Case Report

Coexistant extramedullary hematopoiesisin lymph node and non-hodgkin lymphoma with leukemic spill: A rare case report

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ABSTRACT

Extramedullary hematopoiesis (EMH) commonly occurs in the liver and spleen. Non-hepatosplenic EMH in a lymphnode is rare and with co-existing non-Hodgkin lymphoma is even rarer. Careful screening of cytological slides is a must in order not to miss such rare cases of non-hepatosplenic EMH in lymphnodes. We hereby report a rare case of a 75-year-old male with coexisting lymphnode EMH and NHL, that too with the leukemic spill, which has never been reported before.

Keywords: *Extramedullary, Hematopoiesis, Lymphnode, Megakaryocytes, Non Hodgkin lymphoma.*

Extramedullary hematopoiesis (EMH) is defined as the production of hematopoietic cells outside the bone marrow due to either bone marrow destruction or bone marrow infiltration [1,2]. As is known, physiologic EMH occurs in fetal life, mainly in liver and spleen [3]. The scenario is nearly the same in postnatal life, as most common sites for EMH in adults remain liver and spleen. However, differing from physiologic EMH, non-hepatosplenic EMH does occur in adult life at many other sites also.

Non-hepatosplenic EMH in a lymphnode with coexistent non-Hodgkin lymphoma in the same lymphnode is rare. This rare coexistence of the beforesaid entities, coupled with the leukemic spill of the non-Hodgkin lymphoma has never been described before. We, hereby, for the first time in the literature, report this rare case of coexistent EMH and non-Hodgkin lymphoma with the leukemic spill.

CASE REPORT

A 75-year-old male presented to the emergency department with a complaint of acute onset shortness of breath and cough. The patient was a known case of a chronic obstructive pulmonary disease diagnosed for two years and was on regular treatment. High resolution computed tomography (CT) scan of chest done one month back revealed sub-segmental collapse in the right middle lobe and the left inferior lingular segment with bilateral cervical, axillary and mediastinal lymphadenopathy.

On examination, the vitals were stable with blood pressure 110/70 mm Hg,pulse rate 110/min and temperature 98 degrees Fahrenheit. The patient was maintaining a low spO2 of 88%. On general physical examination, chest auscultation revealed bilateral rhonchi. There was no hepatosplenomegaly on abdominal examination. Rest central nervous system and cardiovascular system were within normal limits. Significant non-tender, discrete, firm lymph node enlargement was noted in bilateral cervical (1.5-2cm) and axillary regions (2-2.5 cm).

A routine complete blood count showed leucocytosis (86000/microlitre), with the presence of 86% atypical lymphoid cells, many of which showed nuclear clefting. Few of the cells showed opened up chromatin with prominent nucleolus (Fig. 1a). A subsequent bone marrow aspirate was performed, which despite being hemodilute revealed predominance of atypical lymphoid cells with similar morphology as seen in peripheral smear (Fig. 1b). The bone marrow aspirate also had a paucity of myeloid and erythroid cells and megakaryocytes were absent.

Flow cytometric immunophenotyping performed on peripheral blood revealed a lymphoid cluster constituting 88% of all events. These were CD19+, dim CD5+, bright CD 20+ and showed kappa chain restriction (Fig. 2 a,b,c,d). These were negative for CD34, CD 23, CD10, CD 200, CD 43, CD 25, CD 123, CD 103 and CD 11c. Flow cytometry study confirmed the diagnosis of B cell chronic lymphoproliferative neoplasm (likely Mantle cell lymphoma) with a spill in peripheral blood.

Simultaneously, fine needle aspiration cytology (FNAC) done from enlarged left cervical lymphnode swelling also revealed features of non-Hodgkin lymphoma. Smears showed a predominance of intermediate-sized atypical lymphoid cells having scant to moderate amount of cytoplasm, granular chromatin and few with cleaved nuclei (Fig. 1c). In addition, careful screening of FNAC smears revealed the presence of few megakaryocytes and very few myelocytes and nucleated

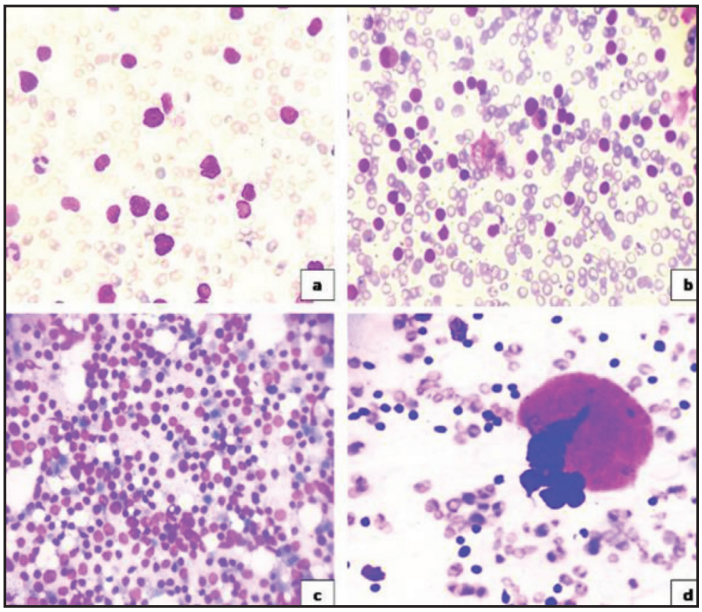

Figure 1: (a)Peripheral smear showing atypical lymphoid cells with nuclear indentation, (Giemsa, 400x); (b)Hemodiluted bone marrow aspirate smear showing predominance of atypical lymphoid cells, (Giemsa, 100x); (c)FNAC smear from lymphnode showing preponderance of atypical lymphoid cells admixed with few mature lymphoid cells and lymphoglandular bodies, (Giemsa, 100x); (d)FNAC smear from lymphnode showing multilobated megakaryocyte, (Giemsa, 100x)

RBC's indicating EMH (Fig 1d). However, the patient could not be started on therapy as he succumbed to his respiratory illness.

DISCUSSION

Non-hepatosplenic EMH is a rare entity. The rarity was highlighted in a retrospective study by Koch *et al* [3] , wherein over a span of 27 years (from 1975 to 2002), 510 patients were found to have EMH, out of which only twenty-seven patients (5.3%) had non-hepatosplenic EMH. Non-hepatosplenic EMH has been reported at numerous sites involving almost each and every organ from head to toe, namely central and peripheral nervous system; ear; pharynx; gastrointestinal tract; endocrine organs like adrenal; mediastinum; lungs; heart; peritoneum; genitourinary system like kidney, prostate etc [3].

The etiology of non-hepatosplenic extramedullary hematopoiesis is varied. Most common are haematological causes of which myelofibrosis with myeloid metaplasia is the commonest [1]. Other haematological causes include red blood cell disorders like thalassemia, hereditary spherocytosis etc; myeloproliferative disorders like polycythemiavera, chronic myeloid leukemia; platelet disorders like immune thrombocytopenic purpura; myelodysplastic syndromes etc [3]. On reviewing the English literature, we could find only two case reports of coexistent leukemia and extramedullary hematopoiesis in lymphnode [2,4]. Also, there was only a single case report of coexistent non-Hodgkin lymphoma and extramedullary hematopoiesis in the same lymphnode [1]. However, there is no case report of

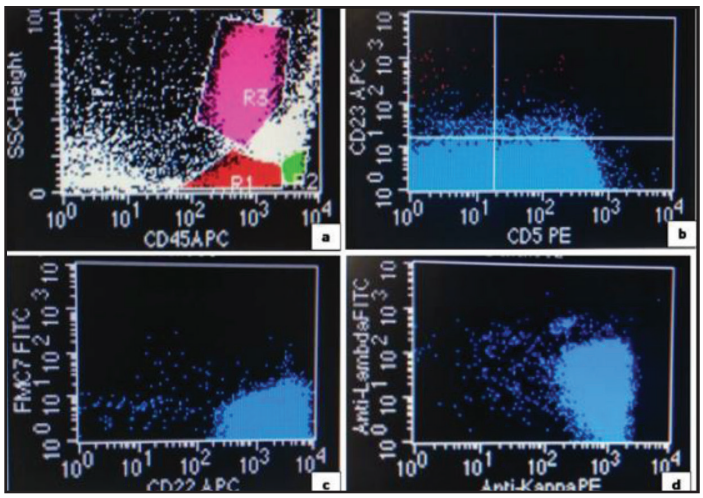

Figure 2: Flow cytometry showing (a)abnormal lymphoid cluster (R1) on side scatter vs CD 45 analysis; (b)on gating R1, the abnormal cluster shows heterogenous positivity for CD 5 and negativity for CD 23; (c) abnormal lymphoid cluster shows positivity for CD 22; (d) abnormal cluster exhibiting kappa restriction

coexistent non-Hodgkin lymphoma with the leukemic spill and extramedullary hematopoiesis in the same lymphnode which was seen in the index case.

Our case highlights the importance of careful screening of cytological smears in order not to miss coexistent EMH in a case of non-Hodgkin lymphoma. The differential diagnosis in such a case varies depending on the predominant cell lineage present. If trilineage hematopoiesis is seen, diagnosis is straightforward. In cases with a large number of mature granulocytic cells, an infectious process comes into the differential. The presence of erythroid and megakaryocytes will help in such cases [1,5]. Megakaryocytes can be mistaken for multinucleated histiocytes of a granulomatous process [1,6]. However, one should keep in mind that megakaryocytes are usually multilobated and not multinucleated. Again, the presence of other lineage cells will help.

Malignant neoplasms, including granulocytic sarcoma, lymphoma, and poorly differentiated carcinoma, also should be considered in the differential diagnosis [1,7]. Erythroid and megakaryocytic cells are absent in granulocytic sarcoma, with the presence of predominantly immature blast-like cells. Immature myeloid forms and atypical megakaryocytes can be mistaken for Reed Sternberg cells in Hodgkin lymphoma [4]. However, these lack the prominent inclusion like nucleolus seen in Reed Sternberg cells as well as lack the typical inflammatory background of Hodgkin lymphoma. Bizarre megakaryocytes can be mistaken for atypical cells of an undifferentiated malignancy. However, these lack hyperchromasia and pleomorphism typical of undifferentiated malignancy [4].

EMH occurs broadly due to overproduction of hematopoietic cells (Myeloproliferative disorders) or replacement of bone marrow by tumor, fibrosis, metastasis, storage disorders etc. Two theories have been proposed to explain the pathogenesis of EMH: (a) EMH in fetal sites is due to due to myelostimulatory factor

which switches on dormant hematopoietic cells in fetal organs like liver, spleen. (b) EMH in non-fetal sites occurs because of secondary involvement due to an abnormality in bone marrow stroma leading to intravascular hematopoiesis and subsequent filtration in various organs (Filtration theory) [3,8,9]. However, the first theory does not explain extramedullary hematopoiesis in non-fetal sites and second theory does not explain extramedullary hematopoiesis in organs which do not filter. So, Koch *et al* [3] proposed a new theory "redirected differentiation theory" according to which a circulating factor causes differentiation of adult stem cells into cells of hematopoietic lineage leading to hematopoiesis.

Antemortem diagnosis of EMH can be made with the help of tissue biopsy, FNAC or radionuclide scanning. Treatment of EMH involves the use of low dose radiotherapy as dividing marrow cells are highly radiosensitive [3]. Treatment of Non-Hodgkin lymphoma with or without the leukemic spill involves use of specific chemotherapy. Hence diagnosing coexistent EMH in a case of Non-Hodgkin lymphoma is of therapeutic importance.

CONCLUSION

To the best of our knowledge, the index case is the first in English literature to report coexistence of non-Hodgkin lymphoma and EMH in the same lymphnode with the leukemic spill. Also, it highlights the importance of careful screening of cytological smears in order not to miss such a rare diagnosis, which will have an impact on treatment.

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