Cardiology in the Young

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Takayasu's arteritis presenting as acute myocardial infarction: case series and review of literature

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Brief Report

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Abstract

This series describes three adolescent females who presented with chest pain and ventricular dysfunction related to acute coronary ischemia secondary to Takayasu's arteritis with varied courses of disease progression leading to a diverse range of therapies including cardiac transplantation. While Takayasu's arteritis is rare in childhood, it should be strongly considered in any adolescent female presenting with systemic inflammation and chest pain consistent with myocardial infarction. A high index of suspicion can lead to early detection and aggressive management of the underlying vasculitis reducing associated morbidity and mortality. The purpose of this report is to describe the challenges in the clinical diagnosis and management of Takayasu's arteritis with myocardial infarction. We also seek to enhance awareness about unique presentations of Takayasu's arteritis within the paediatric community.

Takayasu's arteritis is a chronic granulomatous vasculitis that primarily involves the aorta and its major branches. It is a rare disease with an incidence of 1–3 per million people in the USA and Europe and is most prevalent among females between the ages of 10–40 years.[1,2] Although Takayasu's arteritis has been reported in infancy, the median age of disease onset is 12 years.[3] Diagnosis requires an abnormal angiography with positive findings on physical examination (e.g., pulse deficits, blood pressure discrepancies, bruits, or hypertension) or elevated inflammatory markers.[4]

While lesions associated with Takayasu's arteritis can be detected along the thoracic and abdominal aorta, up to one-third of adult patients present with coronary arterial involvement.[5,6] Adults with coronary arterial involvement have worse clinical outcomes and higher mortality.[5] Takayasu's arteritis accounts for up to 10% of myocardial infarction in women under the age of 40 years.[5] While limited information is available on the prevalence of coronary arterial involvement in children with Takayasu's arteritis, recent studies estimate an incidence of approximately 5%.[6,7] Coronary lesions are mostly seen within the proximal coronaries and ostial disease has been reported in 73% of adults, likely due to direct extension of inflammation from the aorta.[8] We present our case series of three adolescent females with Takayasu's arteritis and myocardial infarction.

Patient #1

A 13-year-old female with a history of antithrombin III deficiency was evaluated for acute chest pain and elevated troponin (5.08 ng/mL). Initial electrocardiogram demonstrated ST segment elevation in leads III/aVF concerning for a myocardial infarction involving the inferior wall. Initial transthoracic echocardiography revealed normal left ventricular function with hypokinesis of the inferior, inferolateral, and inferoseptal segments of the right ventricle. Further evaluation with cardiac CT and MRI demonstrated proximal stenosis of the right coronary artery and a moderate to severe myocardial infarction in the distribution of the right coronary artery, with significant transmural involvement within the basal inferior, inferoseptal, and mid-inferior walls (Fig 1).

Due to suspicion of acute coronary syndrome, a cardiac catheterisation was performed which demonstrated severe ostial narrowing of the right coronary artery (Fig 1). Balloon coronary angioplasty was performed, and a 3.0×15 millimetre drug-eluting stent was placed at the ostium of the right coronary artery.

Magnetic resonance angiography of neck, chest, abdomen, and pelvis did not demonstrate any other areas of arteritis. Based on clinical presentation, angiographic findings, and elevated

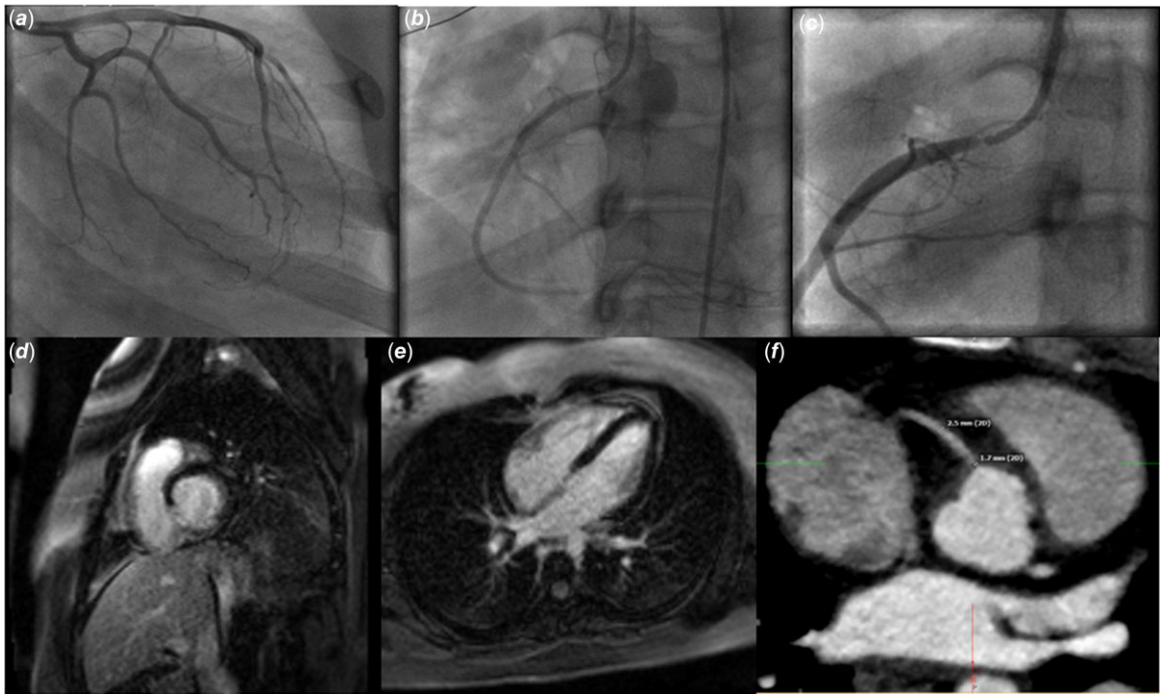

Figure 1. Imaging for Case 1 (A–C) Selective coronary angiography of left coronary artery (A) and right coronary artery (B–C); the left coronary artery appears normal but there is severe ostial narrowing of the right coronary artery; (D–E) cardiac magnetic resonance imaging demonstrating extensive delayed enhancement and fibrosis in the basal inferior and inferoseptal wall of the left ventricle. Overall left ventricular systolic function was preserved (EF: 56%) and right ventricle demonstrated borderline systolic function (EF: 49%); (F) cardiac computerised tomographic angiography demonstrating ostial narrowing of the right coronary artery.

inflammatory markers, she was diagnosed with Takayasu's arteritis and was treated with intravenous pulse dose steroids followed by daily oral steroids and cyclophosphamide. Despite this regimen, her systemic inflammation was not well controlled, and her treatment plan was modified to 10 mg/kg of intravenous infliximab monthly, oral steroids, and methotrexate 30 mg subcutaneously weekly after 4 months. Despite these changes, she developed re-stenosis of her proximal right coronary artery, which was successfully treated with balloon angioplasty. On monthly infliximab, steroid taper (now at 3 mg daily), and weekly subcutaneous methotrexate, she has remained clinically asymptomatic with well-controlled systemic inflammation with no progression of her disease in 2–1/2 years.

Patient #2

A 14-year-old African American female was evaluated for chest pain and an abnormal electrocardiogram. Patient initially presented with secondary haemophagocytic lymphohistiocytosis, deep venous thrombosis with pulmonary embolisation, mesenteric adenopathy, and inflammatory colitis, requiring emergent exploratory laparotomy. During that admission, an extensive rheumatologic, infectious, and haematologic evaluation was inconclusive for the aetiology of her haemophagocytic lymphohistiocytosis.

Her electrocardiogram demonstrated ST segment depression in inferior leads with mildly elevated troponin levels (0.06 ng/mL). A transthoracic echocardiogram demonstrated severe aneurysmal dilation of the right and left coronary arterial systems with normal biventricular function. Coronary angiography revealed extensive fusiform aneurysmal dilation of the left anterior descending coronary artery and circumflex coronary artery with proximal narrowing of the right coronary artery and bilobed fusiform aneurysmal dilation extending distally without evidence of thrombosis (Fig 2). A full body magnetic resonance angiogram demonstrated isolated vasculitis of the bilateral posterior tibial arteries. Based on these findings, she was initially diagnosed with polyarteritis nodosa and was started on intravenous pulse steroids, monthly intravenous cyclophosphamide, rituximab, and oral steroids.

She continued to have evidence of systemic inflammation and active vasculitis despite immunosuppressive therapy. After completing a course of intravenous cyclophosphamide, oral and intravenous steroids, and infusions of intravenous tocilizumab every 2–4 weeks, her immunosuppression was changed to mycophenolate but she continued to have evidence of active systemic vasculitis with recurrent chest pain. Due to her evolving coronary pathology, her diagnosis was changed to Takayasu's arteritis. She required multiple admissions for the management of acute myocardial infarction and ultimately developed ischemic cardiomyopathy necessitating cardiac transplantation at 16 years of age using standard induction and maintenance immunosuppression. Since cardiac transplantation, she has remained on a regimen of tacrolimus, prednisone, and mycophenolate with no evidence of active systemic vasculitis or coronary vasculopathy of her allograft over 4 years.

Patient #3

A 16-year-old Caucasian female was evaluated for possible vasculitis due to an abnormal electrocardiogram and an abnormal CT angiographic study of the chest. A routine electrocardiogram obtained due to an episode of dizziness and weakness with walking was concerning for inferolateral ST segment depression. A transthoracic echocardiogram demonstrated normal biventricular

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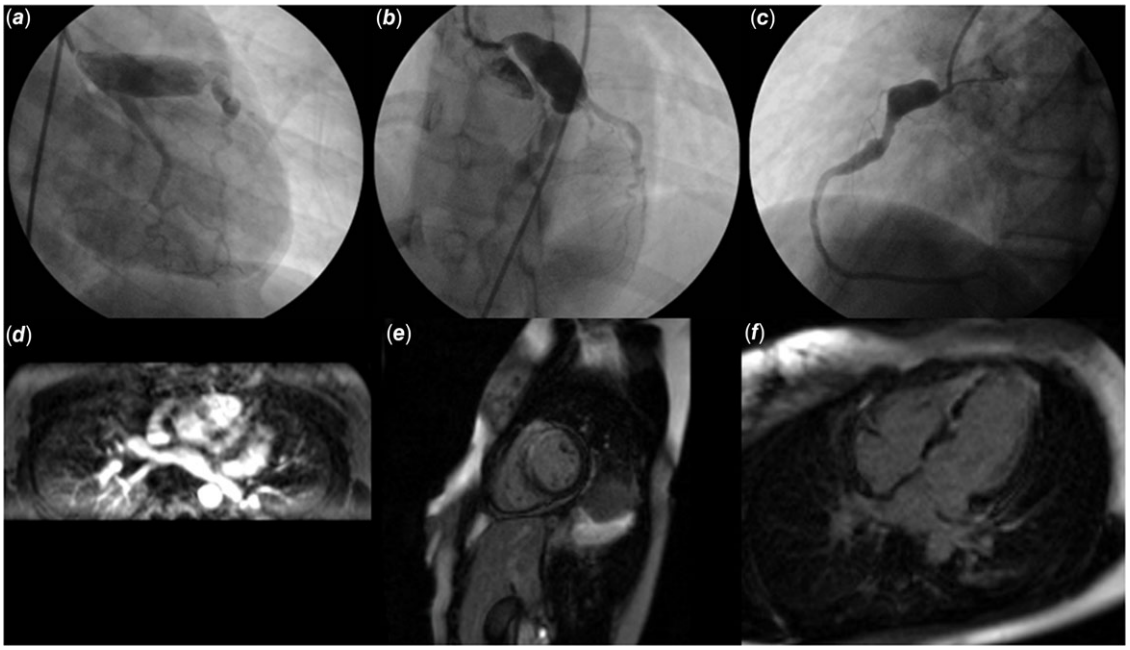

Figure 2. Imaging for Case 2 (A–C) Selective coronary angiography of the left coronary artery (A–B) and the right coronary artery (C); The left coronary artery shows a giant fusiform aneurysm and the right coronary artery shows proximal narrowing with post-stenotic bilobed fusiform aneurysmal dilation; (D) cardiac magnetic resonance angiography demonstrates aneurysmal dilation within the distribution of the left anterior descending coronary artery; (E–F) cardiac MRI showing delayed enhancement in mid-, apical anterior, and apical inferior left ventricular segments.

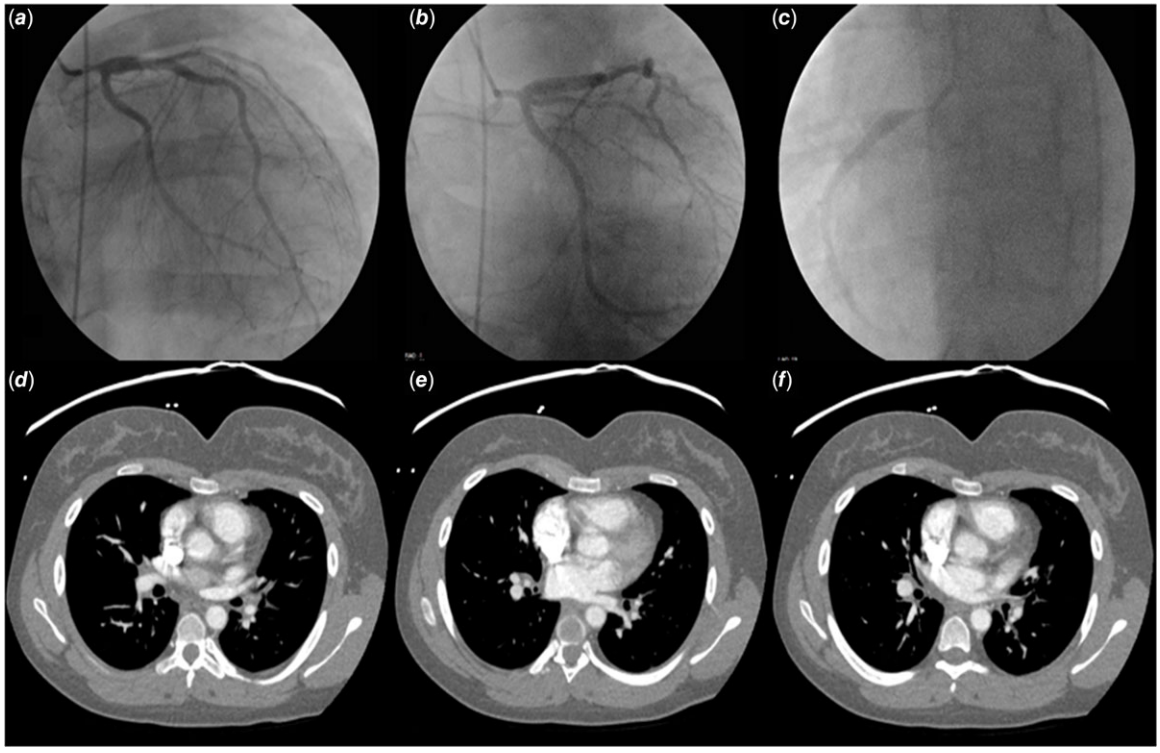

Figure 3. Imaging for Case 3 (A–B) Coronary angiography of the left coronary artery showing diffuse narrowing in the left main coronary artery with approximately 75% stenosis; (C) coronary angiography of the right coronary artery showing diffuse proximal narrowing with approximately 80% stenosis; (D–F) cardiac computerised tomographic angiography demonstrating mild aortic arterial wall thickening.

function, and a follow-up CT chest demonstrated vague soft tissue thickening of the ascending aorta and proximal to mid-descending aorta with a mild outpouching along the medial aspect of the descending thoracic aorta (Fig 3). The patient also had a history of anorexia, unintentional weight loss, and unrelated knee pain for 3 months.

A cardiac MRI study was also obtained and confirmed mild mural thickening of the aortic root, ascending aorta, aortic arch,

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and proximal to mid-descending thoracic aorta, with irregular outpouchings of the descending aorta at level of T4-T6, without obvious evidence for coronary arterial stenosis or aneurysm at that time. Based on these findings and elevated inflammatory markers, she was diagnosed with Takayasu's Arteritis and started on pulse dose steroids followed by oral steroids, monthly intravenous cyclophosphamide (6 months) and two doses of intravenous rituximab followed by mycophenolate.

Despite good medication compliance, she continued to have daily fevers and angina, with elevation of serum troponin. Due to these concerns, she was started on 10 mg/kg of intravenous infliximab, with rapid resolution of her fevers and elevated inflammatory markers but the angina persisted. She was then started on anti-platelet therapy (aspirin and clopidogrel) and amlodipine to minimise her risk of acute coronary syndrome. She ultimately underwent cardiac catheterisation which demonstrated significant ostial stenosis of the left and right coronary arteries and mild to moderate narrowing of the proximal right brachial artery (Fig 3). Based on these findings, she underwent a successful three-vessel coronary arterial bypass grafting procedure. Infliximab was changed to monthly intravenous tocilizumab (per patient request), and the mycophenolate was continued. Her oral steroids were tapered and discontinued within 2 years. Since the coronary arterial bypass grafting and ongoing medical management, she has well-controlled systemic inflammation without any recurrence of chest pain and has clinically stable coronary circulation for the past 8 years.

Discussion

Takayasu's arteritis is a rare systemic vasculitis that primarily affects the aorta and its major branches. Diagnosing Takayasu's arteritis continues to be a challenge because of its rarity, heterogeneity depending on the vessel involvement, and non-specific systemic presentation. The EULAR/PRINTO/PReS classification criteria for Takayasu's arteritis in children have been applied as diagnostic criteria with sensitivity and specificity of 100% and 99.9%, respectively.[4]

Children with Takayasu's arteritis and coronary arterial involvement can often be difficult to identify, given its low incidence and heterogeneity of presentation in the paediatric population compared to adults with atherosclerotic coronary artery disease.[9] Children presenting with angina, syncope, arrhythmias, ventricular dysfunction, or resuscitated from a sudden cardiac death episode typically require a diagnostic workup for congenital anatomic coronary arterial anomalies or systemic inflammatory diseases (e.g., Kawasaki disease and Takayasu's arteritis).

The keys to early diagnosis include a high index of suspicion and positive imaging studies of the affected blood vessels. Two of our cases developed acute myocardial infarction as part of their initial presentations of Takayasu's arteritis, while the third patient presented with a more insidious onset. Based on our experience, diagnosis of Takayasu's arteritis should be strongly considered in any young female presenting with symptoms consistent with myocardial infarction and systemic inflammation regardless of chronicity of symptoms.

Management and treatment of patients with Takayasu's arteritis is challenging because specific biomarkers are not available and randomised control trials have never been performed to guide therapy in children. Corticosteroids have been the mainstay for induction of remission. Since Takayasu's arteritis is often a progressive or relapsing disease, immunosuppressive therapy including methotrexate, mycophenolate, or cyclophosphamide is often required. Biological therapies, such as inhibitors of tumour necrosis factor and interleukin-6, have shown both efficacy and safety in refractory cases[3] and are used commonly in treatment, especially infliximab. While Takayasu's arteritis can be a self-limiting disease in some patients, the majority of patients will develop chronic and progressive disease, requiring long-term immunosuppression.[6,10] The long-term prognosis in patients with Takayasu's arteritis is related to arterial complications, and disease response to appropriate therapies, and disease progression. Up to 20% of adult patients require surgical intervention related to arterial complications and worsening disease,[10] but the need for surgical intervention is less common in children. Early diagnosis and aggressive management are imperative to prevent significant morbidity and mortality.

Our case series illustrates how difficult it is to manage children with Takayasu's arteritis and secondary coronary arterial complications. Our patients demonstrated variable responses to a variety of immunosuppressive medications (in large part due to availability of new biologic treatments over time), interventional and surgical therapies. Without appropriate control of systemic inflammation with immunosuppression, disease progression is imminent regardless of the interventional or surgical treatments performed. The heterogeneous nature of our case series highlights the need for further investigation into the pathophysiology of Takayasu's arteritis and the treatments that will provide the best long-term outcomes. While Takayasu's arteritis is an uncommon disease, optimisation of care has a significant impact on patient outcomes and quality of life.

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