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Title: Large Pericardial effusion and tamponade in young male with Niemann-Pick disease type C

Authors: Ojas Mehta, Robert Anderson, Michael Gonzales

A 27-year-old gentleman with Niemann-Pick Disease type C (NPC) presented to a tertiary hospital with two months of constitutional symptoms including lethargy, chronic cough, exertional dyspnoea and anorexia.

NPC is a rare genetic disease with an incidence of approximately 1/120,000 live births.¹ It is a disease of excessive lipid accumulation resulting from mutations in genes, *NPC1* or *NPC2*, which encode a large membrane glycoprotein and a small cholesterol-binding lysosomal protein, respectively. These defects result in abnormal lipid transport, lysosomal storage and accumulation of cholesterol, phospholipids, glycolipids and sphingomyelin.²

NPC can present at any age from the perinatal period until over 50 years into adulthood. Typical clinical manifestations are visceral and neuropsychiatric. Visceral manifestations commonly include neonatal jaundice and hepatosplenomegaly. Neuropsychiatric manifestations, which ultimately determine the patient's lifespan, include supranuclear vertical gaze ophthalmoplegia, ataxia, dysarthria, dysphagia, cataplexy, epilepsy and cognitive impairment with progressive dementia.³

Our patient was diagnosed at 18 years of age, two years after his initial presentation with acutely worsening ataxic gait on a background of neonatal jaundice, speech impediment and learning disability. He was diagnosed histologically with a skin biopsy from the arm. He has since suffered all the aforementioned manifestations of NPC. His medications included miglustat, valproic acid, quetiapine, codeine linctus and loperamide. Miglustat inhibits glycosphingolipid biosynthesis, as part of a substrate reduction therapy strategy to reduce the rate of glycosphingolipid accumulation in NPC.⁴

On examination, his blood pressure was 135/80mmHg and his electrocardiogram showed sinus rhythm at 100bpm. His jugular venous pulse was elevated. Chest radiography revealed an enlarged cardiac silhouette. Suspicion for a pericardial effusion was confirmed with transthoracic echocardiography, which demonstrated a 3.4cm large, loculated effusion (figure 1). He had early features of tamponade as demonstrated by a leftward septal shift on deep inspiration. His left and right ventricles were of normal size, thickness and systolic function. His valves were also of normal structure and function.

Over the next few days, he developed pulsus paradoxus with systolic blood pressure variation between 120mmHg and 105mmHg, and worsening sinus tachycardia at 120bpm. Serial echocardiograms confirmed clinical deterioration with additional features of tamponade. These included exaggerated leftward septal shift, reduced right ventricular function and size and significant respiratory variation in flow velocities across the mitral and tricuspid valves.

Emergent surgical subxyphoid pericardial window drained 250ml of heavily bloodstained pericardial fluid. There were widespread adhesions and clots with 2-3mm thickened parietal pericardium and visceral pericarditis. Fluid assessment demonstrated an abundance of chronic inflammatory cells and degenerated red cells.

A 10x10x3mm biopsied pericardium segment showed a layer of inflamed granulation tissue covered by a dense layer of fibrin (figure 1). Immunophenotyping of the inflammatory cells showed predominantly CD68+ monocyte-macrophages and a lesser extent of CD3+ T lymphocytes, CD20+ B lymphocytes and scattered plasma cells. The monocyte-macrophages had granular foamy cytoplasm consistent with storage material. Electron microscopy revealed classical features of NPD: histiocytes with granular osmophilic material within lysosomes and cytoplasmic collections of whorled “myelin” figures.

Post-operatively, the patient had significant improvement and eventual resolution of his symptoms. He was subsequently discharged from hospital care.

Conclusion

This is the first reported case of NPC with pericardial involvement manifesting in early cardiac tamponade. Awareness of potential cardiac involvement may lead to earlier detection in individuals known to have NPC with early signs or symptoms. Management of such effusions would involve therapeutic drainage and any treatment of underlying pathophysiological processes of infiltration seen in NPC. Cardiac involvement has very rarely been reported. In 1985, Ferrans and colleagues identified NPD as a potential cause of non-granulomatous lipid-laden histiocytic infiltration of the myocardium, valves and pericardium.⁵ While our patient had normal underlying valves and myocardial function, there is the possibility of deterioration in these elements in addition to recurrent pericardial effusions.

Figure and description

Figure 1. Chest X-ray and TTE demonstrated a large, circumferential effusion with multiple loculations seen across the fibrous and serous pericardial layers (A and B). Pericardial biopsy sections with Haematoxylin and Eosin staining with progressive magnification demonstrates extensive fibrin deposition and granulation tissue with inflammatory cell infiltrate (panels C to F). Panel E shows infiltration with foamy histiocytes. Electron microscopy images show granular osmophilic material (Panel G) and “myelin” figures (Panel H).

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Abstract

We describe a twenty seven year old male with Niemann-Pick disease type C, a rare inherited lysosomal storage disease, who presented with a complex loculated pericardial effusion and early signs of cardiac tamponade prompting drainage via a pericardial window. Pericardial biopsy revealed an underlying infiltrative process consistent with Niemann-Pick disease. With this finding, we suggest that the clinical manifestations of Niemann-Pick disease are broader than previously described.

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