Case report

Primary cardiac lymphoma diagnosed and subtyped on pericardial fluid cytology

ABSTRACT

Primary cardiac lymphoma (PCL) is a very rare malignancy, involving only the heart/pericardium with no or minimal evidence of extra-cardiac involvement.

A 73-year-old lady presented with dyspnoea on exertion. Echocardiography revealed a mass predominantly involving right atrium with moderate pericardial effusion. Pericardiocentesis was done and the smears showed monomorphic population of medium sized atypical lymphoid cells. Immunohistochemistry performed on the cellblock was suggestive of Diffuse large B cell lymphoma (DLBCL), activated B cell (ABC) type. PET-MR revealed a metabolically active large diffusely infiltrative intracardiac mass lesion with no other distant possible sites of primary malignancy or extra cardiac deposits. Thus, a diagnosis of PCL was made. She underwent single fraction of palliative radiotherapy as she was unfit for definitive chemotherapy.

Cytological evaluation of pericardial fluid using cell block is a useful and effective tool in the diagnosis as well as subtyping of PCL presenting as malignant effusion.

Keywords: Primary cardiac lymphoma, cytology, Cell block, pericardial effusion, diffuse large B cell lymphoma

Learning objective:

- Primary cardiac lymphoma (PCL) is a rare cardiac tumor with poor prognosis

- Cytological examination of pericardial fluid is the least invasive technique for diagnosis of Primary cardiac lymphoma
- Cases diagnosed by cytology and cell block immunohistochemistry are sparse in the literature compared to those diagnosed in histology. This emphasizes the importance of awareness among clinicians that cytology can yield an accurate and early diagnosis using minimally invasive procedures.

INTRODUCTION

Primary cardiac lymphoma (PCL) is a rare disease, constituting about 0.01 - 0.5% of all lymphomas and about 1–2% of all cardiac tumours. [1-3] PCL is defined as lymphomas that only involve the heart and pericardium with no evidence of extra-cardiac disease. [2-4] The usual presentation is in the 5th or 6th decade of life, with a slight male predominance. [6] [7] Previously many cases of PCL were diagnosed only post-mortem as can be seen from articles published till early 2000s. [6] With newer imaging modalities, PCL were diagnosed ante-mortem either on cytology or by biopsies. By cytological evaluation of pericardial fluid along with ancillary studies like immunohistochemistry on cellblock, a definite diagnosis of PCL can be achieved. Despite being a minimally invasive diagnostic technique, cases diagnosed on cytology [8-10] are fewer than those diagnosed on biopsy in the literature. [1-3] [7] We present a case of PCL which was diagnosed and subclassified on pericardial effusion cytology.

CASE HISTORY

A 73-year-old lady, presented with progressive dyspnoea on exertion for 6months. Her physical examination revealed irregular tachycardia, normal blood pressure, mild facial puffiness, bilateral infrascapular crepitation and muffled heart sounds. There was no lymphadenopathy or organomegaly. Electrocardiogram revealed atrial flutter with controlled ventricular rate and low

voltage complexes. Chest X-ray revealed globular enlargement of cardiac shadow with increased cardiothoracic ratio (Fig.1). Echocardiography revealed an intracardiac mass in right atrium with extension into the right ventricular wall along with moderate PE. There was no evidence of cardiac tamponade. Computed Tomography (CT) chest showed a lobulated mass predominantly involving the right atrium measuring 9.4 x 5.4cm, encasing right atrial appendage, right coronary artery and causing significant narrowing of distal SVC. The mass also involved right ventricular wall, root of aorta and right superior pulmonary vein. Lung parenchyma, tracheobronchial tree and pleura appeared normal. The patient was subsequently subjected to a pericardiocentesis. It showed elevated total counts and LDH levels, with negative cultures. Smears prepared from the centrifuged sample were of high cellularity showing monomorphic population of medium to large sized cells having scant cytoplasm and round nucleus with opened up chromatin. Cell block also showed cells with similar morphology, suggestive of large cell lymphoma. On immunohistochemistry (IHC), tumour cells were positive for LCA, CD20, MUM1 and BCL2 while negative for MPO, Tdt, Cyclin D1, bcl-6, c-myc with Ki67 of 90% (Fig 2). Morphological and immunohistochemical features were suggestive of Diffuse large B-cell lymphoma (DLBCL), activated B cell type.

Peripheral smear, bone marrow aspirate and biopsy evaluation showed no evidence of lymphoma. PET-MR showed metabolically active large diffusely infiltrative intracardiac mass lesion, suggestive of primary cardiac lymphoma or cardiac sarcoma. No other FDG avid lymph node or distant possible sites of primary were seen (Fig 3). In view of her advanced age and the risk of hemodynamic instability, she was not considered fit for chemotherapy and was given single fraction of palliative radiotherapy. The patient was clinically stable on discharge but was lost in follow up.

DISCUSSION

Criterias for making diagnosis of PCL are (i) Location of the tumour should be limited to the heart (ii) no previous history of lymphoma or primary nodal involvement (iii) not more than two extra-cardiac sites including lymph nodes or extra-nodal organs (iv) exclude if the tumour occurs in sites with abundant lymphoid tissue.[9]

An increase in incidence of PCL has been noted in recent times, especially in patients with immunodeficiency syndromes and organ transplants.[3] Our patient did not have any immunocompromised states. The clinical manifestations include dyspnoea, heart failure, PE, hemopericardium and cardiac arrhythmias. [1]

Diagnostic methods include chest X-ray, echocardiography, CT and magnetic resonance imaging. PCL most commonly occurs in the right atrium and right ventricle [1], with diffuse infiltration of myocardium and subsequent venous extension leading to superior or inferior venacaval obstruction. [7] Such involvement of SVC was seen in the present case. If the pericardium is involved, effusion or bleeding can occur which is followed by constrictive pericarditis and shock due to cardiac tamponade. Lymphatic obstruction is also hypothesized to be a dominant causal agent in development of pericardial effusion which seen in most of the cases. [6]

Angiosarcomas also preferentially involve the right side of heart and may manifest with PE, making radiological distinction from lymphoma difficult. However, central necrosis is more commonly seen in angiosarcoma, than lymphoma. [4]

Definite diagnosis is made on cytological evaluation of PE fluid or on tissue biopsy. [1] Primary cardiac lymphoma is a variant of Non-Hodgkin's lymphoma. More than 80% of PCLs are diffuse

large B-cell lymphomas as was seen in our case. [1] Other low and intermediate B-cell types have also been described [9].The cytological diagnosis of PCL on PE fluid can be obtained in about 67% cases, while diagnostic rate of biopsy by multiple approaches varies from 50-100%. [5] At times, it may be difficult to differentiate PCL from the benign reactive lymphocytosis without performing an immunocytochemical staining, cytogenetic studies or PCR techniques. [6] In our case, IHC was performed on cell block, to confirm as well as subclassify the lymphoma. Differential diagnoses include tumours involving heart like metastatic carcinoma, metastatic melanoma and angiosarcoma. [4] IHC helps in distinction between these neoplasms.

The treatment modalities include chemotherapy, radiotherapy and surgical excision. But the overall prognosis for PCL is generally poor. [1] [8] Even though surgery does not improves prognosis, tumour debulking may be an effective palliative measure in cases with obstructive symptoms. [6] With chemotherapy regimens, patients survive for about 4years whereas with only radiotherapy or surgery, survival is around 1year. [1]

CONCLUSION

PCL is a rare tumor with poor prognosis, where early diagnosis and treatment are important determinants of outcome. Cytology allows for diagnosis as well as subtyping of PCL by the least invasive technique. However, cases diagnosed on cytology are fewer than that on biopsy in published literature. Hence awareness among clinicians and pathologists that PCL can present with pericardial effusion and can be diagnosed accurately on cytology is important.

Statement of Ethics: Patient's details are not being disclosed, hence consent not required.

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FIGURE LEGEND

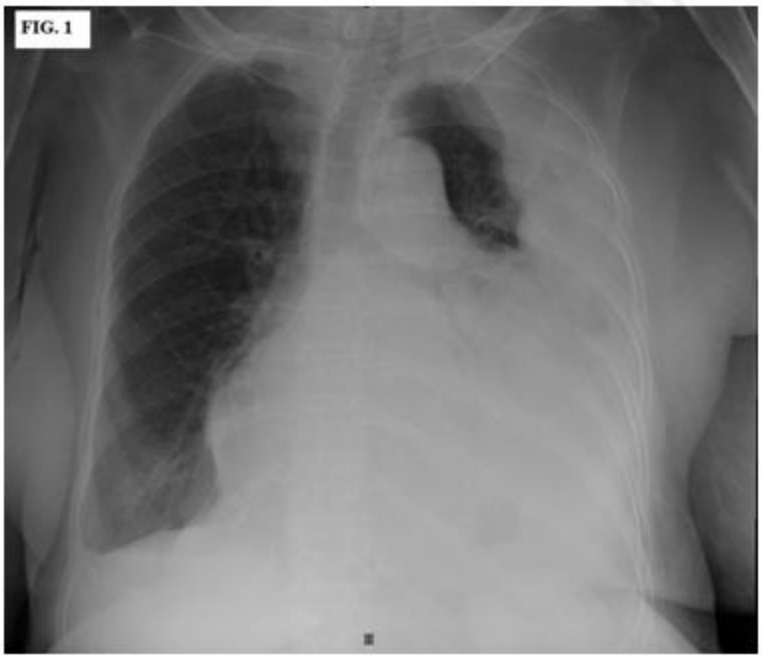

Fig. 1. Chest X-ray showing globular enlargement of cardiac shadow suggestive of pericardial effusion.

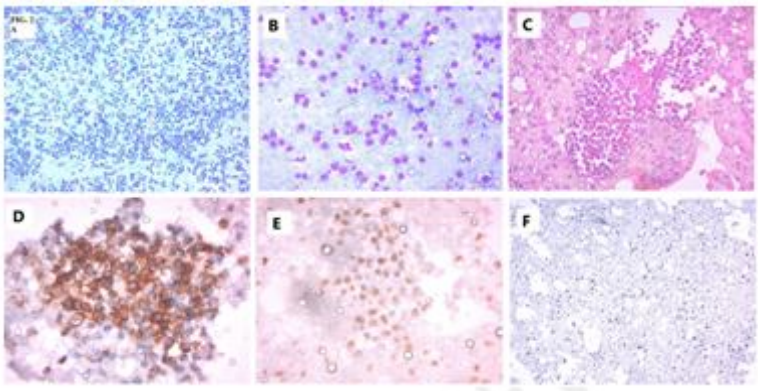

Fig. 2. (A). Highly cellular smears showing monomorphic population of medium sized atypical lymphoid cells **(MGG. 100X)**, (**B)** Individual cells have scant cytoplasm, round nucleus with opened up chromatin, a few showing convoluted nuclei **(MGG. 400X)**, **(C)** Cell block sections showing singly dispersed and aggregates of cells with high N: C ratio, irregular nuclear membrane and conspicuous nucleoli **(H & E. 400X)**. **(D), (E)** Tumour cells showing positivity for CD 20, and MUM 1 respectively **(IHC, 400x)** and **(F)** with a high Ki67 index of 90% **(IHC, 100x)**

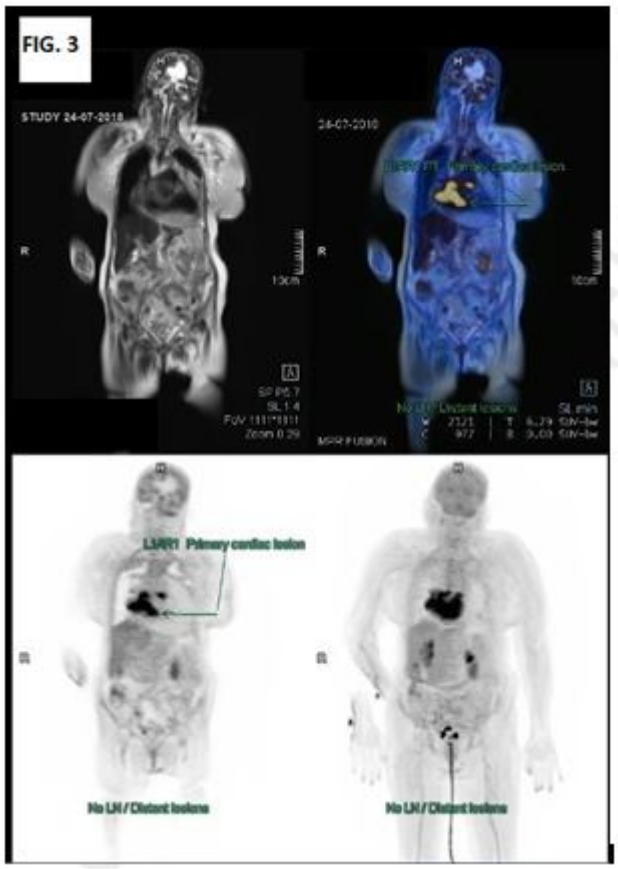

Fig. 3. PET MR showing a metabolically active intra-cardiac mass lesion predominantly involving the right atrium with no other FDG avid lymph node or distant possible sites of primary malignancy