Echocardiographic Findings in Children with Native Mitral Valve Masses Complicated by Systemic Embolization

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INTRODUCTION

Native mitral valve mass with systemic embolization is a rare phenomenon in children. Here, we present two unique pediatric cases of mitral valve masses complicated by systemic embolization. Both children were previously healthy, with no histories of congenital heart disease or other identifiable risk factors for endocarditis. The first case was diagnosed as inflammatory myofibroblastic tumor (IMT), a rare cause of mitral valve mass, with embolization to the right renal and right common femoral arteries. The second case was diagnosed with *Streptococcus pneumoniae* endocarditis with evidence of embolization to the right temporal and temporo-occipital regions, bifurcation of the abdominal aorta, and right kidney. Both patients underwent surgical resection of the mitral valve masses as well as embolectomy.

CASE PRESENTATIONS

Case 1

A 7-year-old girl presented to a community emergency department for evaluation of 2 days of fevers, malaise, flank pain, vomiting, and decreased appetite. Further history revealed episodes of intermittent right leg tingling and pallor over the previous month. She had an illness with vomiting and diarrhea 3 weeks before presentation that had resolved and an episode of cough and congestion treated with azithromycin 2 weeks before presentation. Physical examination was unremarkable for cardiac or abdominal findings, with normal heart sounds without murmur and soft, nontender abdomen without organomegaly or masses. She underwent abdominal computed tomography for worsening right leg and flank pain, which revealed right renal infarct and embolus in the right common femoral artery. Electrocardiography revealed sinus rhythm with a normal QRS axis. Initial transthoracic echocardiography showed a mobile echogenic mass seen in the left atrium and ventricle that appeared to be attached to the underside of the anterior mitral valve leaflet extending into the subaortic area with attachments to the aortic valve leaflet. No significant mitral or aortic valve stenosis or regurgitation (Videos 1-4) was seen. The mass was further delineated with real-time three-dimensional (3D) and full-volume 3D echocardiographic image acquisitions followed by offline postprocessing to help with surgical planning (Figures 1 and 2). She initially underwent right common femoral arterial thromboembolectomy with resection of a whitish-yellow mass of rubbery texture. The next day, she underwent surgical resection of the mitral valve mass. The mass was noted to be globular and pedunculated with attachments to the anterior leaflet of the mitral valve (Figure 3), consistent with the geometric anatomy, orientation, and attachment as seen on 3D echocardiographic imaging. Additional masses were resected from the chordae, papillary muscles, and left ventricular cavity along with a few strings extending into the left ventricular outflow tract. She recovered with no further complications. Surgical pathologic examination revealed the cardiac mass to be an IMT. There was papillary and nodular proliferation of spindle cells in a background of fibromyxoid stroma. Focal areas with increased cellularity with mild to moderate atypia and rare mitoses were seen. The spindled lesional cells were positive for smooth muscle–specific α-actin and focally positive for CD163, CD68, and CDK4. The mass was negative for desmin, myogenin, S100, anaplastic lymphoma kinase (ALK), calretinin, and murine double minute 2. The femoral artery embolectomy specimen was similar to cardiac pathology and consistent with tumor embolization. The femoral embolectomy culture (obtained approximately 18 hours after the initiation of broad-spectrum antibiotics) grew *Cutibacterium acnes*.[1-3] Blood cultures before initiation of antibiotics and culture from the mitral valve (obtained approximately 34 hours after the initiation of antibiotics) were negative. The patient completed a course of antibiotics for infective endocarditis. Follow-up echocardiography and positron emission tomography showed no recurrence of tumor. Echocardiography 4 weeks after surgical resection showed trivial mitral valve regurgitation and no stenosis. She has done well clinically since discharge, with no clinical concerns. She continues to require ongoing follow-up with cardiology and oncology for recurrence surveillance but has not required any ongoing medications or treatment.

Case 2

A healthy 4-year-old boy was seen in an outpatient pediatric cardiology clinic for evaluation of a murmur in the setting of persistent fevers. He was seen at various points during his monthlong febrile illness by his primary care physician, at urgent care, and at an outside emergency department. A blood culture obtained by the emergency department tested positive for *S pneumoniae*, prompting admission and treatment with a 7-day course of intravenous ceftriaxone. However, his fever kept recurring, leading to a referral to the infectious disease clinic at our institution, where a new finding of cardiac murmur prompted evaluation at the pediatric cardiology clinic. Physical examination at the cardiology clinic visit was notable for normal heart sounds and a grade III/VI holosystolic murmur heard best at the apex and left sternal border. Electrocardiography revealed sinus rhythm with a normal QRS axis and right ventricular hypertrophy. Transthoracic echocardiography obtained for further investigation showed a hyperechoic, pedunculated mass (2.6 $\times$ 1.5 cm) adhering to the anterior leaflet of the mitral with moderate mitral

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VIDEO HIGHLIGHTS

Video 1: Case 1: apical four-chamber view of mitral valve mass.
Video 2: Case 1: parasternal long-axis view of mitral valve mass with S-8 probe.
Video 3: Case 1: 3D image of mitral valve mass in parasternal long-axis view.
Video 4: Case 1: parasternal long-axis view of mitral valve mass with X-5 probe.
Video 5: Case 2: parasternal long-axis view of mitral mass.
Video 6: Case 2: apical four-chamber view of mitral mass.
Video 7: Case 2: transesophageal echocardiographic image of mitral valve mass with failure of coaptation due to perforation of anterior leaflet of mitral valve.
Video 8: Case 2: transesophageal echocardiography with color Doppler demonstrating regurgitation through the perforation in anterior leaflet of mitral valve.
Video 9: Case 2: 3D transesophageal echocardiographic image of mitral valve demonstrating anterior leaflet perforation.
Video 10: Case 2: transthoracic echocardiography, apical four-chamber view, demonstrating mitral valve mass.
Video 11: Case 2: transthoracic echocardiography, parasternal long-axis view, showing mitral valve mass.
Video 12: Case 2: transesophageal echocardiography showing preoperative 3D images of mitral mass. *AML,* anterior mitral valve leaflet; *AoV,* aortic valve; *LVOT,* left ventricular outflow tract.
Video 13: Case 2: postoperative transesophageal echocardiography showing mitral insufficiency.

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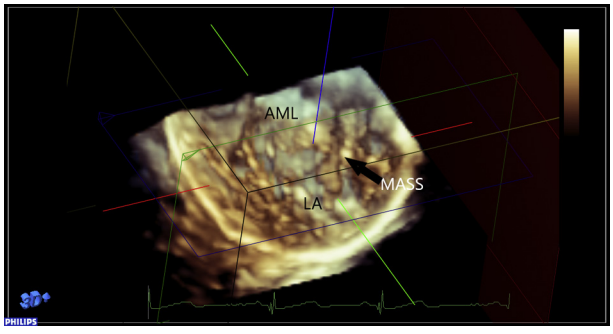

Figure 1 Case 1: 3D image of pedunculated and multilobulated mass from atrial surface of anterior mitral valve leaflet (AML). *LA*, Left atrium.

regurgitation (Videos 5 and 6). Brain magnetic resonance imaging demonstrated septic emboli in the right temporal and temporo-occipital regions with associated focal vasculitis, meningitis, and underlying cerebritis. Surgical vegetation removal was therefore scheduled. Preoperative transesophageal echocardiography showed interval decrease in the size of the vegetation (1.1 × 0.2 cm). There was a small

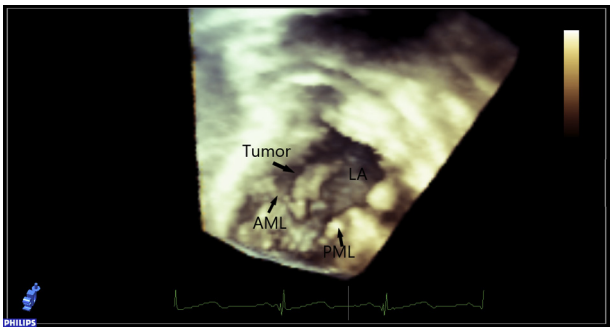

Figure 2 Case 1: 3D image of mitral valve mass from right atrial side. *AML*, Anterior mitral valve leaflet; *LA*, left atrium; *PML*, posterior mitral valve leaflet.

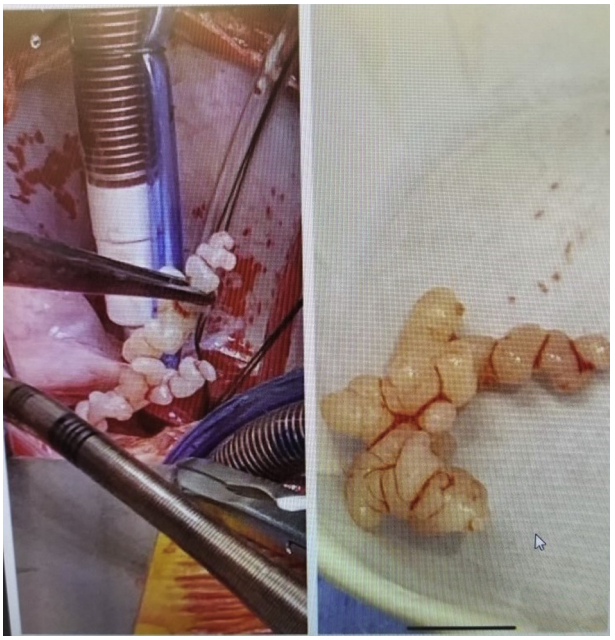

Figure 3 Case 1: surgical resection of mitral valve mass.

perforation in the anterior leaflet of the mitral valve with associated mild regurgitation and mild central regurgitation (Videos 7-9). Surgical intervention was deferred at that time because of the decrease in the size of the mass and concerns that surgical risks outweighed the benefits. However, follow-up transthoracic echocardiography continued to show pedunculated vegetation with measurements of 1.4 × 0.5 cm and worsening moderate mitral regurgitation from two jets (Videos 10 and 11). The picture was further complicated by computed tomography of the abdomen and pelvis showing a nonocclusive thrombus at the bifurcation of the abdominal aorta, insinuating into both common iliac arteries, and a wedge-shaped perfusion defect in the right kidney suspicious for thromboembolic disease. After further discussions the patient was taken back to the cardiac surgical suite and subsequently underwent vegetation removal with mitral valve repair. His preoperative transesophageal echocardiography with real-time 3D echocardiography confirmed before chest opening the presence of vegetation on the atrial surface of anterior mitral leaflet attached by a thin pedicle, freely mobile and with no additional attachments or presence in left

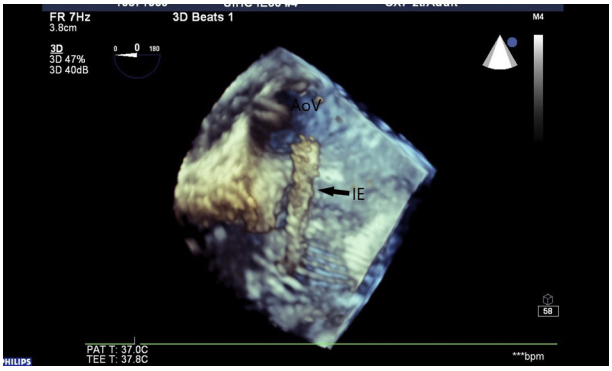

Figure 4 Case 2: 3D transesophageal echocardiographic image of infective endocarditis (IE) mass from atrial side. *AoV*, Aortic valve.

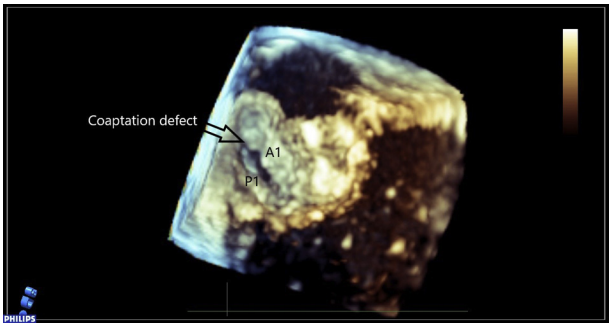

Figure 5 Case 2: 3D transesophageal echocardiographic image of mitral valve coaptation defect from atrial side. A1, A1 scallop of mitral valve; P1, P1 scallop of mitral valve.

ventricular outflow (a concern on two-dimensional imaging; Figure 4). Three-dimensional echocardiography also clarified the mechanism of mitral insufficiency through A1-P1 scallops (Figure 5, Video 12). The vegetation was measured at 1.53 × 0.48 cm on the anterolateral side of the anterior mitral valve leaflet. Surgical exploration revealed a 1.0 × 0.7 × 0.2 cm mass adherent to the anterior leaflet of his mitral valve. His mitral valve tissue was found to be very friable, with destruction of the A1 and P1 scallops of his mitral valve. The vegetation was removed, but the mitral valve was not repaired, because of ongoing inflammation (Figures 6 and 7). Postoperative transesophageal echocardiography showed moderate to severe mitral regurgitation (Video 13). The decision was made to defer mitral valve replacement until after completion of an antibiotic course. Surgical pathology revealed grossly a 1.0 × 0.7 × 0.2 cm tan-yellow to pink, ragged, unoriented soft tissue fragment with central bifurcated patency. Histologic examination revealed fibrin, acute inflammatory cells, and histiocytes. The next day the patient underwent exploratory laparotomy with aortic thrombectomy and reconstruction. He was discharged home on ceftriaxone, enalapril, furosemide, and enoxaparin. Furosemide and enoxaparin were stopped at follow-up visits. His recovery was complicated by development of right common iliac and gastroduodenal artery mycotic aneurysms 6 weeks after his procedures. He underwent invasive aortoiliac angiography and placement of kissing iliac stents as a bridge to more definitive repair in the future. He was incidentally found to have gallbladder sludging, prompting antibiotics to be changed to cefepime, and completed an additional 2 weeks of intravenous antibiotic before being transitioned to oral amoxicillin,

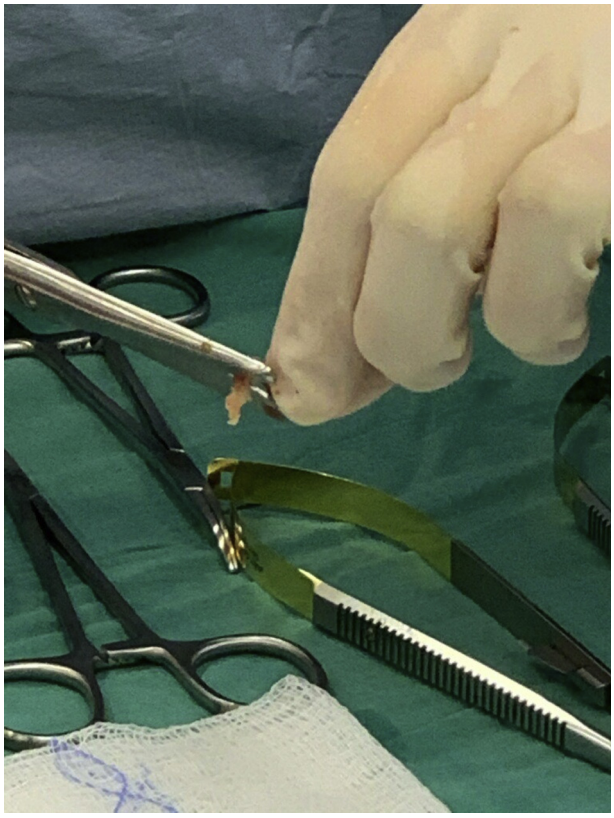

Figure 6 Case 2: Surgical removal of mitral valve mass.

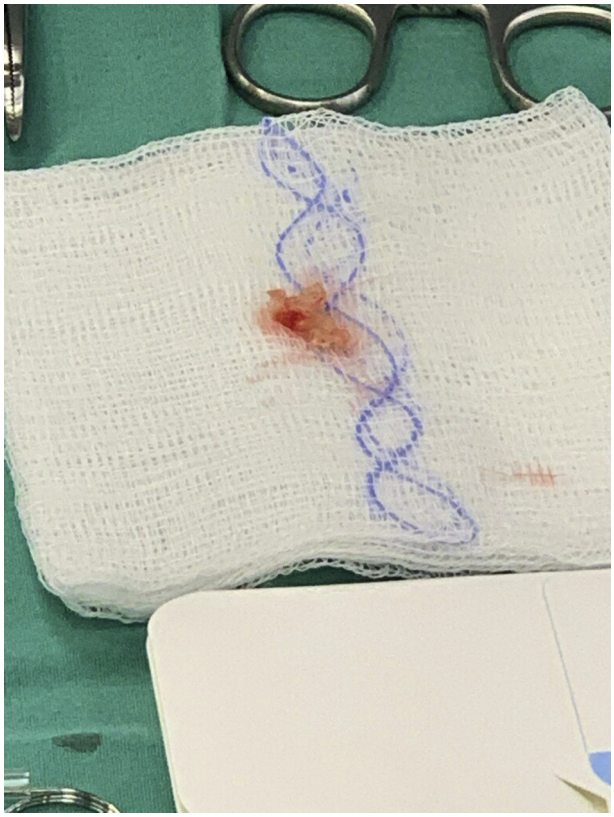

Figure 7 Case 2: mitral valve mass surgical specimen.

which he will remain on as suppressive therapy. He continues aspirin and enalapril and is being closely followed to determine the timing of further interventions on his mitral valve and arterial aneurysms.

DISCUSSION

Risk factors for embolization are well described for endocarditis. Echocardiographic findings of anterior mitral valve leaflet vegetations >10 mm place the patient at highest risk for embolization and indicate consideration for surgical intervention.[4] Other etiologies of mitral valve masses do not have well-described risk factors for embolization.

Our first case demonstrates a primary cardiac tumor with presenting symptoms secondary to embolization.

IMT is a rare mesenchymal neoplasm with unknown etiology.[5] It could be an immunologic response to an infectious agent such as Epstein-Barr virus (in splenic or hepatic IMT)[6,7] or human herpesvirus 8 (pulmonary IMT).[8] Genetic mutations involving the short arm of chromosome 2 in region 23, the genetic location of a tyrosine kinase receptor, ALK, have been shown in IMT.[9-11] The presence of ALK on histopathology has significant clinical relevance, as there are targeted chemotherapeutic agents for ALK alterations. With <60 cases reported in the scientific literature, IMT typically presents in children and young adults in the lungs and abdominopelvic regions.[12] Intracardiac presentations are extremely rare and have a predilection for right-sided cardiac structures.[13] Left-sided intracardiac IMT has been described only in case reports and literature reviews. We found seven case reports of intracardiac IMT involving the mitral valve. Three of these described pediatric patients (two described 11-year olds and the other an infant). All these case reports described identification by echocardiography and subsequent surgical resection. No cases described the use of 3D echocardiography or evidence of embolization.[14-20] When we broadened our literature search to include all locations of cardiac IMT, we found two case reports describing systemic embolic phenomenon.[14,21] Eilers *et al.*[13] reviewed 57 published cases of cardiac IMT and found that cardiac IMT occurs throughout the life span but is most commonly found during the pediatric years, with a slight female predominance and most commonly on the right side. Cardiac or constitutional symptoms were described at the most frequent primary presentation.

Our patient was the age and gender in which IMT are most frequently seen, but her primary symptom of leg pain due to an embolus from a mitral valve lesion was unique. She underwent surgical resection because of her history of embolic phenomenon and was successfully treated with surgical resection and antibiotics, with no further embolic phenomenon. Her femoral embolectomy tissue culture grew *C acnes*, with blood cultures and mitral valve tissue culture remaining negative. The source of *C acnes* could be a secondary infection of the embolus or a contaminant during culture processing. However, we could not rule out a primary infection of mitral valve precipitating IMT. Primary infection of mitral valve was less likely given that the remainder of cultures were negative; however the mitral valve tissue may have been sterilized with the additional day of antibiotics. We could not find any reported cases of *C acnes* infection precipitating IMT.

Our second patient represents *S pneumonia* infective endocarditis. *S pneumonia* is an uncommon cause of endocarditis, representing 3% to 7% of all pediatric endocarditis.[22] Givner *et al.*[23] reviewed 11 cases of pneumococcal endocarditis at eight US children's hospitals, of which only one patient had no history of structural heart disease. Systemic embolization is not uncommon, occurring in 22% to 50% of all cases of infective endocarditis. Embolization occurs most frequently in the first 2 to 4 weeks of antimicrobial therapy. Patients with left-sided infective endocarditis are at a higher risk for central embolization, but there is little evidence to predict which patients are at higher risk for embolization. Some studies have shown the mitral valve, particularly anterior leaflet location and size >1 cm, being associated with higher risk for embolization.[4] Our patient demonstrated evidence of embolization within 24 hours of diagnosis, with no clinical signs or symptoms suggestive of embolization. Follow-up two-dimensional and 3D echocardiography played an important role in his clinical decision-making.

CONCLUSION

Echocardiography has long been used to identify the risk and aid in decision-making regarding cardiac surgery. Newer 3D echocardiographic capabilities in pediatric patients are further enhancing the supportive capabilities of echocardiography in this process. We were able to harness those capabilities in the management of two very rare pediatric cases of native mitral valve masses with systemic embolization.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2020.05.021.

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