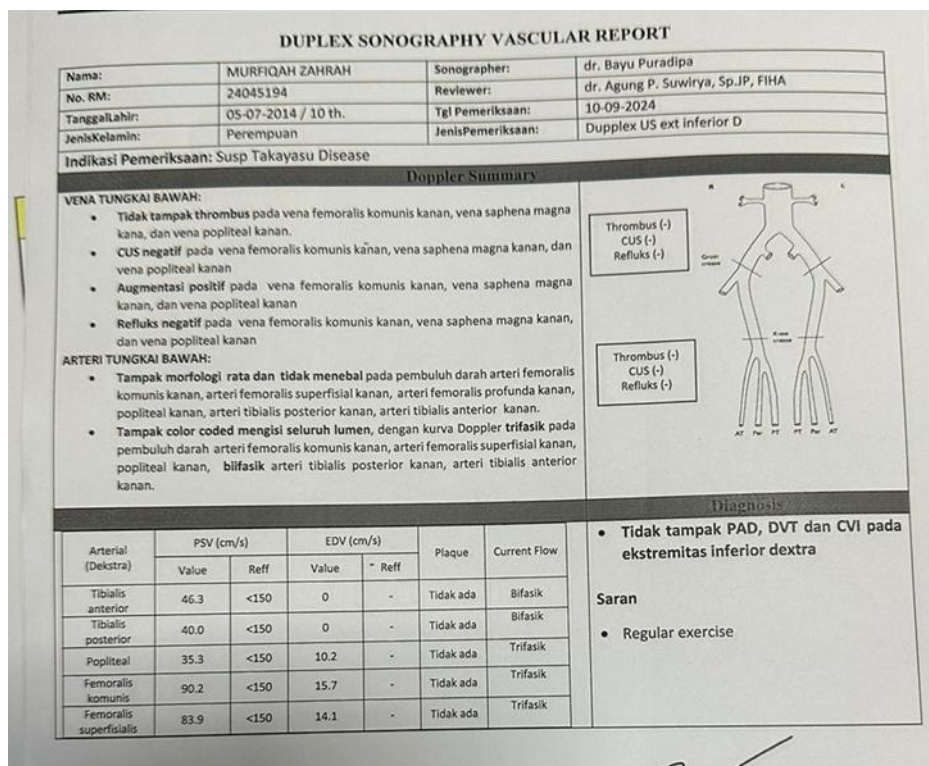


Figure 7. Duplex Sonography Vascular Right Inferior Extremity Examination Results

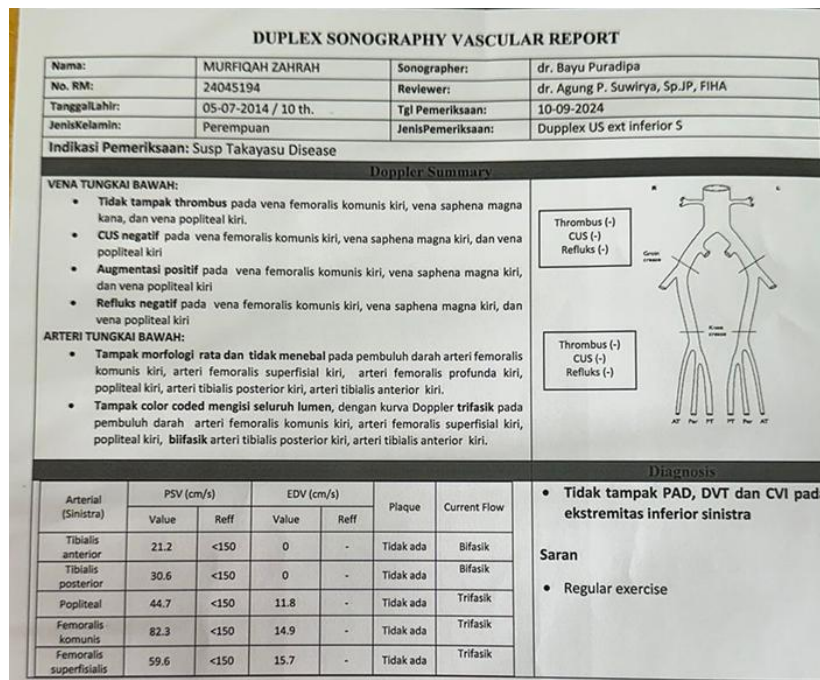


Figure 8. Results of Duplex Sonography Vascular Left Inferior Extremity Examination

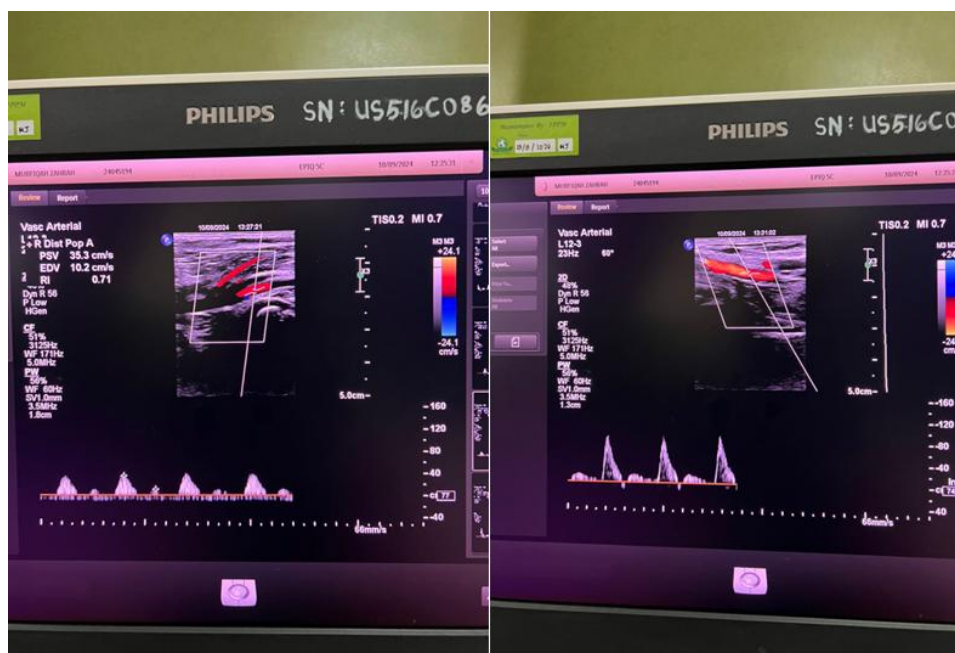


Figure 9. Duplex Sonography Vascular examination results

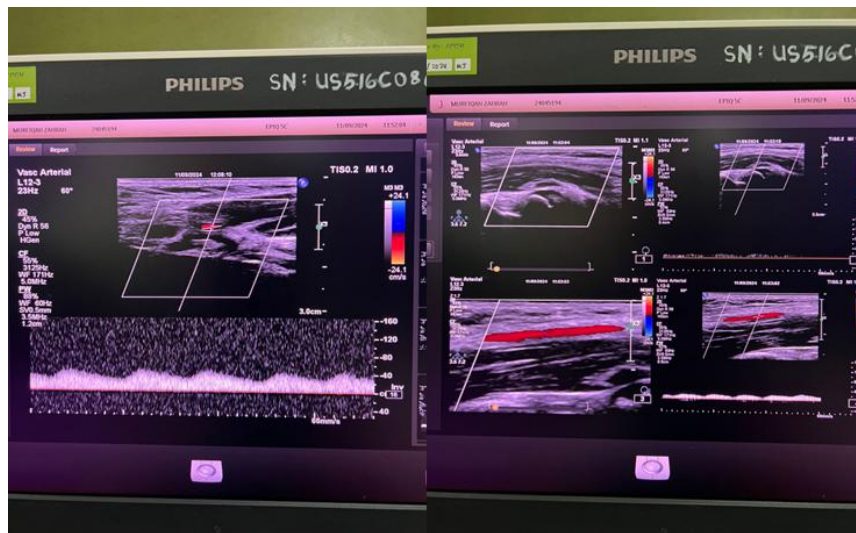


Figure 10. Duplex Sonography Vascular examination results

Examination of *the head CT-scan* without and with intravenous contrast obtained results for now no visible intraparenchymal pathological lesions of the brain and visible bilateral maxillary sinusitis, right ethmoidalis.

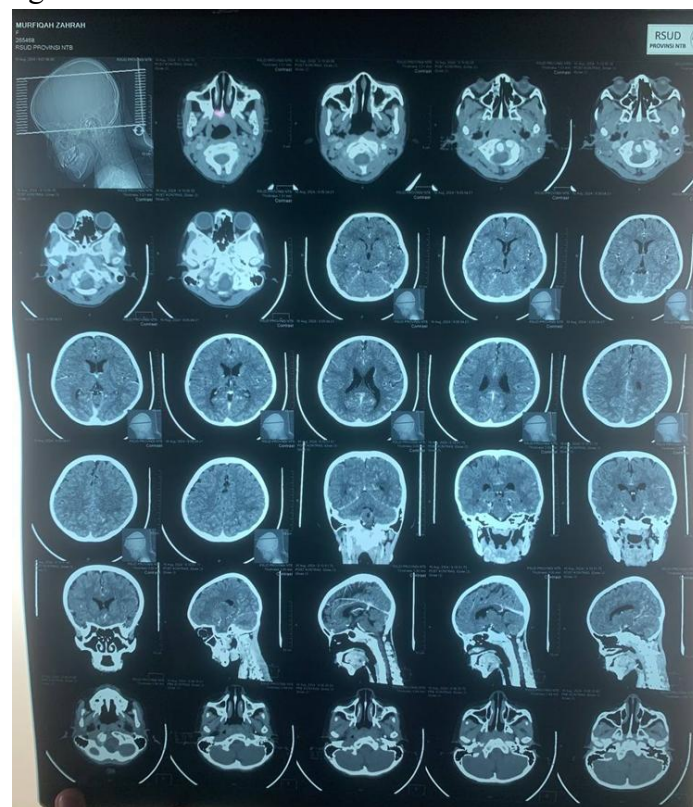


Figure 11. CT-scan results

Laboratory examination showed an increase in LED and CRP infiltration from a complete blood test, a complete urinalysis examination within normal limits, and a molecular rapid test examination with sputum samples showed no detectable MTB bacteria.

Discussion

Takayasu arteritis (TA) is one of the main forms of large vascular vasculitis. TA is a chronic disease characterized by granulomatous inflammation that affects the aorta and its main branches. Complications from blood vessel damage can result in substantial morbidity including stroke, myocardial infarction, mesenteric ischemia, and limb claudication (Jennette *et al.*, 2013).

Unlike diagnostic criteria, the purpose of classification criteria is to ensure that homogeneous populations are selected for inclusion in clinical trials and other research studies (Aggarwal *et al.*, 2015). In 1990, *American College of Rheumatology* (ACR) supports the classification criteria for TA. This criterion was developed using data from only 63 patients with TA and has never been independently validated. In addition, this criterion was derived using data from patients exclusively from North America without representation from Europe or Asia, where the clinical pattern of the disease may be different, thus limiting the generalization of outcomes (Maksimowicz-McKinnon, Clark and Hoffman, 2007). Given these constraints, the 1990 ACR criteria for TA no longer meet the current standards applicable to the development of classification criteria, and updated criteria are required. What further highlights the need for uniform and revised criteria in the TA is the use of different eligibility criteria to determine the study population in two recent randomized clinical trials conducted in North America and Japan, making it difficult to compare clinical trial findings (Langford *et al.*, 2017; Nakaoka *et al.*, 2018).

The TA classification has been created to classify diseases based on angiography findings. The clinical classification and diagnostic criteria of TA according to Ishikawa are shown in Table 2 and Table 3. The initial system, revised by Lupi-Herrera *et al.*, has been superseded by a new TA classification. This system is useful because it provides a comparison of patient characteristics according to the blood vessels involved and aids in surgical planning (Setty *et al.*, 2017).

Table 1. 1990 ACR criteria for TA

Criteria	Definition
Age at disease onset <40 years	Development of symptoms or findings related to Takayasu arteritis at age <40 years
Claudication of extremities	Development and worsening of fatigue and discomfort in muscles of 1 or more extremity while in use, especially the upper extremities
Decreased brachial artery pulse	Decreased pulsation of 1 or both brachial arteries
Blood pressure difference >10 mm Hg	Difference of >10 mm Hg in systolic blood pressure between arms
Bruit over subclavian arteries or aorta	Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta
Arteriogram abnormality	Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta. Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not caused by arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

Table 2. Ishikawa's clinical classification for TA

Group	Clinical Features
Group I	Uncomplicated disease, with or without pulmonary artery involvement
Group IIA	Mild/moderate single complication together with uncomplicated disease
Group IIB	Severe single complication together with uncomplicated disease
Group III	Two or more complications together with uncomplicated disease

Table 3. Ishikawa's diagnostic criteria in TA

Criteria	Definition
Obligatory criterion: Age \leq40 years	Age \leq 40 yr at diagnosis or at creel of "characteristic signs and symptoms" of 1 month duration in patient history.
Two major criteria: 1) Left mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid portion from the point 1 cm proximal to the left vertebral artery orifice to that 3 cm distal to the orifice determined by angiography.
2) Right mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid portion from the right vertebral artery orifice to the point 3 cm distal to the orifice determined by angiography.

Table 4. Nine Minor Criteria

Nine Minor Criteria	Definition
1) High ESR	Unexplained persistent high ESR \leq 20 mm/h (Westergren) at diagnosis or presence of the evidence in patient history.
2) Carotid artery tenderness	Unilateral or bilateral tenderness of common carotid arteries by physician palpation : neck muscle tenderness is unacceptable.
3) Hypertension	Persistent blood pressure \geq 140/90 mmHg brachial or \geq 160/90 mmHg popliteal at ages 40 years, or presence of the history at age \leq 40 years
4) Aortic regurgitation or Annuloaortic ectasi	By auscultation or Doppler echocardiography or angiography. By angiography or two-dimensional echocardiography
5) Pulmonary artery lesion	Lobar or segmental arterial occlusion or equivalent determined by angiography or perfusion scintigraphy; or presence of stenosis, aneurysm, luminal irregularity or any combination in pulmonary trunk or in unilateral or bilateral pulmonary arteries determined by angiography
6) Left mid common carotid lesion	Presence of the most severe stenosis or occlusion in the mid portion of 5 cm in length from the point 2 cm distal to its orifice determined by angiography.
7) Distal brachiocephalic trunk lesion	Presence of the most severe stenosis or occlusion in the distal third determined by angiography
8) Descending thoracic aorta lesion	Narrowing, dilation or aneurysm, luminal irregularity or any combination determined by angiography; tortuosity alone is unacceptable.
9) Abdominal aorta lesion	Narrowing, dilation or aneurysm, luminal irregularity or any combination and absence of lesion in aorto-iliac region consisting of 2 cm of terminal aorta and bilateral common iliac arteries determined by angiography; tortuosity alone is unacceptable.

TA classification criteria based on *American College Rheumatology (ACR) /European Alliance of Association for Rheumatology (EULAR) 2022* has been validated and intended for the purpose of classification of vasculitis and should not be used to establish a diagnosis of vasculitis. The purpose of the classification criteria is to distinguish cases of TA from similar types of vasculitis in a study setting. Therefore, the criteria should only be applied when a diagnosis of LVV or vascular vasculitis is being made and all potential similarities of a disease to vasculitis have been removed from the list of suspicions. For example, this criterion was not developed to distinguish patients with TA from patients with atherosclerosis or other non-inflammatory genetic diseases that damage large arteries. The 1990 ACR classification criteria for vasculitis perform poorly when used for diagnosis enforcement (i.e., when used to distinguish between cases of vasculitis vs mimics without vasculitis) (Grayson *et al.*, 2022).

2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EULAR
CLASSIFICATION CRITERIA FOR TAKAYASU ARTERITIS

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- These classification criteria should be applied to classify the patient as having Takayasu arteritis when a diagnosis of medium-vessel or large-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

ABSOLUTE REQUIREMENTS

Age ≤ 60 years at time of diagnosis	
Evidence of vasculitis on imaging ¹	

ADDITIONAL CLINICAL CRITERIA

Female sex	+1
Angina or ischemic cardiac pain	+2
Arm or leg claudication	+2
Vascular bruit ²	+2
Reduced pulse in upper extremity ³	+2
Carotid artery abnormality ⁴	+2
Systolic blood pressure difference in arms ≥ 20 mm Hg	+1

ADDITIONAL IMAGING CRITERIA

Number of affected arterial territories (select one) ⁵	
One arterial territory	+1
Two arterial territories	+2
Three or more arterial territories	+3
Symmetric involvement of paired arteries ⁶	+1
Abdominal aorta involvement with renal or mesenteric involvement ⁷	+3

Sum the scores for 10 items, if present. A score of ≥ 5 points is needed for the classification of TAKAYASU ARTERITIS.

<ol style="list-style-type: none"> Evidence of vasculitis in the aorta or branch arteries must be confirmed by vascular imaging (e.g., computed tomographic/catheter-based/magnetic resonance angiography, ultrasound, positron emission tomography). Bruit detected by auscultation of a large artery, including the aorta, carotid, subclavian, axillary, brachial, renal, or iliofemoral arteries. Reduction or absence of pulse by physical examination of the axillary, brachial, or radial arteries. Reduction or absence of pulse of the carotid artery or tenderness of the carotid artery. 	<ol style="list-style-type: none"> Number of arterial territories with luminal damage (e.g., stenosis, occlusion, or aneurysm) detected by angiography or ultrasonography from the following nine territories: thoracic aorta, abdominal aorta, mesenteric, left or right carotid, left or right subclavian, left or right renal arteries. Bilateral luminal damage (stenosis, occlusion, or aneurysm) detected by angiography or ultrasonography in any of the following paired vascular territories: carotid, subclavian, or renal arteries. Luminal damage (stenosis, occlusion, aneurysm) detected by angiography or ultrasonography involving the abdominal aorta and either the renal or mesenteric arteries.
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Figure 12. ACR/EULAR 2022 classification criteria for TA

The patient in this case report is a woman, 10 years old, coming with complaints of weakness in both legs and the whole body. The patient was a referral patient from another hospital with complaints of weakness in both legs since 2 months ago. Tremors were also found

since 1 month ago, felt on the tips of the hands, with a duration of 30 seconds, and appeared 2-3 times every day, especially when the patient felt tired. Other complaints in the form of cough and fever for approximately 2 weeks, felt to disappear. A history of weight loss, decreased appetite, night sweats, or coughing with bloody sputum is denied. Physical examination found no pulsation in both radial arteries, brachialist arteries, and left dorsalis pedis arteries. Laboratory examination showed an increase in LED and CRP infiltration from a complete blood test, a complete urinalysis examination within normal limits, and a molecular rapid test examination with sputum samples showed no detectable MTB bacteria. The patient underwent a *Duplex Sonography Vascular examination* of the inner extremity with results on the inferior extremities of the dextra and sinistra no PAD, DVT, and CVI were found. On the right and left superior extremities, an image of PAD with the suspect *Takayasu Arhtritis was found*. Examination of *the head CT-scan* without and with intravenous contrast obtained results for now no visible intraparenchymal pathological lesions of the brain and visible bilateral maxillary sinusitis, right ethmoidalis.

The cases reported in this report support the diagnosis of takayasu arteritis, ranging from the clinical manifestations found in patients with weakness in both legs and the rest of the body. Physical examination found no pulsation in both radial arteries, brachialist arteries, and left dorsalis pedis arteries. The results of the anamnesis and physical examination were then supported by the supporting examination modality of *Duplex Sonography Vascular* on the interior extremities with results on the inferior extremities of the dextra and sinistra not found PAD, DVT, and CVI. On the right and left superior extremities, a picture of PAD with the suspect Takayasu Arhtritis relates. Based on the classification of criteria by ACR/EULAR 2022, patients who are women get 1 point, reduced pulsation in the superior extremities get 2 points, and there are abnormalities in the communist carotid get 2 points. So that a total of 5 points was obtained which indicates takayasu arteritis. Further classification of TA can be enforced if a supporting examination in the form of angiography has been carried out. After that, the classification of TA will be known so that the administration can also be carried out immediately.

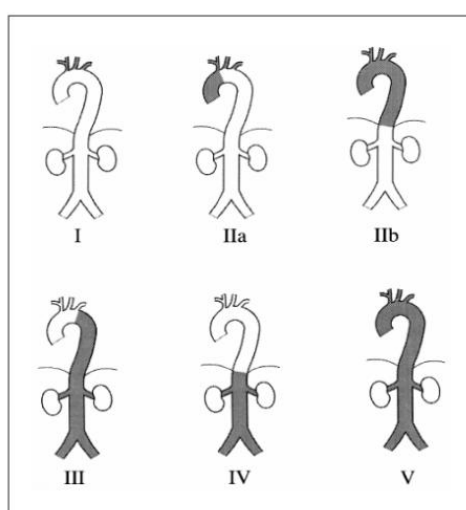


Figure 13. Angiography classification of Takayasu arteritis

Table 5: Types of Vascular Involvement

Type	Vessel Involvement
Type I	Branches from the aortic arch
Type IIa	Ascending aorta, aortic arch and its branches
Type IIb	Ascending aorta, aortic arch and its branches, thoracic descending aorta
Type III	Thoracic descending aorta, abdominal aorta and/or renal arteries
Type IV	Abdominal aorta and/or renal arteries
Type V	Combined features of types IIb and IV

Takayasu's arteritis is named after Japanese ophthalmologist Mikito Takayasu, who first documented the case in 1905. The aorta, its main branches, coronary arteries and lungs, and other large and moderate blood vessels, are all affected by the chronic inflammatory vasculitis known as TA (Khadka, Singh and Timilsina, 2022). Due to the frequent occurrence of blockages of large arteries originating from the aorta, this condition is also known as a condition without pulse or occlusive thromboarthopathy. The pathophysiology of this disease is still unknown to this day. However, pan arteritis, which has substantial intima hyperplasia, medial and adventitial thickening, mononuclear cell infiltration, and sometimes giant cells, is thought to be the underlying cause of the occurrence of TA. The condition is mostly observed in women of Asian descent, with its peak in the 30s. Takayasu's disease affects 2 out of 10,000 people each year, with a male-to-female ratio of 8:1.6. The patient in this case study is a 10-year-old girl.

Atherosclerotic, inflammatory, infectious, and genetic conditions affecting the major arteries are included in the differential diagnosis of TA. Examples include atherosclerosis, fibromuscular dysplasia, TB, and arteritis *Giant Cell*. *Standard Gold* to diagnose TA is angiography. However, Doppler and non-invasive MRA can also provide equally good results (Alibaz-Oner and Direskeneli, 2015). In patients, a series of supporting examinations were carried out to be able to exclude several diseases, in laboratory examinations in the form of molecular rapid tests with sputum samples showed that MTB bacteria were not detected.

Acute phase markers such as ESR and CRP also provide additional evidence supporting the diagnosis. The main treatments are expected to be systemic glucocorticoids and immunosuppressants, which are believed to reduce inflammation and limit disease progression. If irreversible arterial stenosis develops due to conditions such as cerebral ischemia, hypertension with critical renal artery stenosis, claudication of the extremities, or both, surgical (endovascular) intervention may be necessary. To avoid problems, surgical intervention is usually not recommended during active disease and is recommended during calm disease (Soto *et al.*, 2022). Supporting examinations were carried out on patients, namely laboratory examinations, and an increase in ESR and CRP was obtained.

A retrospective cohort study involving 183 TA patients during 1979 to 2018 showed a time duration of 4 years or more from the onset of TA symptoms to diagnosis verification was associated with a higher risk of cardiovascular events and lower survival rates (Popov, Borodina and Shardina, 2021). Studies conducted on 318 TA patients collected from 1970 to 2004 showed that there was no difference in mortality by year in which the diagnosis of TA was upright in those patients, found in 126 of the 318 sample patients had at least one vascular-

related complication, and mortality was generally found on average after 6.1 years *Follow-up* (Mirouse *et al.*, 2019).

CONCLUSION

A 10-year-old girl presented with bilateral lower extremity and generalized weakness persisting for two months, diagnosed with Takayasu arteritis (TA) type I—a nonspecific inflammatory arterial disease more prevalent in Asian countries and primarily affecting women, with variable presentations across populations and disease phases. Angiography serves as the gold standard for diagnosis and treatment planning, often complemented by comprehensive evaluation leading to percutaneous angioplasty and stent placement in suitable cases. Key complications at diagnosis include Takayasu's retinopathy, secondary hypertension, aortic regurgitation, and aneurysm formation, classified as mild/moderate or severe. For future research, longitudinal studies should investigate the long-term efficacy and safety of early percutaneous interventions combined with immunomodulatory therapies in pediatric TA patients from diverse ethnic backgrounds to optimize outcomes and reduce complication rates.

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