

Myeloid Sarcoma in Lymph Node: An Uncommon Presentation in Case of Chronic Myeloid Leukemia

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ABSTRACT

Hematological malignancies may manifest as extramedullary soft tissue masses causing significant diagnostic and therapeutic dilemma. We herein report a case of 25-year-old male who presented with pain abdomen and lymphadenopathy, with no previous history of any haematological abnormality. A lymph node excision biopsy was conducted with simultaneous haematological work up. The case was finally diagnosed as extramedullary myeloid sarcoma in lymph node in newly detected case of CML in chronic phase.

Myeloid sarcomas (MS), may occur in isolation, or more commonly in patients with a history of myeloid malignancy. MS is an uncommon condition and exact mechanism of occurrence is unclear. It should be considered in the differential diagnosis of any atypical cellular infiltrate at any site. In all cases a thorough, diagnostic work-up including genetic profiling is important to stratify risk and guide treatment strategies.

Keywords: Chronic Myeloid Leukemia, Lymph node, Myeloid Sarcoma

INTRODUCTION

Extramedullary soft tissue masses known as myeloid sarcomas (MS) can develop in isolation or more frequently in people with myeloid neoplasms, particularly acute myeloid leukemia (AML).^[1] Males are more likely to experience it than females (M:F 1.2:1), and it typically affects elderly people (median age 56 years).^[2] The skin (26%), lymph node (15%), testis (6%), and gut (6%), are the most frequently affected anatomic locations. Additionally, it could affect the biliary tract (3%), CNS (3%), and bone (3%).^[3] It can be quite difficult to diagnose MS clinically and pathologically. Any unusual cellular infiltration, wherever, especially but not primarily where there has been a history of myeloid neoplasia, should raise the possibility of MS.^[1] We herein discussing a case who presented for the first

time with pain abdomen later on diagnosed having CML.

CASE REPORT

A 25-year-old male, with no previous history of any haematological abnormality presented with pain abdomen which was sudden in onset, severe in intensity and radiate toward back since last 20 days which relied on medication. There was no history of fever, headache or any chronic illness. He was non-alcoholic and non-smoker.

On general physical examination revealed enlarged cervical and inguinal lymph nodes. Per abdomen examination revealed splenomegaly 7 cm below costal margin. Ultrasonography shows enlarged spleen along with partially distended gallbladder and multiple enlarged hypoechoic lymph nodes in bilateral cervical, axillary and

inguinal region, most of them have maintained fatty hilum. A lymph node excision biopsy was conducted with simultaneous haematological work up.

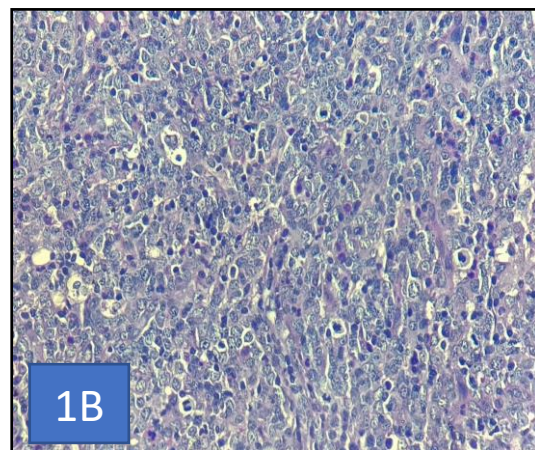
His complete blood count revealed haemoglobin 10.4 gm/dl, total leucocyte count $61 \times 10^9/L$, platelet count $430 \times 10^9/L$ with predominance of myeloid precursors 09% myelocytes 11% metamyelocytes 02% promyelocytes and 1% blast.

Microscopic evaluation of excised inguinal lymph node revealed effacement of lymph node architecture by intermediate size atypical cell having high N:C ratio, vesicular nuclear chromatin and scant cytoplasm. 1-2 mitosis/HPF was also seen. [Figure 1A & 1B] On immunohistochemistry these cells were positive for CD34, MPO, CD117 and negative for CD19, CD3 and

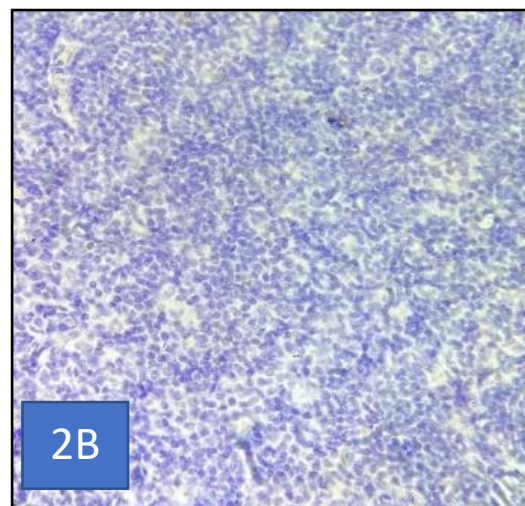
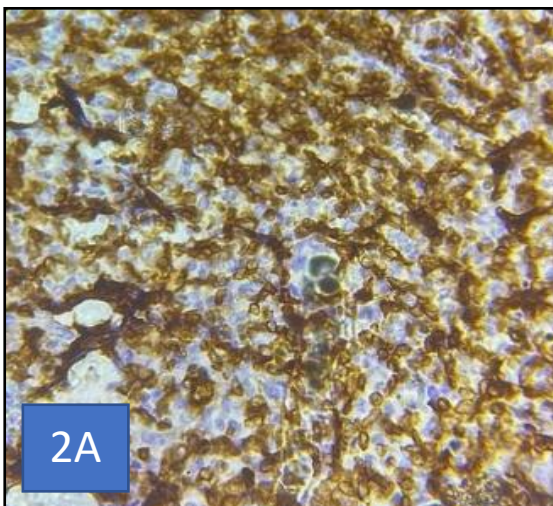
CD5. [Figure 2A, 2B, 2C & 2D] Histological findings are suggestive of MPO positive chloroma.

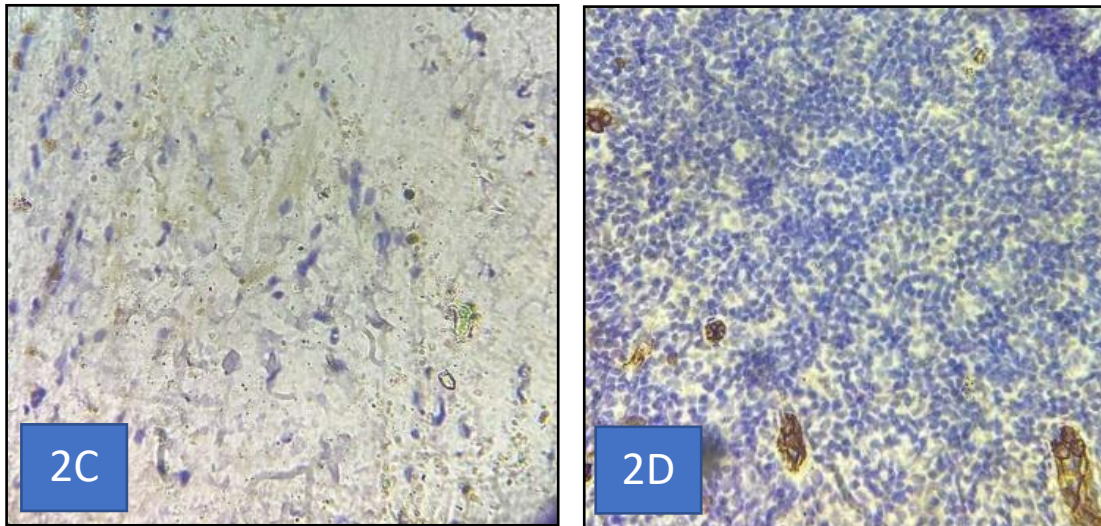
Bone marrow examination showed hypercellular marrow with increased myeloid: erythroid ratio and prominence of myeloid precursors with blast constituting 3%. Megakaryocytes were increased although normal in morphology. [Figure 3A & 3B] Based on these findings diagnosis of chronic myeloproliferative neoplasm was given. Cytogenetic evaluation confirmed t(9:22) favouring the diagnosis of Chronic Myeloid Leukemia; Chronic phase.

On correlation with haematological findings final diagnosis of extramedullary myeloid sarcoma in lymph node in freshly detected case of CML in chronic phase was made. Patient is now on tyrosine kinase inhibitor (imatinib) and responding.

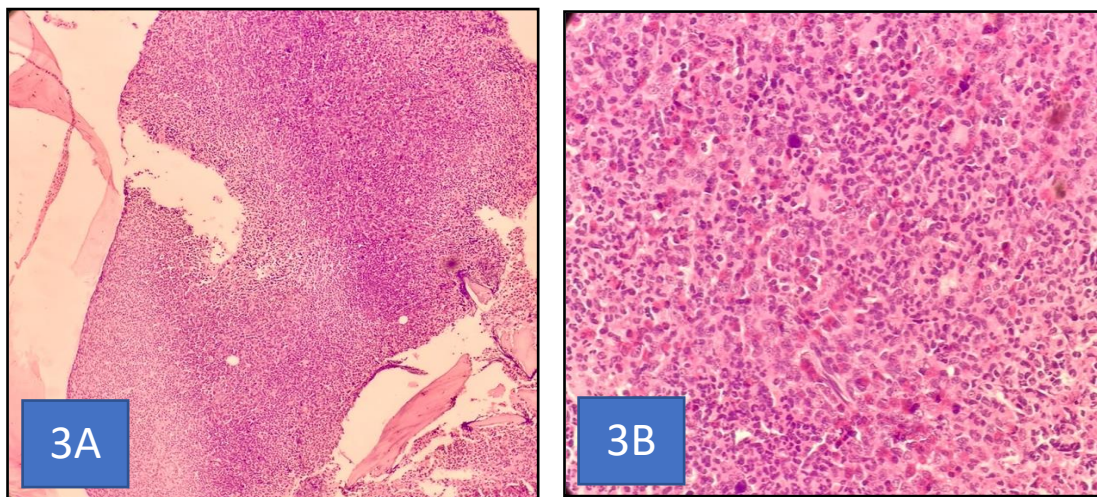


(H&E stain) Fig 1A & 1B biopsy shows effacement of lymph node architecture by atypical cell which on immunohistochemistry proved to be immature myeloid cells. (100X, 400X)





(IHC) Fig 2A, 2B, 2C & 2D immunohistochemistry proved to be immature myeloid cells these cells are MPO positive, CD3, CD117, CD20 negative



(H&E stain) Fig 3A & 3B Bone marrow biopsy revealed hypercellular marrow with prominence of myeloid precursors (100X, 400X)

DISCUSSION

MS is a neoplasm of immature granulocytes, monocytes, or both involving any extramedullary site. Chloroma, Granulocytic Sarcoma, Myeloblastoma, and Extramedullary Leukemia are other names for it. Because of its high MPO concentration and its greenish tint (Chloros = Green in Greek), the word "Chloroma" was first used historically.^[3]

According to the 2016 World Health Organization (WHO) classification, a myeloid sarcoma is a tumour mass consisting of myeloid blasts, with or without maturation, occurring at an anatomical site other than the bone marrow. Infiltration of any site of the body by myeloid blasts in a patient with leukemia is not classified as

myeloid sarcoma unless it presents with tumour masses in which the tissue architecture is effaced.^[2]

The exact mechanism of occurrence of MS is unclear. Most of the cases occur as de novo neoplasms, however some may be therapy-related. The incidence of MS appears to be rising with up to 9% in patients with acute or chronic myeloid leukemia. The reason may be presence of another homing signal that allows the blast cells to re-localize to secondary sites following allogeneic hematopoietic stem cell transplantation or therapy with novel targeted agents including small molecule inhibitors, histone deacetylase inhibitors, DNA methyltransferase inhibitors, and nucleoside analogues.^[1,3]

The incidence of EM blast crisis in the newly diagnosed patients is extremely rare. EM blast crisis almost always followed by hematological blast crisis within few months, therefore it is to be considered as the earliest sign, or pathognomonic for, blast crisis in the bone marrow.^[4]

Although it is possible for MS to exist before a CML diagnosis in some circumstances, MS development and progression are mainly caused by the advancement of CML. Therefore, if remission is not attained by treatment, the diagnosis of MS may signal disease progression towards its terminal stages. Prior to the onset of CML in our patient's chronic phase, where CML's hematological development had not yet begun, MS was also identified.^[5]

The literature and isolated case reports mentioned lymph node involvement in MS in cases of CML as an unusual clinical site. However, very few of them had MS as a presenting feature leading to the diagnosis of CML as in our case. Out of which only Ai et al^[6] reported a case which have a presented as lymphadenopathy in case of CML.^[3]

Bangerter et al^[7], Paydas et al^[8] and Jadhav et al^[3] reported MS in patients with CML in one, 11 and one cases respectively out of 26, 32 and 4 cases with MS. Chen et al^[9], in their study of 307 patients diagnosed with CML, reported 42 cases with MS. Dhar et al^[10], also described a case where a female patient presented with prolonged febrile illness with generalized lymphadenopathy who on extensive workup turned out to be MS as a first presentation of CML in blast crisis.

Symptoms typically result from tumour mass effect or local organ dysfunction and clinical presentation is based on tumor location. MS is typically diagnosed using a combination of clinical characteristics, radiological examinations, and tissue biopsies.

Non-Hodgkin lymphoma (NHL), small round cell tumours (neuroblastoma, rhabdomyosarcoma, Ewing sarcoma/PNET,

and medulloblastoma), and undifferentiated carcinoma are among the conditions that MS is frequently mistaken for. Infiltrating myeloid cells at various stages of maturation that exhibit either granulocytic or monocytic maturation, similar to that seen in AML, are frequently seen in histological sections. When cytochemistry and immunohistochemistry are not used, the diagnosis is missed in about 50% of cases.^[11] It has been demonstrated that using molecular methods such as fluorescence in situ hybridization and flow cytometry can improve diagnostic precision.

Age, sex, anatomical site(s) involved or the mode of presentation do not appear to have any effect on clinical behavior and therapeutic response in MS cases. Treatment options include chemotherapy regimens, allogeneic or autologous bone marrow transplants, surgical excision in cases where patients require quick symptom relief or debulking, and targeted therapies specific to the tumour's site.^[4,5] Only a few thorough studies have been conducted on myeloid sarcoma, which is indicative of both the disease's rarity and the challenges associated with its management. More than 2000 case reports about the disease have been indexed in PubMed.^[2]

CONCLUSION

It can be difficult to make the right MS diagnosis, which calls for a high degree of suspicion and use of auxiliary methods. The differential diagnosis of any atypical cellular infiltrate at any site, with or without involvement of the bone marrow, should take this rare disease into account. The management of MS can be greatly improved by early diagnosis in the era of targeted therapy and sophisticated risk stratification. This increases patient survival. Large prospective clinical trials are required to more accurately determine the best treatment approach for this condition.

Declaration by Authors

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