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EC CARDIOLOGY

Case Report

A Complex Cardio-Hematological Case

Alvin Ee Zhiun Cheah[1], Krishan Gupta[1] and Seshasayee Narasimhan[1,2,3,4]*

[1]*Internal Medicine, Manning Base Hospital, Taree, NSW, Australia*

[2]*Cardiology, Manning Base Hospital, Taree, NSW, Australia*

[3]*Conjoint Senior, University of Newcastle, Callaghan, NSW, Australia*

[4]*Adjunct Senior Lecturer, University of New England, Armidale, NSW, Australia*

***Corresponding Author:** Seshasayee Narasimhan, Cardiology, Manning Base Hospital, Taree, NSW, Australia.

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Abstract

A 61-year-old female presents to a rural hospital with recurrent admissions for myopericarditis diagnosed 3 weeks while on a holiday in Bali, Indonesia. Echocardiogram revealed a mild pericardial effusion, but no regional wall abnormalities were identified. She was initially treated symptomatically with NSAIDs and colchicine for myopericarditis. During admission, she began to develop thrombocytosis and suffered unexplained thrombotic events. A bone marrow aspirate revealed hypercellular bone marrow aspirate suggestive of Myeloproliferative Neoplasm (MPN) including Essential Thrombocythemia (ET) pre-fibrotic primary myelofibrosis (PMF). JAK2 V617F mutation was positive on peripheral blood film. This case report highlights the rare cause of extramedullary haematopoiesis leading to cardiac involvement associated with MPN.

Learning Objective: Extramedullary haematopoiesis with cardiac involvement is uncommon and may lead to complications such as myopericarditis, pericardial effusion and cardiac tamponade. Thus, a high index of suspicion is required to ascertain the underlying cause for recurrent myopericarditis for appropriate management to be commenced promptly.

Keywords: *Chest Pain; Pericarditis; ST Elevation; Myeloproliferative Neoplasm*

Introduction

Myopericarditis is an inflammatory condition involving the myocardium and pericardium which can be caused by various aetiologies, including rare causes such as myeloproliferative neoplasms. Typical clinical features include pleuritic chest pain, reduced exercise tolerance, cardiac failure and EC changes of diffuse saddle ST elevation with PR depression. Treatment of myopericarditis involves symptomatic management of pain with anti-inflammatories and restriction of physical activities for 3 months. We report an unusual case of a 61-year-old female who presented with recurrent myopericarditis secondary to extramedullary haematopoiesis associated with MPN.

Case Report

61-year-old female presented to Emergency Department with nausea, vomiting and general malaise on a background of recent trip to Bali, Indonesia. She reports feeling slightly unwell two days before holiday trip to Bali. Whilst on holidays, she developed chest pain and inferior ST elevation and troponin rise. Echocardiogram revealed mild pericardial effusion and no regional wall abnormalities were identified. She was subsequently diagnosed with myopericarditis and was discharged home from the Balinese hospital with colchicine and NSAIDs.

On return to Australia, she experienced further headaches, fever, pleuritic chest pain and dyspnoea which prompted her to visit the nearest Emergency Department. She denies history of recent coryzal symptoms or trauma. It was of interest to note that she had a root canal procedure 3 weeks prior to her holiday in Bali. She had a past medical history of migraines and does not take any regular medications. She lives with her family and is independent with her activities of daily living. She is a non-smoker, drinks alcohol occasionally and leads a fit and active lifestyle.

Initial investigations revealed leucocytosis of 18.4 x 10^9, thrombocytosis of 565 x 10^9 and haemoglobin of 127 g/L. Troponin was elevated at 2017. Peripheral blood film showed leucocytosis with neutrophilia, monocytosis, thrombocytosis and large platelets. Electrocardiogram showed deep t-wave inversions. She was admitted, treated symptomatically as myopericarditis and was discharged home the next day.

Three days later, she represented to hospital again due to ongoing pleuritic chest pain. She was found to have thrombocytosis which was initially thought to be a reactive process due to her myopericarditis. However, during her admission she was found to have rapidly progressive thrombocytosis with a peak platelet levels of 1424 x 10^9/L. Computed Tomography(CT) scan of chest, abdomen and pelvis showed an enlarged spleen, a 56 x 58 x 40 mm hypodense region in the spleen suggestive splenic infarction or abscess, left pleural effusion and multifocal low density areas on kidneys suggestive of pyelonephritis.

She was commenced on intravenous ceftriaxone for pyelonephritis. However, she continued to spike temperatures up to 38.8 degrees Celsius on antibiotic therapy. Blood and urine cultures showed no growth. Diagnostic tap of the left pleural effusion was unremarkable. Autoimmune screen including anti-nuclear antibody, double stranded DNA, extra-nuclear antibodies were negative. Hepatitis B, C, Human Immunodeficiency Virus (HIV) Q-fever, cytomegalovirus, norovirus, herpes simplex (HSV), varicella zoster (VZV), enterovirus and adenovirus serologies were also unremarkable. However, she was positive for Hepatitis A and Epstein Barr virus (EBV) IgG indicating previous exposure. She developed temporary right-hand weakness for 15 minutes which self-resolved. CT-Brain and Carotid Doppler Ultrasound were unremarkable. She was then transferred to Intensive Care Unit (ICU) for closer monitoring.

Due to intermittent pyrexia and unexplained thrombotic shower, he underwent a transoesophageal echocardiogram (TOE) where subacute bacterial endocarditis was excluded. TOE also revealed normal Left Ventricular Ejection Fraction (LVEF) of 60percent and mild grade 1 diastolic dysfunction. Her condition continued to deteriorate and underwent splenectomy as per haematology advice. Histopathology of the spleen was consistent with splenic infarction with no signs of malignancy. post-splenectomy, she was administered with Haemophilus *influenza* type B, pneumococcal and meningococcal vaccinations according to the vaccination schedules and lifelong amoxicillin.

Bone marrow aspirate demonstrated a hypercellular picture, moderately increased megakaryopoiesis with hyperlobulated megakaryocytes, atypical lymphocytes with cleaved nucleus and moderately increased plasma cells suggestive of MPN including Essential Thrombocythaemia (ET) and prefibrotic PMF. JAK2 V617F mutation was identified on cytogenetic testing but BCR-ABL1 was negative.

She was then commenced on hydroxyurea for myelosuppression, aspirin and apixaban for prevention of further thrombotic events. Her platelet levels were on the downtrend after commencement of hydroxyurea. However, she developed neutropenia and recovered after three days of Granulocyte-colony stimulating factor (GCSF). She has made a remarkable recovery since and follows up regularly with her haematologist.

Discussion

Myopericarditis refers to the combination of pericarditis and myocarditis with predominant pericarditis picture. Contrasting to the term perimyocarditis which presents largely as a myocarditis picture. The European Society of cardiology has recommended distinguishing these two terms as focus of management would differ from one another [1].

Myopericarditis and acute pericarditis share similar aetiologies, with viral infections being the commonest cause in developed countries. Common viruses included coxsackieviruses, adenoviruses, echovirus, cytomegalovirus, epstein barr virus, HHV and parvovirus B19 [2]. In developing countries, atypical infections such as tuberculosis remains an important cause of myopericarditis [3]. These cardiotropic viruses either cause direct cytolytic or cytotoxic leading to pericardial and myocardial inflammation with subsequent immune mediated hypersensitivity response. Other autoimmune conditions such as inflammatory bowel disease and connective tissues disease and rarely, radiation, drugs and small-pox vaccine [4] can also trigger similar immune pathways resulting in eosinophilic myocardial infiltrates. Infrequently, malignancies can also trigger eosinophilic response and myocarditis [5]. Myocarditis has been associated in solid lung, gastrointestinal and urogenital tumours as well as a variety of haematological malignancies such as T cell leukaemia, acute lymphoblastic leukaemia, acute and chronic myeloid leukaemia, myelodysplastic and myeloproliferative syndromes and Hodgkin's lymphoma. It is believed that eosinophilia is a result of neoplastic clone in myeloid cell line disorders [6].

Myeloproliferative Neoplasms (MPN) are a group of haematopoietic stem cells disorders that leads to an excess of myeloid cells in the peripheral blood. MPN consists of polycythaemia rubra vera, essential thrombocythemia, primary myelofibrosis, chronic myeloid leukemia (CML), chronic neutrophilic leukemia and chronic eosinophilic leukemia. Clinical presentations of MPN include unusual thrombotic events, massive splenomegaly, fever, night sweats, and loss of weight. MPN can progress to Acute Myeloid Leukemia, Myelodysplastic Syndrome and secondary fibrosis of the bone marrow due to clonal evolution and disease progression. The most common mutations found in MPN such as primary myelofibrosis, essential thrombocytosis and polycythaemia rubra vera are *JAK2, CALR* and *MPL*. The sensitivity of *JAK2* mutations found in PV is 100 percent and 60 - 65 percent in both ET and PMF [7,8].

Myopericarditis have a myriad of clinical features including subclinical asymptomatic disease. It is not uncommon for the symptoms to be preceded by an acute respiratory tract infection such as pneumonia, sinusitis or tonsillitis. Symptoms included those of pericarditis such as pleuritic chest pain relieve leaning forward, dyspnoea, reduced exercise tolerance and occasionally fever. Depending on severity of myocarditis, symptoms of failure may be present, or arrhythmias leading to syncope and palpitations. Examination may reveal a pericardial friction rub, reduced heart sounds in significant pericardial effusion or signs of heart failure including elevated jugular venous pulsations, peripheral oedema and pulmonary congestion.

An electrocardiogram typical of myopericarditis includes saddle shape diffuse ST elevation and PR depression. It then evolves to normalisation of ST and PR segments followed by diffuse T wave inversions. Localised myopericarditis can also result in localise ST and T wave inversion changes. Occasionally arrhythmias can also be seen in those with significant myocardial involvement such as ventricular ectopic, non-sustained ventricular tachycardia and supraventricular tachycardia.

Blood test almost always show signs of inflammation such leucocytosis, raised C-reactive protein and erythrocyte sedimentation rate. Serum cardiac biomarkers such as troponin, B natriuretic peptide and CK-MB is also raised reflecting myocardial injury in myopericarditis.

An echocardiogram when performed may reveal an associated pericardial effusion or increased pericardial brightness reflecting underlying inflammation. If regional wall abnormalities or reduce left ventricular function is seen, this should point instead to myopericarditis. In some circumstance of diagnostic uncertainty, a coronary angiogram can be done to rule out acute coronary syndrome. A cardiac MRI is diagnostic in determining the involvement of myocardium and pericardial tissue. The presence of myocarditis can be confirmed with an endomyocardial biopsy, however this is rarely required in the absence of heart failure.

Myopericarditis is diagnosed based on presence of diagnostic criteria of pericarditis with significant elevation of cardiac biomarkers in the absence of regional or global impairment of left ventricular function.

The treatment of myopericarditis is similar to acute pericarditis. This includes administration of anti-inflammatory agents such as aspirin, ibuprofen, indomethacin for symptomatic management of chest pain [9]. Corticosteroids is second line if NSAIDs are contrain-

dicated or in cases of inadequate symptom control. Some have suggested using reduced doses of NSAIDs due to animal studies showing increased mortality of NSAID use in coxsackie related myocarditis [10]. However, this argument have been found to be controversial due to poor study conditions.

Other non-pharmacological treatments include strict physical activity restriction in the first 3 months. Athletes and high demanding sport activities should be avoided for a further 6 months due to risk of sudden cardiac death [11]. The prognosis for perimyocarditis is generally good especially for idiopathic and viral causes. A great majority of patient achieve full recovery demonstrated on imaging at 12 months [12].

Conclusion

This is an unusual case of MPN JAK2 V617F mutation positive presenting initially with myopericarditis and leading to widespread thrombotic events. It is a rare observation to have MPN that presents with cardiac involvement. Thus, a high clinical suspicion and prompt recognition is required to obtain an accurate diagnosis in order to provide appropriate management for optimal patient outcomes. Further studies of mutation pathways including *JAK2, CALR* and *MPL* would allow for a clearer and reliable diagnostic system for MPN and account for their various clinical presentations.

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