Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.64, No.5(2024). p.454-8 ; DOI: https://doi.org/10.14238/pi64.5.2024.454-8

Case Report

Undetected Takayasu arteritis presenting as severe hypertension in children: a report of two cases

Muhammad Taufik Wirawan, Indah Kartika Murni, Suryono Yudha Patria, Nadya Arafuri, Noormanto, Sasmito Nugroho

Takayasu arteritis (TA) is a rare chronic granulomatous vasculitis mainly affecting the aorta and its main branches. Clinical presentations of TA are non-specific, especially in the initial phase, which likely contributes to delayed diagnosis besides the rarity of the disorder. Childhood-onset of TA is associated with significant morbidity and mortality. This case report aimed to present two rare cases of acute symptomatic severe hypertension in children due to TA. **[Paediatr Indones. 2024;64:454-8; DOI: https://doi.org/10.14238/pi64.6.2024.454-8**].

Keywords: *Takayasu arteritis; vasculitis; hypertension; pediatric; percutaneous transluminal angioplasty*

Case 1

A 15-year-old girl was referred to our hospital due to severe hypertension, which was detected by chance. At admission to the hospital, the patient was in good general condition. There was a history of 3 weeks of intermittent fever, mild cephalgia, and dyspnea during heavy activity, but no nausea or blurred vision. On initial examination, there was significant hypertension, blood pressure 210/100 mmHg in the upper extremity and 140/90 mmHg with a weak pulse in the lower extremity. Bruit audible over the abdomen area, but no sign of heart failure.

Initial laboratory examination showed an elevated ESR (68 mm/hour) and CRP (34 mg/L). The complete blood count, urinalysis, urea, creatinine, and electrolyte were normal. Antineutrophil cytoplasmic antibody (ANCA) and antinuclear antibody (ANA) tests were negative. Chest X-ray and ECG showed marked LVH. Echocardiography showed that the left ventricle was mildly dilated and had reduced LV function (LVEF: 48%). CT angiography of the aorta revealed stenosis of the abdominal aorta with thickening of the wall and stenosis of the proximal right renal artery, in accordance to type IV TA (**Figure 1**). We diagnosed the patient with type IV TA according to clinical manifestation and angiographic abnormalities.

The hypertension was treated intravenously by nicardipine drip and two oral anti-hypertension, such as amlodipine and furosemide. We treated the patient with methylprednisolone drug at an initial dose of 1 mg/kg/day. Percutaneous transluminal angioplasty (PTA) was performed after inflammation and hypertension condition was controlled. The ballooning procedure was performed at multiple sites, with multiple balloon catheter sizes 3.5/20 mm and 5.0/60 mm in the left renal artery and sizes 5.0/60 mm and 6.0/60 mm in the abdominal aorta. The stenosis

From the Department of Child Health, Dr. Sardjito Hospital/Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada, Yogyakarta, Central Java, Indonesia.

Corresponding author: Muhammad Taufik Wirawan. Jalan Kesehatan 1, Sekip, Yogyakarta 55284, Central Java, Indonesia. Email: mtaufikwirawan@gmail.com.

Submitted December 19, 2022. Accepted October 8, 2024

was relieved from 70% to <20% in the abdominal aorta and from 90% to < 20% in the left renal artery. The patient was discharged from the hospital 3 days after the procedure with steroid and antiplatelet clopidogrel therapy (**Figure 2**). After 1 month, the dose of methylprednisolone was tapered down, and we maintained the low dose of steroid for 6 months until 1 year. During the one-year follow-up, the hypertension was controlled, the ventricular function improved, and the nonspecific inflammatory markers returned to normal level.

Case 2

A 10-year-old girl was referred to our hospital with a history of chronic cephalgia and pain in both legs on walking for 2 months. The symptoms associated with intermittent fever. Three years before, she had a history of admission to a district hospital with complaint of dyspnea and whole-body swelling. She was diagnosed with heart failure concurrent with pneumonia. The symptoms were relieved with anti-

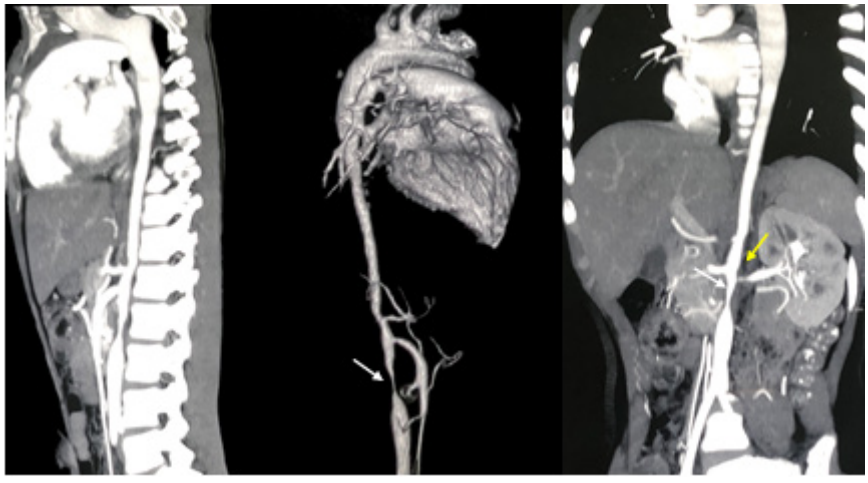

Figure 1. MSCT angiography showed the stenosis of the descending aorta along 17.8 cm, from thoracal part (VTh) 8th until abdominal part (VL) 3rd with smallish caliber 2.85 mm (indicated with white arrow) and stenosis proximal part of the left renal artery with caliber 1.58 cm (indicated with yellow arrow). The aortic wall was thickened and irregular, but no aneurysms or thrombus existed.

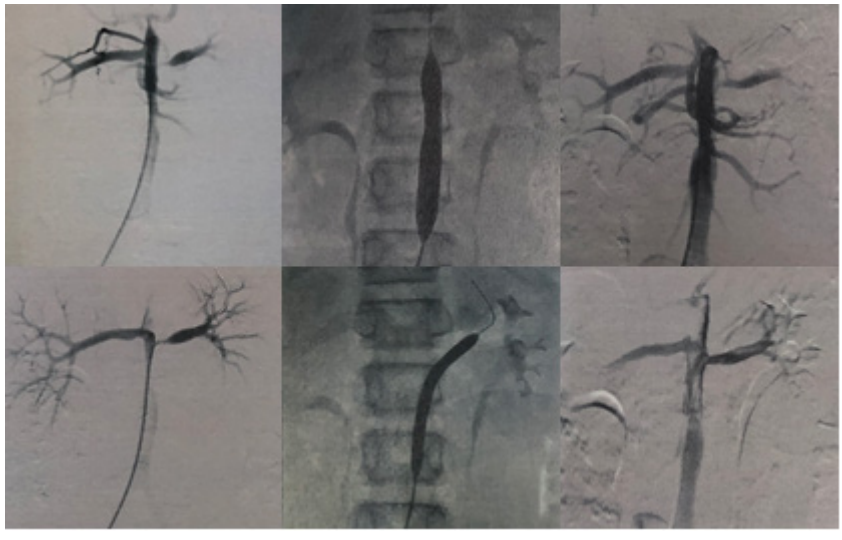

Figure 2. PTA procedure with ballooning in the abdominal aorta and left renal artery

failure medication, such as furosemide and captopril, the drugs had stopped a year before. However, there was no previous data on blood pressure and echocardiography.

On examination, the patient was looking well. She had tachycardia (HR 142/min), mild tachypnea (RR: 28/min), low-grade fever (temp: 37.8°C), and hypertension in the upper extremity(BP: 188/128 mmHg). The blood pressure could not be detected at the lower extremities, which had a very weak pulse compared to the upper extremities. There was no murmur at the heart and abdomen area. Physical examination also revealed there was no evidence of heart failure. Laboratory examination showed mild anemia (Hb: 9.6 g/dL), elevated ESR (74 mm/hour), and elevated CRP (>150 mg/dL). The urea, creatinine, electrolyte, and urinalysis were normal. Chest X-ray and ECG showed LAH and LVH. Echocardiography showed concentric left ventricle hypertrophy and trivial aortic regurgitation with normal ventricular function (LVEF: 62%). CT angiography showed multiple stenoses in the thoracal and abdominal aorta with thickening of the wall (**Figure 3**). The diagnosis of the type III TA was made according to the new angiographic classification.

We treated hypertension with nicardipine drip and oral anti-hypertension such as nifedipine, furosemide, and carvedilol. We gave methylprednisolone at a dose of 1 mg/kg/day. After controlling the inflammation and hypertension, we performed the PTA and ballooning using multiple balloon sizes 4.0/40mm and 6.0/80 in the abdominal aorta and thoracic aorta. The stenosis was relieved from 80% to <40% in the abdominal aorta and from 60% to <40% in the thoracic aorta (**Figure 4**). The patient was discharged after the procedure with steroid and antiplatelet clopidogrel therapy. Inflammatory markers gradually back to the normal level. We tapered off the steroid after 1 month and maintained the low dose of steroid for 6 months until 1 year from the start of treatment. She has been free of claudication symptoms, and there have been no hypertension or other cardiac events after a year of follow-up.

Discussion

Takayasu arteritis (TA) is a chronic granulomatous vasculitis mainly affecting the aorta and its main branches.[1] Takayasu arteritis commonly affects young women between 20-40 years of age, and childhood-onset is rare.[2] Cardiovascular manifestation such as hypertension is the most common symptom of TA in both children and adults. According to the previous report, hypertension occurred in 70- 80% of patients.[2,3] Besides cardiovascular manifestation, TA in children has various clinical manifestations, and the rate of underdiagnosis and misdiagnosis is high due to atypical symptoms.

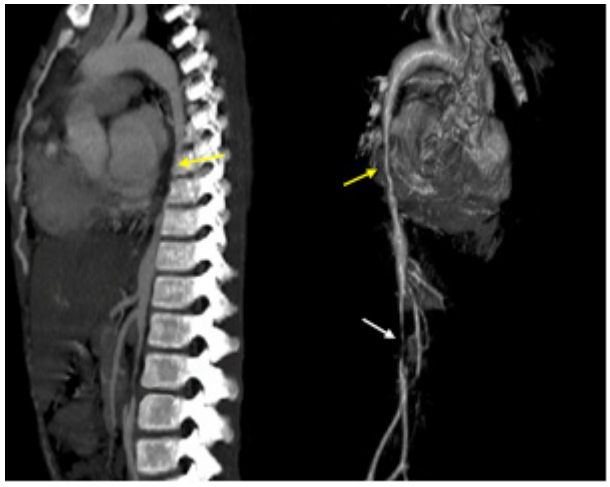

Figure 3. MSCT angiography showed multiple stenoses of descending aorta thoracic part (Vth) level 7-8 (0.39 cm) (indicated with yellow arrow) and abdominal part (VL) level 1-3 (0.07 cm) (indicated with white arrow). The bilateral renal artery, superior mesenteric, inferior mesenteric, and bilateral iliac were within normal limits. The aortic wall was thickened and irregular, but there were no aneurysms or thrombus.

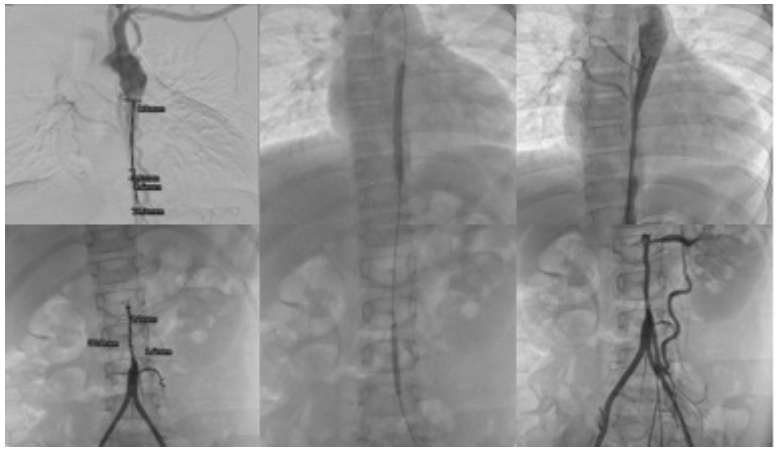

Figure 4. PTA procedure with ballooning in the thoracal and abdominal aorta

The diagnosis of childhood TA follows the criteria set by the *European League Against Rheumatism* (EULAR), *Paediatric Rheumatology International Trial Organisation* (PRINTO), and *Paediatric Rheumatology European Society* (PRES), including angiographic abnormality (mandatory criterion) plus at least one of the following: (1) absence of the peripheral artery pulse or claudication induced by physical activity; (2) a >10mm Hg difference in systolic blood pressure in all four limbs; (3) bruits over large arteries; (4) hypertension and (5) increased levels of acute phase reactants. These criteria demonstrate sensitivity and specificity of 100% and 99.9%, respectively.[4] The first patient met all diagnosis criteria, and five of six criteria were met in the second patient. Patients had elevated inflammatory markers, which reflects the inflammatory process. Both patients also had severe hypertension and cardiac manifestation, which reflect the history and echocardiography findings. Poorly controlled hypertension is a major cause of cardiac complication.

The renal arteries are frequently involved, usually with renovascular hypertension. The incidence of renal arteries involvement was 24-68% of patients. The renal artery involvement is often bilateral and frequently ostial and proximal.[5] Previous research reported that in patients with TA-related renal artery stenosis, the prevalence of hypertension was 60%, with 30% of patients having refractory hypertensive cases.[6] Besides renal artery involvement, pathogenesis hypertension due to TA is complex and multifactorial. It is thought to result from mechanical, neural, and hormonal mechanisms.[7] Hypertension in TA is also related to the involvement of abdominal aorta and severe aortic regurgitation.[8] In our first case, stenosis occurred in the abdominal aorta and unilateral renal artery. However, in the second case, stenosis occurred in the thoracic and abdominal part of the aorta.

Hypertension is one of the leading causes of heart failure and aortic dissection in TA, which are important causes of mortality.[9] In a recent review, the mortality rate of childhood TA reported varied between 0% and 27%.[2] A previous study reported that the majority of patients with vasculitis (73%) were initially misdiagnosed and 82% of patients with vasculitis with a delayed diagnosis with had negative health consequences.[10] Early recognition and therapeutic strategies have shown a decrease in mortality and morbidity. Therapeutic strategies include revascularization procedures such as angioplasty.[2]

Initially, we managed both patients with multiple anti-hypertension drugs for severe hypertension and corticosteroids for the disease activity. Corticosteroid is the first-line agent for controlling disease activity in TA. However, most patients initially achieve disease remission, but 46-84% of patients will need a second-line agent to maintain remission.[11] Our two patients responded well to a single corticosteroid regimen and did not need the second-line agent to achieve or maintain disease remission. Percutaneous transluminal angioplasty intervention was also done in both patients after we controlled the inflammation. Compared to other procedures, the PTA procedure offers a less invasive, cost-effective, and safe method

for relieving stenotic lesions in patients with TA. The previous study also reported that the restenosis rate of PTA in a patient with TA was about 17-32%, and compared to other interventions, the restenosis rate of stenting was higher, with the incidence about 12-66% in overall arteries.[12] Revascularization can reduce the need for multiple medications in hypertensive therapy.[13] As in our cases, after the successful procedure, the hypertension was controlled without any anti-hypertension medication in a year follow-up.

These two case reports highlight the importance of investigating acute symptomatic hypertension in children, and vasculitis etiology must be considered. The diagnosis of TA and other vasculitis is still challenging for the physician. Clinical suspicion and proper imaging are crucial for the correct diagnosis in the earlier phase. Initiation of multi-modal aggressive therapy in TA, including antihypertension, anti-inflammatory therapy, and angiography intervention. It is important to prevent severe complications and mortality in children.

Conflict of interest

None declared.

References

1. Kothari S. Takayasu's arteritis in children - a review. Images Paediatr Cardiol. 2001 ;3:4-23. PMID: 22368604.
2. Aeschlimann FA, Twilt M, Yeung RSM. Childhood-onset Takayasu arteritis. Eur J Rheumatol. 2020;7:S58-66. DOI: https://doi.org/10.5152/eurjrheum.2019.19195
3. Brunner J, Feldman BM, Tyrrell PN, Kuemmerle-Deschner JB, Zimmerhackl LB, Gassner I, *et al.* Takayasu arteritis in children and adolescents. Rheumatology (Oxford). 2010;49:1806-14. DOI: https://doi.org/10.1093/rheumatology/keq167
4. Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, *et al.* EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis. 2010;69:798-806. DOI: https://doi.org/10.1136/ard.2009.116657
5. Li Cavoli G, Mulè G, Vallone MG, Caputo F. Takayasu's disease effects on the kidneys: Current perspectives. Int J Nephrol Renovasc Dis. 2018;11:225-33. DOI: https://doi.org/10.2147/IJNRD.S146355
6. Ying S, Sifan W, Yujiao W, Rongyi C, Qingrong H, Lili M, *et al.* Clinical characteristics, imaging phenotypes and events free survival in Takayasu arteritis patients with hypertension. Arthritis Res Ther. 2021;23:196. DOI: https://doi.org/10.1186/s13075-021-02579-8
7. Sadurska E, Jawniak R, Majewski M, Czekajska-Chehab E. Takayasu arteritis as a cause of arterial hypertension. Case report and literature review. Eur J Pediatr. 2012;171:863-9. DOI: https://doi.org/10.1007/s00431-012-1674-z
8. Sun Y, Dai X, Lv P, Dong Z, Ma L, Yan Y, et al. Characteristics and medium-term outcomes of Takayasu arteritis-related Renal artery stenosis: Analysis of a large Chinese cohort. J Rheumatol. 2021;48:87-93. DOI: https://doi.org/10.3899/jrheum.190965
9. Mathew AJ, Goel R, Kumar S, Danda D. Childhood-onset Takayasu arteritis: an update. Int J Rheum Dis. 2016;19:116-26. DOI: https://doi.org/10.1111/1756-185X.12718
10. Sreih AG, Cronin K, Shaw DG, Young K, Burroughs C, Kullman J, *et al.* Diagnostic delays in vasculitis and factors associated with time to diagnosis. Orphanet J Rare Dis. 2021;16:184. DOI: https://doi.org/10.1186/s13023-021-01794-5
11. Kötter I, Henes JC, Wagner AD, Loock J, Gross WL. Does glucocorticosteroid-resistant large-vessel vasculitis (giant cell arteritis and Takayasu arteritis) exist and how can remission be achieved? A critical review of the literature. Clin Exp Rheumatol. 2012;30:S114-29.
12. Jeong HS, Jung JH, Song GG, Choi SJ, Hong SJ. Endovascular balloon angioplasty versus stenting in patients with Takayasu arteritis: A meta-analysis. Medicine (Baltimore). 2017;96:e7558. DOI: https://doi.org/10.1097/MD.0000000000007558
13. Casalini E, Sfondrini MS, Fossali E. Two-year clinical follow-up of children and adolescents after percutaneous transluminal angioplasty for renovascular hypertension. Invest Radiol. 1995;30:40-3. DOI: https://doi.org/10.1097/00004424-199501000-00006