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Title : **Myeloid Sarcoma – A Masquerade**

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Myeloid Sarcoma – A Masquerade

Abstract:

Myeloid sarcoma (MS), is a tumor mass of myeloblasts or immature myeloid cells occurring at a site other than the bone marrow. MS may either occur de novo, precede or coincide with acute myeloid leukemia (AML) and its presentation as the initial manifestation is rare. We present a series of six cases of myeloid sarcoma in an age group ranging from 15 to 62 years, involving paraspinal area, lymph node, ileum and appendix. Three cases had a prior diagnosis of AML and in the rest, a diagnosis of myeloid sarcoma preceded further investigations which did not reveal any other site of involvement. The diagnosis of myeloid sarcoma is important especially in patients who do not have associated hematologic abnormalities at presentation. Immunohistochemistry is an invaluable tool that assists in arriving at a correct diagnosis. The diagnosis of myeloid sarcoma can be challenging due to its varied clinical presentations and should be kept in mind as a differential diagnosis.

Key words: extramedullary, immunohistochemistry, myeloid sarcoma

Introduction:

Myeloid sarcoma (MS) is defined as a tumor mass of myeloblasts or immature myeloid cells occurring at a site other than bone marrow. First described by Burns^[1] in 1811, it was later also termed chloroma by King^[2] because of its green appearance on gross morphology owing to myeloperoxidase enzymes in the myeloblasts. These tumors are also known as granulocytic sarcomas, myeloblastoma or myelocytoma. Though the tumor may arise at any site, commonly involved sites are skin, lymph nodes, gastrointestinal tract, bone, soft tissue and testis.^{[3][4]} Other rare sites include heart, spinal cord and liver.^[5,6-9] The diagnosis of myeloid sarcoma can be challenging due to its varied clinical presentations and overlap with other lymphoid malignancies with respect to cytomorphology, cytochemistry and cytogenetic findings. Immunohistochemistry can assist in the proper diagnosis and thereby guide the treatment protocol which includes chemotherapy and bone marrow transplantation.

Case Series:

The present study at our institute included 6 cases over a period of six years. A review of case records, histopathology and immunohistochemistry was done correlating with the available bone marrow aspirates. Immunohistochemistry was done with the polymer technology method using prediluted primary antibodies from Dako and Envision Secondary kit (Dako; Carpinteria, CA). Follow up data of the patients were retrieved.

Results:

Of the six cases included in the study, the male to female ratio was 5:1. The age ranged from 15 to 62 years, (median age = 33). The location of the lesion at presentation in these cases was paraspinal area, lymph node, ileum and appendix. The commonest presenting symptom was localized swelling in accordance with the site. Three cases had a

prior diagnosis of AML and in the other three, a diagnosis of myeloid sarcoma lead to further investigations which did not reveal any other sites of involvement. In five of these cases, immunohistochemistry was performed for confirmation. The details of the cases are summarized in Table 1.

Table 1: Details of all the 6 cases of myeloid sarcoma

Case No.	AGE(in yrs)	SEX	SITE	BM/PS FINDINGS	POSITIVE MARKERS	NEGATIVE MARKERS	FINAL DIAGNOSIS
1	15	M	Paraspinal Region	No prior diagnosis of AML at presentation	MPO , LCA , CD99 , Vimentin	CK, Myogenin , CD79a , CD138 , ALK , CD20 , CD3 , CD5 , CD30 , TdT	Myeloid sarcoma
2	16	F	Appendix	Diagnosed case of AML	MPO	-	Myeloid sarcoma
3	24	F	Cervical LN	Diagnosed case of AML	MPO ,LCA,CD31 , CD61	CD20, CD3, CD34	Myeloid sarcoma with megakaryoblastic differentiation
4	38	F	Cervical LN	No prior diagnosis of AML at presentation	MPO , CD117 , CD34 , Bcl- 2 , TdT , CD68	CD20, CD79a, CD3, CD5, CD10, CD23.	Myeloid sarcoma
5	45	F	Ileum	No prior diagnosis of AML at presentation	MPO ,LCA , CD117 ,TdT , CD34 , Bcl – 2	CD20, CD5, CD56, Cyclin D1, CD10, CD23, ALK, CK, Cd1a	Myeloid sarcoma
6	62	F	Cervical LN	Diagnosed case of AML	MPO , CD117 , CD3 , CD5 , CD8 , CD4 , CD7	CD20, CD15, PAX5, CD23 , CD10	Myeloid sarcoma

Pathologic Findings:

All Cases showed diffuse infiltration of mononuclear cells effacing the architecture of the underlying tissue. The cells showed scant cytoplasm, round nuclei, fine nuclear chromatin and prominent nucleoli. (Figure1)

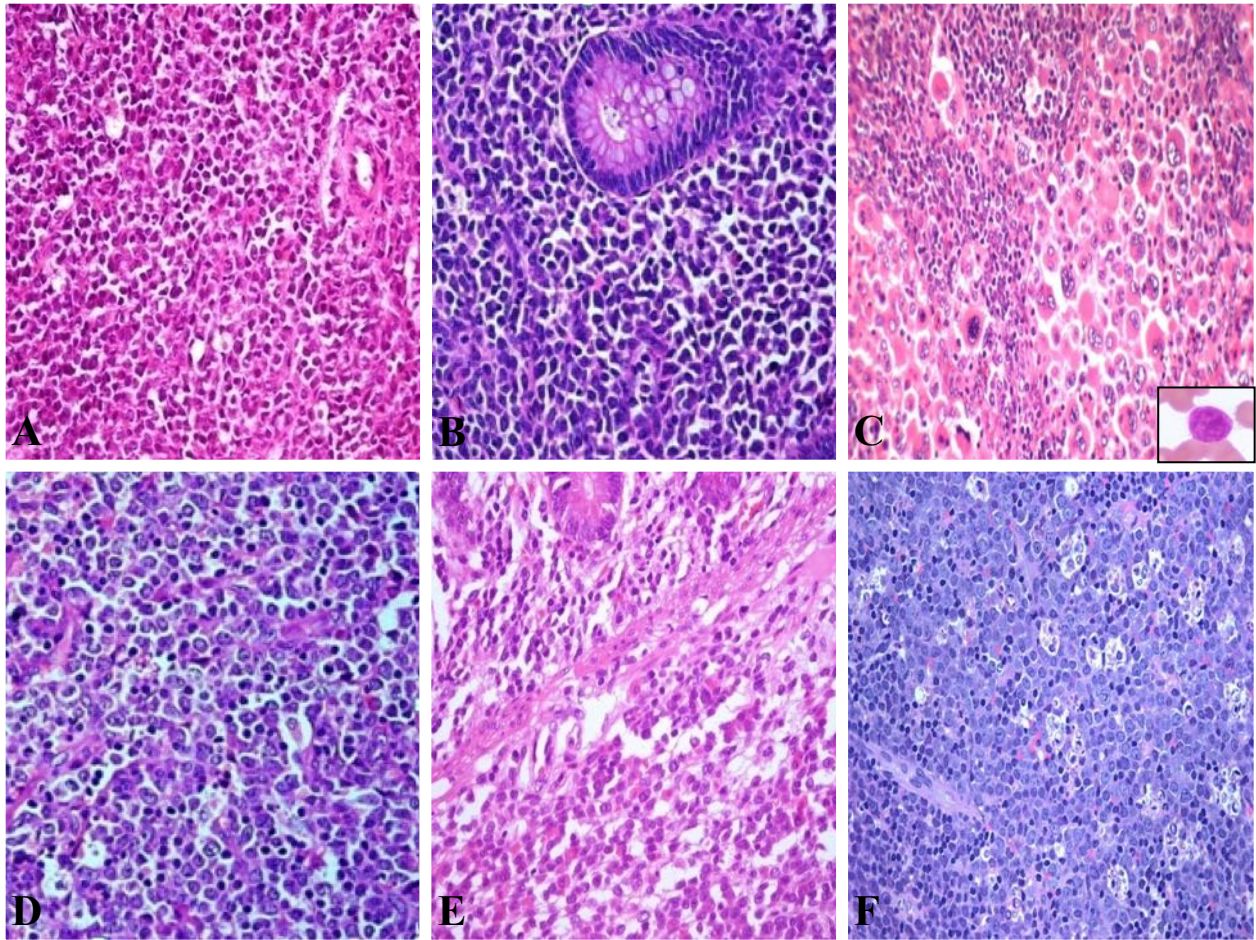


Figure 1: Atypical lymphoid cells of myeloid sarcoma (A) paraspinal region (B) Appendix (C) (D) cervical lymph node (E) Ileum (F) cervical lymph node. (C) cervical lymph node - Atypical lymphoid cells with megakaryoblastic differentiation (inset)

The IHC panel included LCA, MPO, CD 68, CD 117, Ki67, CD3, CD20 and TdT. All the cases were positive for MPO and two cases were positive for CD68. (Figure2)

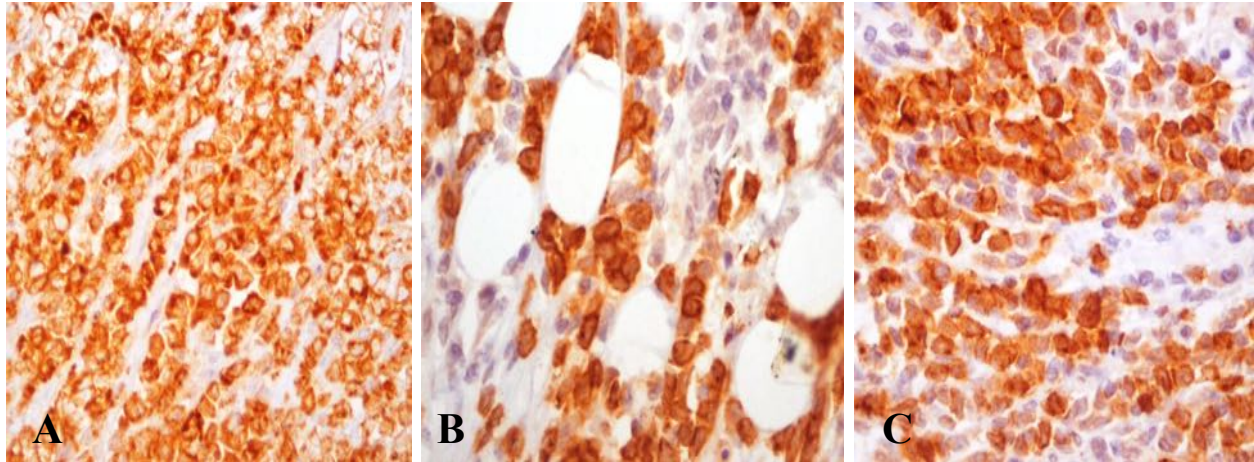


Figure 2: The tumor cells show diffuse strong positivity for (A) myeloperoxidase (MPO) immunostain (x 400)(B) CD117 (x400) (C) CD34 (x400)

Discussion:

Myeloid Sarcoma is a rare disease and the differential diagnosis of MS is often a clinical challenge. The incidence of myeloid sarcoma in patients without leukemia (primary myeloid sarcoma) is 2 per million in adults. ^[10] In adults, roughly one third of myeloid sarcomas present with concurrent myeloid neoplasm and one third have a history of myeloid neoplasms. The secondary forms of myeloid sarcoma occur in 1.4% to 9% of patients with AML. ^[11, 12]

Though MS may involve any organ or system in the body, the symptoms are substantially related with the anatomic location that is involved. Lymph nodes were the most frequent site of localization in our series.

The diagnosis of myeloid sarcoma is important in patients who do not have associated hematologic abnormalities at presentation. Only leukemic infiltrates that form tumor are called myeloid sarcomas. Mature or immature types of MS can be confused with Hodgkin lymphoma, T-cell lymphomas, extramedullary hematopoiesis (myeloid metaplasia) or infectious processes. Additionally, blastic types of MS can be confused with non-Hodgkin lymphoma (diffuse large B-cell lymphoma, lymphoblastic lymphoma, blastoid mantle cell lymphoma), lymphoblastic lymphoma, poorly differentiated carcinoma, or melanoma.^[13] A high degree of suspicion and immunohistochemistry are necessary to arrive at a diagnosis.

Immunophenotyping of MS includes variable positivity for MPO, CD68, CD34, CD117, TdT. Immunohistochemistry for MPO, which is commonly expressed by cells of the myeloid lineage was positive in 100% of our cases. Also, CD68, which is more common in cells of monocytic lineage, was expressed in 40% of the cases.

In making a diagnosis of MS, histopathology and cytomorphology are less informative than cytogenetics, cytochemistry and immunophenotyping. Audouin *et al.* noted that the infiltrate in MS can be massive, obscuring and destroying normal tissue, with perivascular infiltration being a common histopathologic finding.^[14] Cytomorphologic classification of tumors by degree of differentiation does not change the prognosis of the patient and is clinically insignificant.^[15,16] While it was previously thought that the presence of eosinophilic myelocytes was a means to a definitive diagnosis, this finding is much less sensitive than originally thought and should not be used as a hallmark of disease.^[15,16]

The role of cytogenetics in the diagnosis of MS is becoming increasingly important.

Pileri *et al.*^[17] found that monosomy 7 (10.8%), trisomy 8 (10.4%), and mixed lineage leukemia splitting (8.5%) were the most frequently encountered abnormalities. The t(8;21) (p22;q22) translocation, previously thought to be the most common cytogenetic abnormality, is now known to be more common in childhood or in MS involving the orbit.^[18,19] Overall, the recorded incidence of chromosomal aberrations appears to be in line with that seen in adult AML.^[18]

The importance of arriving at a diagnosis of MS cannot be overemphasized, considering the fact that early diagnosis and appropriate treatment strategies need to be implemented before the disease progresses to AML, thereby ensuring better prognosis.^[20]

Conclusion:

Myeloid sarcoma poses a diagnostic dilemma due to its variable clinical attributes. Myeloid sarcoma usually consists of diffuse pattern of mononuclear cells but immunohistochemical and cytogenetic analysis are required for a definitive diagnosis. A high index of suspicion and application of myeloid markers for any poorly differentiated neoplasm at an extramedullary site is important. This study highlights the rare incidence and varied presentation of myeloid sarcoma. Early detection is essential for appropriate and prompt treatment to prevent or delay the progress to the leukemia stage.

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