

A Rare Case of Hodgkin's Lymphoma Presenting as Hypereosinophilia

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ABSTRACT

Although eosinophilia is a recognised associated feature of Hodgkin's Lymphoma, hypereosinophilia is seldom the presenting feature in the patient. Here, the authors report an unusual case of a 21-year-old male patient who presented to the General Medicine outpatient department of the hospital with a history of multiple episodes of left-sided pleural effusion in addition to mediastinal and cervical lymphadenopathy. Baseline investigations revealed hypereosinophilia which was persistent despite Diethylcarbamazine (DEC) and steroid therapy. Computer Tomography (CT) guided biopsy of an anterior mediastinal mass, likely to be thymus, led to the diagnosis of Hodgkin's Lymphoma. The patient was transferred to the Haematology department where he was started on Adriamycin, Bleomycin, Vinblastine and Dacarbazine (ABVD) chemotherapy regimen. Despite the fact that blood eosinophilia is an associated finding, it is rare for a patient to present with it. The authors also discuss the discrepancies related to the credibility of eosinophilia as a prognostic marker for Hodgkin's disease.

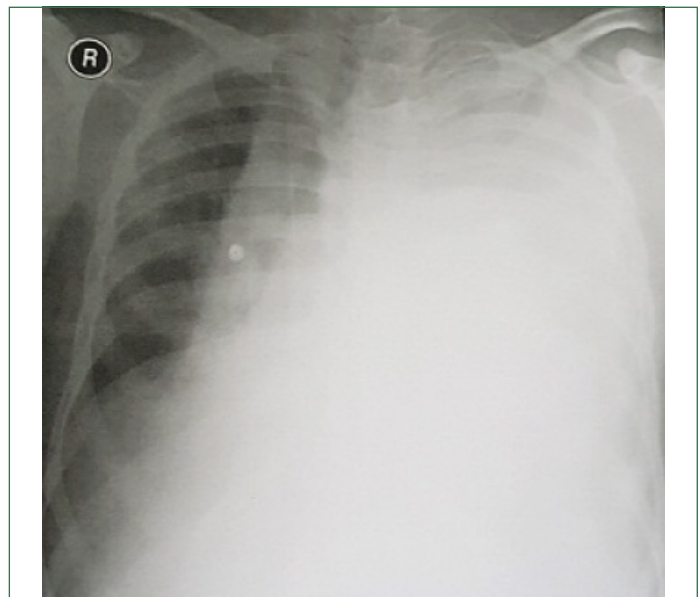
Keywords: Haematological malignancies, Lymphomas, Reed-Sternberg cells

CASE REPORT

A 21-year-old male farmer, with no known co-morbidities, presented to the General Medicine outpatient department of the hospital with complaints of breathlessness on exertion (grade 3) since the past six months. He had not experienced such episodes before. The exertion was associated with dry cough and left-sided pleuritic chest pain. This was preceded by multiple episodes of fever, with an evening rise, which was associated with loss of weight, but without history of haemoptysis. He was admitted at various hospitals for the same and diagnosed with left-sided pleural effusion. In spite of carrying out extensive investigations, the cause of the pleural effusion could not be ascertained. Multiple sessions of therapeutic thoracentesis had been performed over the past six months, with over one-litre fluid removed each time. Examination of pleural fluid revealed high protein and lymphocytic counts. However, tests for *Mycobacterium tuberculosis*, including GeneXpert, were found to be negative each time. The fluid cytology for malignant cells was also negative. The patient was empirically started on Anti-Tubercular Therapy five months ago, which he stopped after one month.

Chest X-ray revealed massive left-sided pleural effusion [Table/Fig-1]. The patient also underwent a Positron Emission Tomography (PET) scan two months prior to the present visit, which revealed hypermetabolic soft tissue in the collapsed left lung along with increased uptake in the mediastinal lymph nodes along with a right perivascular node mass [Table/Fig-2]. There were no other areas of increased uptake in the body. A biopsy done from the area of hypermetabolic soft tissue in the lung revealed only inflammatory cells on histopathological examination.

The patient had undergone a recent Intercostal Drainage tube (ICD) insertion, eight days prior to admission at our centre. At the time of admission, the patient had stable vitals, requiring supplemental oxygen by a face mask. On examination, he had decreased air entry on the left-side and the ICD column was

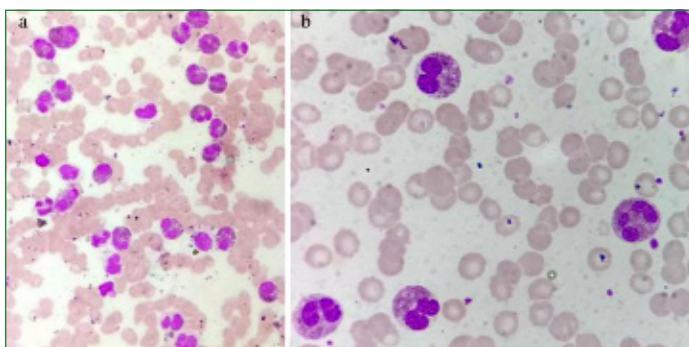


[Table/Fig-1]: X-ray chest (PA view) showing massive left-sided pleural effusion.



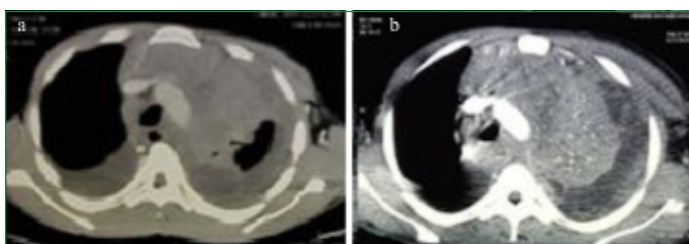
[Table/Fig-2]: PET scan of patient showing hypermetabolic soft tissue in the collapsed left lung, upper lobe measuring 10.2x5.1x10.5 cm (Standardised Uptake Value (SUV) : 8.65) abutting the mediastinal pleura. It also showed increased uptake in the mediastinal lymph nodes with a right perivascular node mass 6.7x3.7 cm in size (SUV: 6.5) along with bilateral cervical level 3-5 and upper abdominal lymph nodes- largest 1.9x1.3 cm (SUV: 1.96-8.39).

moving with respiration. There was no palpable lymphadenopathy. The fluid in the drainage bag was purulent. His baseline haematological investigations showed a Total Leucocyte Count (TLC) of 19,400/cmm with 83% eosinophils [Table/Fig-3]. The Absolute Eosinophil Count (AEC) was 16,102/mm³. Wet mount for microfilaria was negative. The pleural fluid was examined and it reported 5.15 gram of protein and showed 30 polymorphs and 480 lymphocytes. The next complete blood count report, on day 5, revealed a TLC of 31,000 with 94% eosinophils (AEC: 29,140). A haematology reference was ordered in view of the persistent eosinophilia and a bone marrow biopsy was done. The bone marrow biopsy showed 27% eosinophils with normocellular marrow. There were no atypical cells. The patient developed fever and was started on broad spectrum antibiotics for secondary bacterial infection and a 28 day course of DEC. The patient was also started on prednisolone 1 mg/kg/day for hypereosinophilia. The TLC (11,800) and fever settled but the eosinophilia (81%) and AEC (9,558) remained high.



[Table/Fig-3]: Photomicrograph of the patient's peripheral blood smear stained with Wright-Giemsa stain (a - 40x and b - 100x, oil) revealing numerous eosinophils (leucocytes with coarse orange-red cytoplasmic granules and a bilobed nucleus) with Total Leucocyte Count (TLC) of 19,400/cmm with 83% eosinophils (hypereosinophilia).

Further, a CT scan was performed which showed soft tissue density in the anterior mediastinum, with minimal postcontrast enhancement, likely to be an enlarged thymus [Table/Fig-4]. Also, multiple lymph nodes were seen in the pretracheal, paratracheal, prevascular, subcarinal and bilateral hilar regions. A trans-sternal CT-guided biopsy of the anterior mediastinum was done and the histopathology revealed classical Hodgkin's Lymphoma with Reed-Sternberg cells. The immunohistochemistry showed CD 30 positivity. The patient was diagnosed with Hodgkin's lymphoma (stage 3E) and transferred to the Haematology department, where he was started on Adriamycin, Bleomycin, Vinblastine and Dacarbazine (ABVD) chemotherapy regimen.



[Table/Fig-4]: CT scan (Axial images both pre and postcontrast) showing increased soft tissue density in the anterior mediastinum, with minimal postcontrast enhancement, likely to be an enlarged thymus.

DISCUSSION

Hypereosinophilia is defined as an eosinophil count greater than 1,500 cells per microlitre for 6 months with or without end organ damage [1]. The causes for increased eosinophil count

include allergic causes (asthma, atopy, drug reactions etc.), infectious causes (helminth, ectoparasites, endoparasites, fungi etc.), neoplastic disorders, eosinophilic disorders (idiopathic eosinophilia, gastrointestinal disorder related eosinophilia etc.) and other miscellaneous causes (radiation, cholesterol emboli, hypoadrenalism etc.). Neoplastic causes include acute or chronic eosinophilic leukaemia, other myeloid neoplasms and lymphoid malignancies [1].

Eosinophilia is reported in 15% of Hodgkin's Lymphoma patients [2]. However, the exact mechanism for the same is unknown. The postulated theories include production of IL5 and GM-CSF by the Reed-Sternberg cells and this leads to increased production of eosinophils by the bone marrow. The interaction between eosinophils and Reed-Sternberg cells has been studied and it is postulated that eosinophils provide cellular ligands for TNF-superfamily receptors (CD40, CD30, CD95/Fas) and are able to transduce proliferation and anti-apoptotic signals at the surface of Hodgkin Reed-Sternberg cells [3].

Whether eosinophilia serves as a prognostic marker for Hodgkin's Lymphoma, has been a matter of debate. A few studies have found no significant differences as regards to disease stage, general symptoms and gender in relation to tissue eosinophilia and mast cell infiltration and thus, no prognostic value of the same [4-6]. A study has shown blood eosinophilia to be a positive prognostic indicator in some of the subsets of patients with Hodgkin's lymphoma [7]. Another study by Axdorph U et al., reported increased eosinophilic infiltration in patients having bulky tumours and guarded prognosis [8]. A study by von Wasielewski R et al., found lymph node eosinophilia to be prognostic, especially in Nodular Sclerosis type of Hodgkin's Lymphoma and it also proved to be a negative prognostic indicator for survival and successful treatment [9].

CONCLUSION(S)

Persistent eosinophilia may be a clue to an underlying haematological malignancies, either an associated finding or a presenting feature. If hypereosinophilia is resistant to steroids then it raises the suspicion of underlying haematological malignancy. A high index of suspicion would help us in early diagnosis and prompt treatment with improved clinical outcomes.

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