Cardiology in the Young

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Catastrophic antiphospholipid antibody syndrome associated with ischaemic cardiomyopathy

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Brief Report

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Abstract

We report the case of a 16-year-old female with previously diagnosed bilateral sub-segmental pulmonary emboli who presented in cardiogenic shock from depressed biventricular function with cardiac MRI demonstrating concern for microvascular coronary injury. She was ultimately diagnosed with catastrophic antiphospholipid antibody syndrome-induced ischaemic cardiomyopathy, potentially associated with an underlying autoimmune connective tissue disease.

Introduction

Catastrophic antiphospholipid antibody syndrome is a heterogeneous disease process frequently with multi-organ microvascular thrombotic involvement.[1] Cardiac involvement typically manifests as heart failure, valvular disease (mitral and/or aortic), and/or acute myocardial infarction.[2] We present a novel case of acute decompensated heart failure in a paediatric patient due to catastrophic antiphospholipid antibody syndrome-induced microvascular coronary injury with resultant ischaemic cardiomyopathy.

Case presentation

A 16-year-old female with a history of bilateral sub-segmental pulmonary emboli and left lower extremity deep venous thrombosis managed on Lovenox with known triple-positive antiphospholipid antibodies presented to the emergency department with dyspnoea and chest pain. She was found to be in cardiogenic shock with biventricular dysfunction and left ventricular regional wall motion abnormalities, elevated troponins, and ST segment changes on electrocardiogram.

She was admitted to the cardiac ICU and quickly underwent cardiac catheterisation, which showed a low cardiac index of 1.78 L/min/m^2, grossly normal coronary filling (Figure 1), elevated left ventricular end diastolic pressure (40 mmHg), right ventricular end-diastolic pressure (18m mmHg), and pulmonary artery pressure (50 mmHg) in the setting of known pulmonary emboli. Following catheterisation, milrinone, epinephrine, and bumetanide were initiated. Epinephrine was transitioned to dobutamine due to tachycardia, and dobutamine and milrinone were discontinued after 1 week. A cardiac MRI was obtained demonstrating hypoperfusion of the basal and mid inferoseptal, inferior, and inferolateral segments on resting first-pass perfusion with late gadolinium enhancement of the mid inferoseptal, basal inferior, mid-inferior, and mid-anteroseptal segments (Figure 2). With normal coronary origins without focal stenosis or occlusion on cardiac catheterisation and her history of triple antiphospholipid antibody positivity, these findings were felt to be most consistent with microvascular injury related to antiphospholipid disease with resultant ischaemic cardiomyopathy. Throughout this time, she was on bivalirudin before initiating warfarin with a Lovenox bridge.

The heart failure team was consulted and assisted with transitioning her to goal-directed oral heart failure therapy with daily metoprolol, spironolactone, dapagliflozin, and lisinopril. Sacubitril/valsartan had been trialled and was not tolerated due to profound hypotension.

Haematology and rheumatology were consulted for assistance in diagnosing and treating her catastrophic antiphospholipid antibody syndrome with microvascular coronary injury. Immunosuppression, including eculizumab, rituximab, and methylprednisolone, was initiated followed by a prednisone taper. She underwent multiple rounds of therapeutic plasmapheresis. She required intermittent transfusions to maintain platelets $> 50 \times 10^3$/mL and haemoglobin > 7 gm/dL. She was started on aspirin per the recommendations of the adult congenital heart

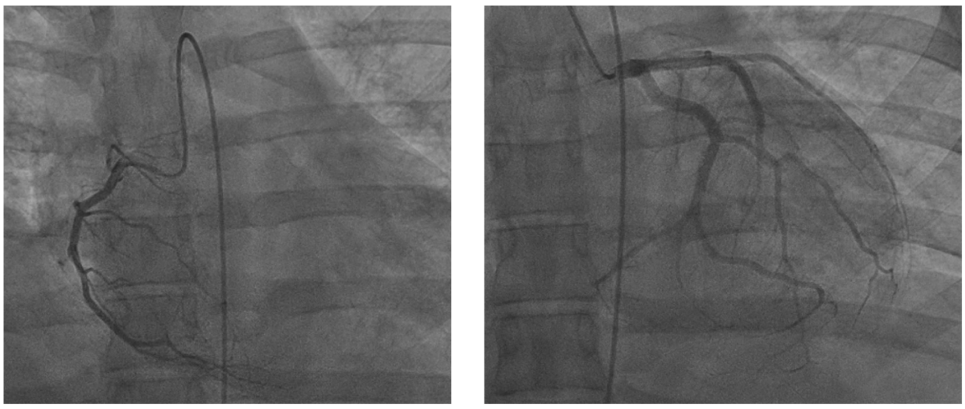

Figure 1. Selective coronary angiography demonstrating normal right and left coronary anatomy and filling.

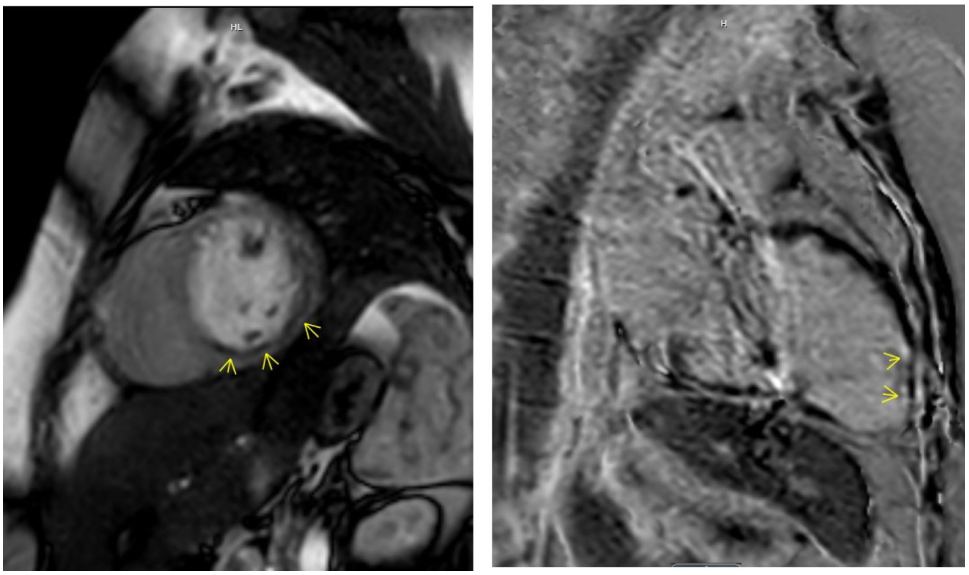

Figure 2. Cardiac MRI from day 2 of hospitalisation demonstrating hypoperfusion on resting first-pass perfusion (left) and multifocal late gadolinium enhancement (right).

disease team based on usage in adult patients with myocardial infarction with nonobstructive coronary arteries. Her echocardiogram prior to discharge showed stable moderately diminished biventricular dysfunction with improved left ventricular apical regional wall motion abnormalities and global longitudinal strain. Workup for primary rheumatic disease was significant for isolated positive anti-La (anti-Sjögren syndrome antigen B (SSB)) antibody. She had a negative antinuclear antibody and specific lupus antibodies (anti-double-stranded DNA, anti-Smith antibodies) and absence of typical clinical features of lupus or Sjögren (e.g arthritis and mucocutaneous involvement). However, the isolated positive anti-La (anti-Sjögren syndrome antigen B (SSB)) was concerning for possible underlying autoimmune systemic connective tissue disease, such as lupus or lupus-like disease.

At her most recent follow up, she was asymptomatic and remained on a regimen of daily aspirin, warfarin, dapagliflozin, lisinopril, metoprolol, and spironolactone. A rhythm monitor demonstrated a 10-beat run of non-sustained ventricular tachycardia after which we increased her metoprolol dose. She continues to follow up with cardiology, rheumatology, and haematology outpatient.

Discussion

Cardiac involvement in catastrophic antiphospholipid syndrome is relatively common, with about 52% of patients in an adult registry with this syndrome having cardiac manifestations.[2] The major cardiac manifestation was heart failure (49%). About 14% of patients with cardiac involvement had dilated cardiomyopathy with 25% experiencing segmental hypokinesia and 46% having decreased ventricular function (Ejection Fraction <40%). A few patients (~14%) completed histologic studies: cardiac thrombotic microangiopathy was predominantly found (~83%).

There have been reports of acute dilated cardiomyopathy from thrombotic microangiopathy in adult patients with catastrophic antiphospholipid antibody syndrome.[3–5] These patients typically required inotropic agents, initiation of heart failure therapy, immunosuppression, and anti-coagulation. On the contrary, acute heart failure due to ischaemic cardiomyopathy is particularly rare in children.[6] To date, there have been no reports of paediatric patients with ischaemic/dilated cardiomyopathy and microvascular coronary injury due to catastrophic antiphospholipid syndrome. The few reported cases of cardiovascular involvement in paediatric patients manifested as myocardial infarctions in two patients, one of which was fatal, and polyvalvar disease in another.[7–9]

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The diagnosis was supported by her known triple-positive antiphospholipid antibodies, biventricular dysfunction with left ventricular regional wall motion abnormalities, normal coronary angiography on cardiac catheterisation, and multifocal hypoperfusion defects with abnormal first-pass perfusion and multifocal late gadolinium enhancement on cardiac MRI. While histopathological confirmation of thrombotic microangiopathy is part of the definitive diagnostic criteria for catastrophic antiphospholipid antibody syndrome, cardiac biopsy was not pursued in this case given high clinical suspicion for this aetiology based on the available data and the high risk of the procedure in her acute inflammatory state.

Cardiac MRI has emerged as a non-invasive tool to assess myocardial injury from coronary ischaemia. While microvascular injury cannot be definitively demonstrated by MRI, the combination of clinical concern for a thrombotic microangiopathic process, grossly normal coronary flow by angiography, and MRI features such as late gadolinium enhancement and abnormal resting first-pass perfusion can be highly suggestive.[10]

Reported outcomes of catastrophic antiphospholipid antibody syndrome with cardiac involvement, in general, are favourable, though mortality was 34% in an adult cohort.[2] Our patient has been transitioned to an oral heart failure regimen, immunosuppressive therapies, anti-coagulation, and anti-platelet therapy, which is similar to goal medical therapy in adult patients with similar presentation, and she is currently doing well as an outpatient.[2]

Conclusion

In summary, we report a novel case of a paediatric patient with ischaemic cardiomyopathy and acute heart failure in the setting of catastrophic antiphospholipid antibody syndrome and possible underlying lupus or lupus-like disease. Thrombotic microangiopathy with microvascular coronary injury-induced cardiomyopathy is a unique manifestation of this syndrome that requires a high degree of clinical suspicion to diagnose.

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Competing interests. The authors declared no potential conflicts of interest.

References

1. Asherson RA, Cervera R, de Groot PG, et al. Catastrophic antiphospholipid syndrome registry project group. Catastrophic antiphospholipid syndrome: international consensus statement on classification criteria and treatment guidelines. Lupus 2003; 12: 530–534.
2. Pons I, Jeréz A, Espinosa G, et al. Cardiac involvement in the catastrophic antiphospholipid syndrome (CAPS): Lessons from the "CAPS registry". Semin Arthritis Rheum 66: 2024; 152439.
3. Hermel M, Hermel D, Azam S, et al. Acute dilated cardiomyopathy in the setting of catastrophic antiphospholipid syndrome and thrombotic microangiopathy: a case series and review. EJHaem 2020; 1: 44–50.
4. Mandal B, Rathore S, Douglas AF. Catastrophic antiphospholipid syndrome presenting as dilated cardiomyopathy with bilateral branch retinal artery thrombosis. Int J Clin Pract 2000; 54: 550–551.
5. Tulai IM, Penciu OM, Raut R, Rudinskaya A. Catastrophic antiphospholipid syndrome presenting as congestive heart failure in a patient with thrombotic microangiopathy. Tex Heart Inst J 2019; 46: 48–52.
6. Lipshultz SE, Law YM, Asante-Korang A, et al. Cardiomyopathy in children: classification and diagnosis: a scientific statement from the American heart association. Circulation 2019; 140: e9–e68.
7. Moreno-Ruiz LA, Mendoza-Pérez BC, Santillano-Gómez E, Jiménez-Arteaga S, Borrayo-Sánchez G, Alva-Espinosa C. Non-ST-elevation acute myocardial infarction secondary to antiphospholipid antibody syndrome in an adolescent female. Cir Cir 2010; 78: 435–438.
8. Miller DJ, Maisch SA, Perez MD, Kearney DL, Feltes TF. Fatal myocardial infarction in an 8-year-old girl with systemic lupus erythematosus, Raynaud's phenomenon, and secondary antiphospholipid antibody syndrome. J Rheumatol 1995; 22: 768–773.
9. Clauss SB, Manco-Johnson MJ, Quivers E, Takemoto C, Spevak PJ. Primary antiphospholipid antibody syndrome and cardiac involvement in a child. Pediatr Cardiol 2003; 24: 292–294.
10. Edvardsen T, Asch FM, Davidson B, et al. Non-Invasive imaging in coronary syndromes: recommendations of The European Association of Cardiovascular Imaging and the American Society of Echocardiography, in collaboration with The American Society of Nuclear Cardiology, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Cardiovasc Comput Tomogr 2022; 16: 362–383.

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