A 15-Year-Old with Aphasia and Right Hemiparesis

Benjamin Wadowski¹ Tanya Chadha^{2,3} Andy Y. Wen^{1,4}

¹ Department of Pediatrics, NYU School of Medicine, New York, United States

² Division of Critical Care, Department of Pediatrics, Wolfson Children's Hospital, Jacksonville, Florida, United States

³ Department of Pediatrics, University of Florida College of Medicine, Jacksonville, Florida, United States

⁴ Division of Critical Care, Department of Pediatrics, NYU Langone Medical Center, New York, United States

Address for correspondence Andy Y. Wen, MD, Division of Critical Care Medicine, Department of Pediatrics, Bellevue Hospital Center, NYU School of Medicine, 462 First Avenue, NBV Suite 8E11, New York, NY 10016, United States (e-mail: andy.wen@nyumc.org).

J Pediatr Intensive Care 2017;6:221–224.

Abstract

Keywords

- ▶ aphasia
- ▶ arteritis
- ▶ stroke
- ▶ Takayasu
- ▶ vasculitis

Takayasu arteritis (TA) is the third most common vasculitis in childhood, peaking in the second to third decades of life but affecting patients as young as 6 months of age. It often presents with nonspecific systemic symptoms, although at late stages, it may present with cardiac, renal, or focal neurologic sequelae of vascular compromise. In this case, we describe a 15-year-old patient who presented acutely with stroke. In the absence of more classic rheumatological symptoms and significant laboratory abnormalities on initial testing, the diagnosis of TA was only reached through extensive vascular imaging following consultation with multiple subspecialty teams. This case demonstrates the need to maintain a high index of suspicion for vasculitis in pediatric patients presenting with new onset stroke in the absence of known predisposing factors. Doing so may reduce the time to diagnosis, hasten treatment, and optimize outcomes.

Introduction

A 15-year-old Hispanic female with a history of aortic and mitral insufficiency presented with right-sided weakness and aphasia that began 1 day prior to arrival. The patient had returned home from school when the patient's mother noticed that she was confused, had slurred speech, and had weakness of the right upper and right lower extremities. Medical attention was not sought until the following morning when the weakness had progressed and she began having difficulty ambulating without improvement in her speech. There was no history of trauma, fever, chills, chest pain, palpitations, rashes, syncope, sick contacts, or travel. She was brought to the emergency room by ambulance.

On examination, the patient's vital signs showed a temperature of 97.8°F, heart rate of 90, respiratory rate of 18, oxygen saturation of 100%, and blood pressure of 87/54 in the right upper extremity and 145/50 in the left lower extremity. A II/VI soft systolic murmur was appreciated at the left upper sternal border. Extremities were warm and well perfused

throughout; however, the patient had a decreased left radial pulse and absent right radial pulse. Neurologic examination revealed complete expressive aphasia with intermittently intact ability to follow commands, right facial nerve palsy, 2/5 strength in the right upper and lower extremities, inability to feel light touch, and temperature on the right upper and lower extremities, but intact withdrawal from nail bed pain and normal reflexes. The remainder of the neurologic examination was normal. Noncontrast head computed tomography (CT) scan revealed a dense infarct in the left middle cerebral artery (MCA) distribution.

The patient was immediately evaluated by the stroke team and started on low-dose aspirin. Magnetic resonance imaging/angiography (MRI/MRA) of the brain and neck performed approximately 36 hours after onset of symptoms revealed a large left MCA infarct (→ **Fig. 1**), complete opacification of the left common carotid artery, and bilateral subclavian artery stenosis. Echocardiogram showed mild aortic valve insufficiency and trivial mitral valve insufficiency without valvular lesions, thrombi, or intracardiac shunts. Thrombolytic

received

September 28, 2016

accepted after revision

December 29, 2016

published online

February 17, 2017

Copyright © 2017 by Georg Thieme
Verlag KG, Stuttgart · New York

DOI <https://doi.org/10.1055/s-0037-1598205>.
ISSN 2146-4618.

Fig. 1 (A) Magnetic resonance imaging brain showing large left middle cerebral artery (MCA) infarct. (B) Magnetic resonance angiography showing absence of flow within the MCA distal to the proximal M1 segment (white arrow).

therapy was withheld due to delayed presentation and prolonged time from onset of symptoms beyond the 4.5-hour window of opportunity.

The patient remained in the pediatric intensive care unit under close monitoring. CT angiography showed total occlusion of the left common carotid artery, high grade stenosis of the left subclavian artery, absent flow in the left vertebral artery, and >50% stenosis of the right proximal subclavian artery (►Fig. 2). Hypercoagulability work-up was negative. Rheumatological panel was significant for normal erythrocyte sedimentation rate (ESR), marginally elevated C-reactive protein (CRP), and positive antineutrophil cytoplasmic

antibody–myeloperoxidase. Albumin was 3.6 g/dL and total protein was 6.5 g/dL. MRI chest and renal ultrasound were performed revealing narrowed aortic caliber at the diaphragmatic hiatus, stenosis of the superior mesenteric artery, and left renal artery stenosis. Cerebral angiography performed on hospital day 2 revealed 99% stenosis of the left common carotid artery with evidence of clots distal to the stenosis and multiple large vessel stenoses involving the descending aorta, right and left subclavian arteries, and right and left vertebral arteries, in a characteristic vasculitic pattern consistent with Takayasu arteritis (TA).

The patient was started on intravenous steroids, aspirin was discontinued, and the patient was started on a 72-hour course of anticoagulation therapy with unfractionated heparin due to the discovery of common carotid artery clots to minimize the risk of artery-to-artery embolism. Her neurologic status did not worsen, and she was started on methotrexate (MTX), infliximab, and fluoxetine. She resumed antiplatelet therapy and was subsequently discharged to inpatient rehabilitation. Over the course of 7 weeks, she regained partial strength in her right-sided extremities, was able to transfer with assistance, and could perform activities of daily living. However, at 3- and 6-month follow-up appointments, the patient remained wheelchair-bound, only answering questions with single word responses, and had no functional movement of the right upper extremity.

Fig. 2 Computed tomography angiography with reconstruction showing occlusion of the left common carotid artery (yellow arrow) and stenosis of the left and right subclavian arteries.

Discussion

TA is the most common large vessel vasculitis and the third most common vasculitis in childhood, representing 2% of pediatric vasculitides in the United States.^{1,2} It has an overall incidence of approximately 2.6/million/year in the United States. TA has a strong female predominance,³ most often occurs in the second and third decades of life, but has been known to affect children as young as 6 months of age.¹ Studies

quantifying the incidence of this disease specifically in the pediatric population are lacking.⁴ The precise pathophysiology of TA is unknown, but commonly understood to involve autoimmune inflammation, fibrosis, and thrombosis, with aneurysm formation and stenosis of the aorta and its major branches.⁴

TA can be roughly divided into an acute early or “prepulseless systemic” phase and a late or “occlusive” phase.^{3,5} The clinical features at presentation are varied and depend largely on the stage of disease. The early phase, characterized by nonspecific systemic symptoms such as headache, fever, myalgia, arthralgia, and weight loss, may go unrecognized for weeks to months.¹ Vascular involvement in the late and chronic phase may lead to end-organ damage and may present as cardiac, renal, or focal neurologic deficits. Physical examination findings play a key role in diagnosing TA in patients that have an atypical presentation like our patient. Hypertension is the most frequently observed clinical feature of childhood TA (c-TA) (57% in the United States, up to 93% in Korea), followed by headache, fever, dyspnea, weight loss, and vomiting.^{6,7} Absent extremity pulses are found in 62.5% of cases, with secondary cardiac involvement seen in 19% of c-TA patients. Some reports suggest an overall rate of neurologic involvement of approximately 20% in c-TA.² Duarte et al found a 15.8% overall stroke/transient ischemic attack prevalence among all patients with TA, whereas stroke alone was found in just 11.7% of patients.⁸ There are few reports in literature describing stroke as the first manifestation of c-TA.^{9,10}

This patient represented a unique diagnostic challenge given the acuity of her presentation with severe neurologic impairment, absence of systemic symptoms more typical for TA, and only minor elevation of inflammatory markers. Several diagnostic and classification criteria for TA have been proposed, the original being Ishikawa’s criteria dating to 1988.¹¹ In 2010, the EULAR/PRINTO/PRES criteria (European League Against Rheumatism [EULAR], the Paediatric Rheumatology European Society [PRES], and the Paediatric Rheumatology International Trials Organization [PRINTO])

were validated and designed to apply specifically to patients younger than 18 years¹²; these are reproduced in ►Table 1. Angiographic abnormalities are a mandatory criterion, and therefore a diagnosis of c-TA cannot be made until angiographic studies are performed.¹³

A general approach to diagnosing TA is to combine a thorough history and physical examination with laboratory testing and imaging to assess for major and minor criteria and rule out alternative diagnoses. ESR and CRP have been shown to correlate with disease activity, and studies have observed an association between elevated CRP and risk of thrombotic complications.¹ When thromboembolic complications are present, hypercoagulability testing (i.e., coagulation studies, factor V Leiden, protein C and S deficiency, antiphospholipid antibodies) and radiographic assessment of thrombotic disease (Doppler studies, echocardiography) is warranted. An autoimmune panel should be sent to assess for other underlying autoimmune diseases. Conventional angiography with digital subtraction technique is considered the gold standard reference modality for diagnosis of TA, but several studies have shown that MRA has comparable accuracy with lower radiation dose and fewer complications in the pediatric population.¹⁴ Imaging of the thoracic and abdominal aorta and its major branches should be obtained to assess the extent of disease. Despite geographic variation in the distribution of TA lesions, the aorta remains the most affected artery, followed by the subclavian, common carotid, and renal arteries.¹³ In the adult population, fluorodeoxyglucose-positron emission tomography is being used to diagnose TA, as well as for follow-up of TA in the presence of negative inflammatory markers.¹

Most cases of c-TA present with nonspecific symptoms in the early phase; therefore, the goal of treatment is to prevent vessel damage and preserve end-organ perfusion. For patients presenting with more severe symptoms, treatment must address the acute complications as well as the underlying vasculitis. Systemic corticosteroids are the mainstay of treatment in the acute phase. Immunosuppressant

Table 1 The EULAR/PRINTO/PRES criteria for childhood Takayasu arteritis¹² requires angiographic abnormalities of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation plus one of the five following criteria: pulse deficit or claudication, four limb BP discrepancy, bruits, hypertension, or elevated acute phase reactants

Criterion	Definition
Angiographic abnormality (mandatory criterion)	Angiography (conventional, CT, or MRI) of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation, narrowing, occlusion or thickened arterial wall not due to fibromuscular dysplasia or similar causes; changes are usually focal or segmental
Pulse deficit or claudication	Lost/decreased/unequal peripheral artery pulse(s)
	Claudication: focal muscle pain induced by physical activity
BP discrepancy	Discrepancy of four limb systolic BP > 10 mm Hg difference in any limb
Bruits	Audible murmurs or palpable thrills over large arteries
Hypertension	Systolic/diastolic BP greater than 95th percentile for height
Acute phase Reactants	Erythrocyte sedimentation rate >20 mm per first hour or C-reactive protein any value above normal (according to the local laboratory)

Abbreviations: BP, blood pressure; CT, computed tomography; MRI, magnetic resonance imaging; EULAR, European League Against Rheumatism; PRES, Paediatric Rheumatology European Society; PRINTO, Paediatric Rheumatology International Trials Organization.

medications such as MTX can be used in combination with steroids and can also maintain remission during steroid tapers. Biologic agents targeting tumor necrosis factor, interleukin-6, and CD-20 have gained favor as adjuncts in the treatment and maintenance of adult TA.^{1,15} Long-term antiplatelet therapy is instituted in nearly all cases, with double-agent therapy (e.g., aspirin and clopidogrel) being administered in the acute phase if risk of bleeding is considered to be acceptable.¹ Endovascular intervention in the acute phase has shown mixed results. Overall, restenosis rates are typically higher than following open surgery (30–50% at 5–10 years vs. 15–30% at 5–20 years) and also appear to be higher when the intervention is performed in the acute phase; therefore, it is recommended that revascularization procedures be performed once disease activity is controlled.¹²

The prognosis for c-TA varies widely depending on extent of vessel involvement and end-organ damage at presentation. Mortality rates in early studies have exceeded 35%, but with the advent of improved medical and surgical therapies, fatality has decreased significantly.¹ Early recognition and treatment is key for reducing morbidity and mortality. Beyond the initial presentation, identifying optimal biomarkers and imaging techniques for monitoring of this chronic disease represents an ongoing challenge for providers worldwide.¹

Note

Benjamin Wadowski drafted the initial manuscript and approved the final manuscript as submitted. Tanya Chadha drafted, reviewed, and revised the initial manuscript and approved the final manuscript as submitted. Andy Y. Wen also drafted the initial manuscript, critically reviewed the manuscript, and approved the final manuscript as submitted.

Funding

None.

Conflict of Interest

None.

References

- Mathew AJ, Goel R, Kumar S, Danda D. Childhood-onset Takayasu arteritis: an update. *Int J Rheum Dis* 2016;19(2):116–126
- Weiss PF, Corao DA, Pollock AN, Finkel TH, Smith SE. Takayasu arteritis presenting as cerebral aneurysms in an 18 month old: A case report. *Pediatr Rheumatol Online J* 2008;6:4. Doi: 10.1186/1546-0096-6-4
- Gulati A, Bagga A. Large vessel vasculitis. *Pediatr Nephrol* 2010; 25(6):1037–1048
- Gedalia A, Cuchacovich R. Systemic vasculitis in childhood. *Curr Rheumatol Rep* 2009;11(6):402–409
- Brunner J, Feldman BM, Tyrrell PN, et al. Takayasu arteritis in children and adolescents. *Rheumatology (Oxford)* 2010;49(10): 1806–1814
- Hong CY, Yun YS, Choi JY, et al. Takayasu arteritis in Korean children: clinical report of seventy cases. *Heart Vessels Suppl* 1992;7:91–96
- Szugye HS, Zeff AS, Spalding SJ. Takayasu arteritis in the pediatric population: a contemporary United States-based single center cohort. *Pediatr Rheumatol Online J* 2014;12:21. Doi: 10.1186/1546-0096-12-21
- Duarte MM, Gerales R, Sousa R, Alarcão J, Costa J. Stroke and transient ischemic attack in Takayasu's arteritis: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis* 2016;25(4): 781–791
- Sikaroodi H, Motamedi M, Kahnouji H, Gholamrezaezhad A, Yousefi N. Stroke as the first manifestation of Takayasu arteritis. *Acta Neurol Belg* 2007;107(1):18–21
- Benjaminsen ER, Reigstad A, Cengija V, Lilleby V, Carlsson M. Stroke as the sole manifestation of Takayasu Arteritis in a 15-year-old boy with latent tuberculosis. *Case Rep Neurol Med* 2016;2016. Doi: 10.1155/2016/8736248
- Ishikawa K. Diagnostic approach and proposed criteria for the clinical diagnosis of Takayasu's arteriopathy. *J Am Coll Cardiol* 1988;12(4):964–972
- Ozen S, Pistorio A, Iusan SM, et al; Paediatric Rheumatology International Trials Organisation (PRINTO). 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(5):798–806
- de Souza AW, de Carvalho JF. Diagnostic and classification criteria of Takayasu arteritis. *J Autoimmun* 2014;48–49:79–83
- Soliman M, Laxer R, Manson D, Yeung R, Doria AS. Imaging of systemic vasculitis in childhood. *Pediatr Radiol* 2015;45(8): 1110–1125
- Catanoso M, Pipitone N, Magnani L, Boiardi L, Salvarani C. New indications for biological therapies. *Intern Emerg Med* 2011;6 (Suppl 1):1–9