1 Case report

2 # Primary cardiac lymphoma diagnosed and subtyped on pericardial fluid cytology

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5 ## ABSTRACT

6 Primary cardiac lymphoma (PCL) is a very rare malignancy, involving only the
7 heart/pericardium with no or minimal evidence of extra-cardiac involvement.
8 A 73-year-old lady presented with dyspnea on exertion. Echocardiography revealed a mass
9 predominantly involvingthe right atrium with moderate pericardial effusion. Pericardiocentesis
10 was done and the smears showed a monomorphic population of medium-sized atypical lymphoid
11 cells.Immunohistochemistry performed on the cellblock wassuggestive of Diffuse large B cell
12 lymphoma (DLBCL), activated B cell (ABC) type. PET-MR revealed a metabolically active
13 large diffusely infiltrative intracardiac mass lesion with no other distant possible sites of primary
14 malignancy or extracardiac deposits. Thus, a diagnosis of PCL was made. She underwent a
15 single fraction of palliative radiotherapy as she was unfit for definitive chemotherapy.
16 Cytological evaluation of pericardial fluid using cell block is a useful and effective tool in the
17 diagnosis as well as subtyping of PCL presenting as malignant effusion.

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

20 **Learning objective:**

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

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

28 **INTRODUCTION**

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

40 **CASE HISTORY**

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

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

61 Peripheral smear, bone marrow aspirate, and biopsy evaluation showed no evidence of
62 lymphoma. PET-MR showed metabolically active large diffusely infiltrative intracardiac mass
63 lesion, suggestive of primary cardiac lymphoma or cardiac sarcoma. No other FDG avid lymph
64 nodes or distant possible sites of primary were seen(Fig 3).In view of her advanced age and the
65 risk of hemodynamic instability during an extended treatment, she was not considered fit for
66 chemotherapy and was given only asingle fraction of palliative radiotherapy (5 Grays). The
67 patient was clinically stabilizedprior to discharge but was lost tofollow-up.

68 **DISCUSSION**

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

73 An increase in the incidence of PCL has been noted in recent times, especially inpatients with
74 immunodeficiency syndromes and organ transplants.[3]Our patient did not have any
75 immunocompromised states.The clinical manifestations include dyspnea, heart failure,
76 pulmonary embolism, hemopericardium, andcardiac arrhythmias. [1]

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

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

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

90 large B-cell lymphomas as was seen in our case.[1] Other low and intermediate B-cell types have
91 also been described [9].The cytological diagnosis of PCL onPE fluid can be obtained in about
92 67% of cases, while the diagnostic rate of biopsy by multiple approaches varies from 50-
93 100%.[5]At times, it may be difficult to differentiate PCL from benign reactive lymphocytosis
94 without performing immunocytochemical staining, cytogenetic studies, or PCR techniques.[6] In
95 our case, IHC was performed on the cell block, to confirm as well as subclassify the
96 lymphoma.Differential diagnoses include tumors involving the heart like metastatic carcinoma,
97 metastatic melanoma, and angiosarcoma.[4] IHC helps in the distinction between these
98 neoplasms.

99 The treatment modalities include chemotherapy, radiotherapy, and surgical excision. But the
100 overall prognosis for PCL is generally poor.[1][8] Even though surgery does not improve
101 prognosis, tumor debulking may be an effective palliative measure in cases with obstructive
102 symptoms.[6]With chemotherapy regimens, patients survive for about 4 years whereas, with
103 onlyradiotherapy or surgery, survival is around 1 year.[1][11]

104 **CONCLUSION**

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

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120 **Acknowledgments**: For their contribution to reporting the PET CT imaging

121 • Dr.Shanmuga Sundaram DRM, DNB, MNAS, FANMB, Department of Nuclear
122 Medicine and Molecular Imaging, Amrita Institute of Medical Sciences, Kochi
123 • Dr. Rajesh Kannan M.D, DNB, PDCC, Department of Radiology, Amrita institute of
124 Medical Sciences, Kochi

125 **Conflict of interest statement:** The authors have no conflict of interest to declare

126 **Author contributions:**

127 **Dr. Deepthi S Pillai** has contributed to theacquisition, interpretation of data, and drafting of the
128 manuscript**. Dr. Archana George Vallonthaiel**has made substantial contributions to the
129 conception and design of the work, drafting the manuscript. **Dr.Ajit Nambiar, Dr. K**
130 **Pavithran,** and **Dr. Praveen G Pai** have been involved in revising it critically for important
131 intellectual content and given final approval of the version to be published.

132 **Statement of Ethics:** The patient's details are not being disclosed, hence consent is not required.

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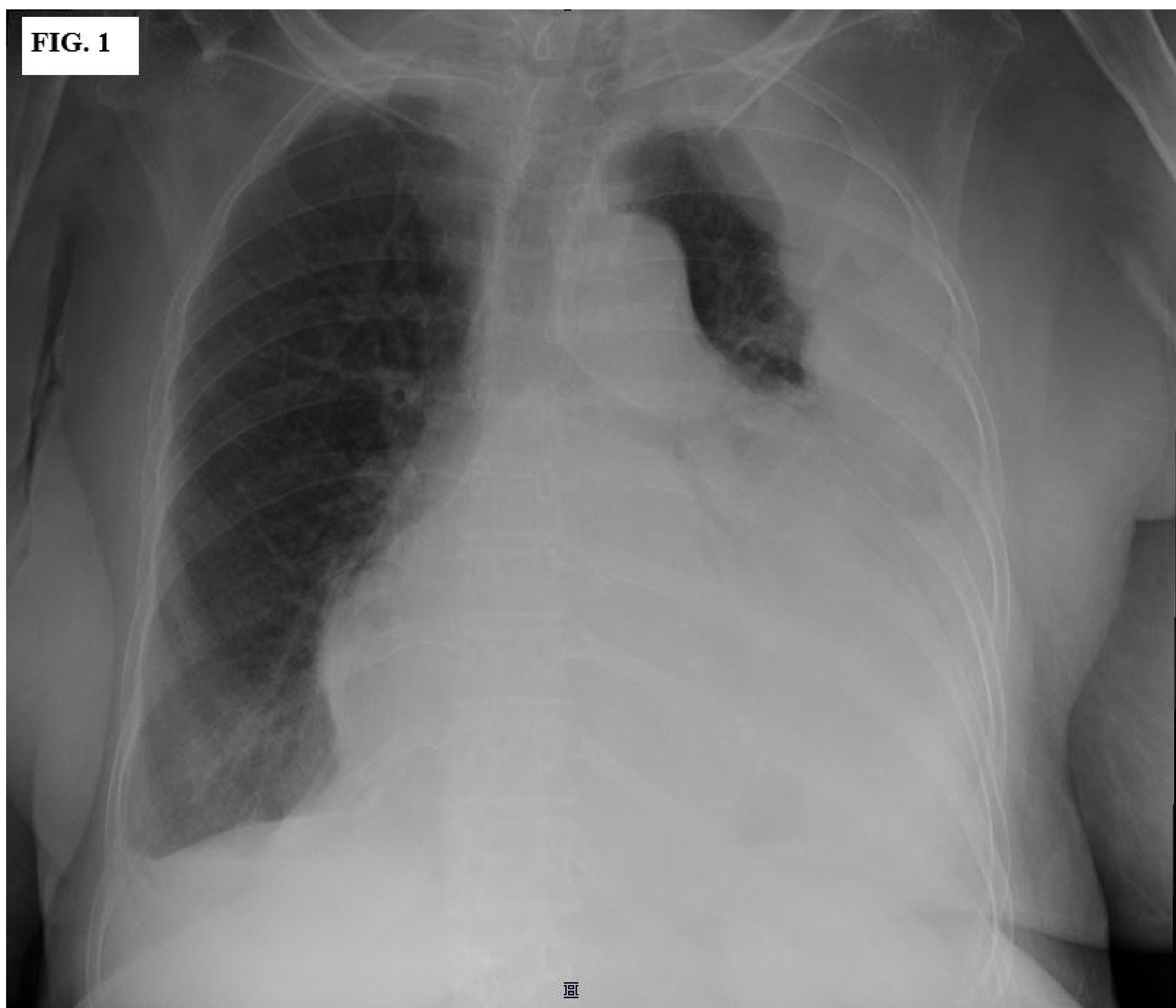
199 **FIGURE LEGEND**

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201 **Fig. 1.** Chest X-ray showingglobular enlargement of cardiac shadow suggestive of pericardial

202 effusion.

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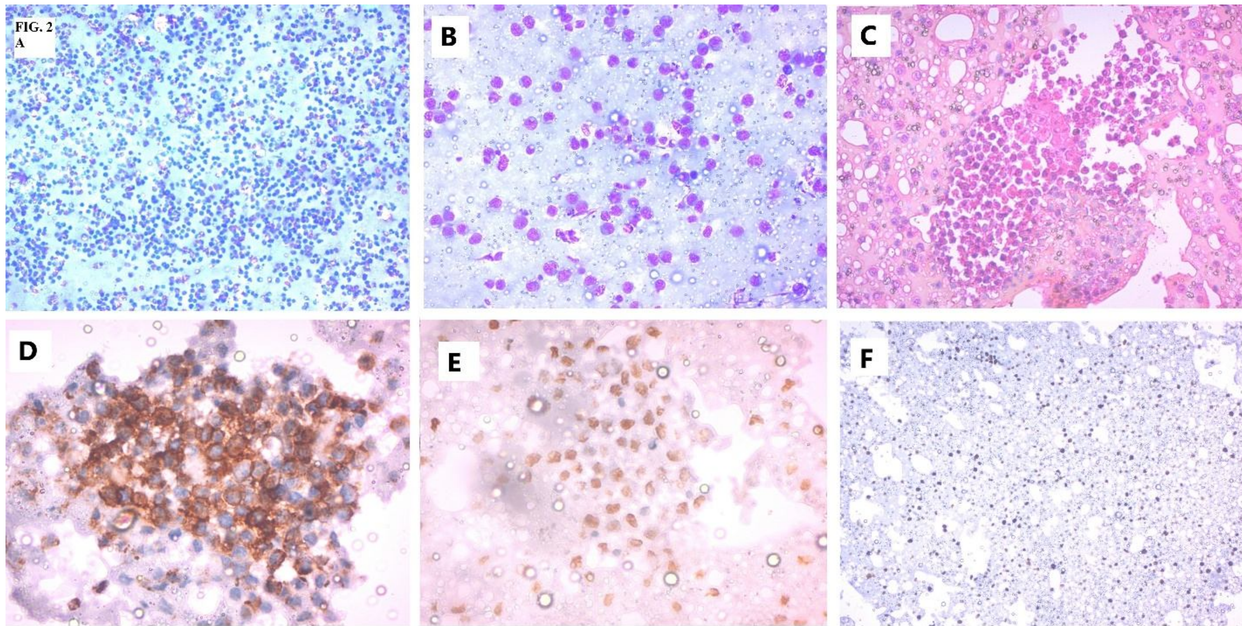


204 **Fig. 2. (A)**. Highly cellular smears showinga monomorphic population of medium-sized atypical
205 lymphoid cells **(MGG. 100X)**, **(B)** Individual cells have scant cytoplasm, round nucleus with
206 opened up chromatin, a few showing convoluted nuclei **(MGG. 400X)**, **(C)** Cell block sections
207 showing singly dispersed and aggregates of cells with high N: C ratio, irregular nuclear
208 membrane and conspicuous nucleoli **(H & E. 400X)**. **(D), (E)** Tumour cells showing positivity
209 for CD 20, and MUM 1 respectively **(IHC, 400x)**and **(F)** with a highKi67 index of 90% **(IHC,**
210 **100x)**

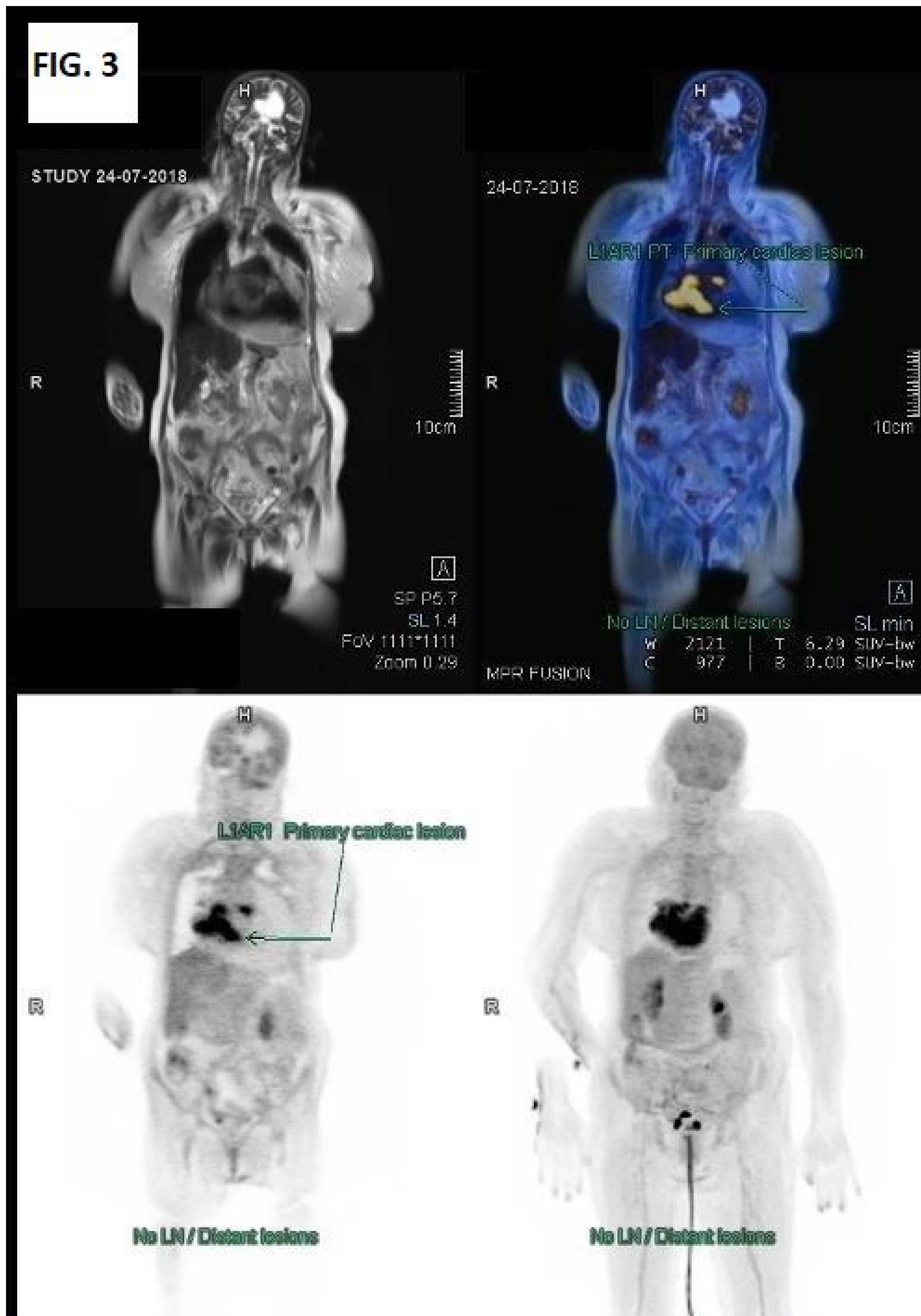


**Fig. 3.** PET MR showing ametabolically active intra-cardiac mass lesion predominantly involving the right atrium with no other FDG avid lymph node or distant possible sites of primary malignancy

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