Original Research Paper

Volume-10 | Issue-1 | January - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pathology

MYELOID SARCOMA – RARE DIFFERENTIAL OF A SUSPECTED LYMPHOMA

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KEYWORDS :

INTRODUCTION:

Myeloid sarcoma is defined as infiltration of tissues and organs other than bone marrow by precursor myeloid series cells. They are rare entities and usually mimic a non Hodgkin lymphoma by presenting as tumors composed of diffusely infiltrating round cells and/or with lymph node enlargement. The bone marrow examination has either not been done or deferred and is performed once the histopathological result proposes the diagnosis.

At our institute there were 8 cases diagnosed as myeloid sarcoma over a period of 3 years. We present the clinical, histopathological and immunohistochemical features of these cases.

MATERIAL AND METHODS:

We reviewed a total of 8 cases which were diagnosed at our institute as myeloid sarcoma to define their clinical, histopathologic and immunophenotypic features.

A broad panel of immunohistochemistry markers had been applied in workup of the cases including lymphoid markers CD45, CD20, CD3, CD2, CD10, Pax-5, CD99, TdT and myeloid / precursor differentiation markers CD34, CD117, MPO, CD15 and Cd68.

RESULTS:

Out of total 08 cases studied, the age range of patients was 18 to 62 years, mean (32.5y), M:F sex ratio was 1:1.5. Sites involved were lymph node (4), bone, colon, duodenum, cervix (1 each). Most common presentation was lymph node enlargement followed by clinically appreciated mass lesion, abdominal pain and bleeding per vaginum.

Clinical Presentation:

CASE 1: 18 years old male presented with left cervical lymph node enlargement. The biopsy was evaluated at regional center and histopathological impression given was high grade non Hodgkin lymphoma, morphologically lymphoblastic lymphoma.

CASE 2: 40 years female known case of CML for one year, presented with left humerus mass

CASE 3: 21 years female presented with left supraclavicular lymphadenopathy which was diagnosed as non Hodgkin lymphoma at the regional center on histopathology alone.

CASE 4: 62 years old male presented with right supraclavicular lymph node enlargement. The clinical diagnosis was NHL.

CASE 5: 32 years old female whose colonic mucosal biopsy histopathology was interpreted as non Hodgkin lymphoma, high grade.

CASE 6: 48 years male presented with abdominal pain since 1 month. Examination showed generalized lymphadenopathy. Lymph node biopsy at the regional center was reported as suggestive of NHL. Peripheral blood TLC- 21,000/cmm out of which 70% atypical cells. Bone marrow aspirate shows infiltration by atypical lymphoid cells. Bone marrow biopsy- Infiltration with B-Cells, Ki-67 inconclusive.

CASE 7: 20 years female with past history of leukemia presented with hematemesis and vomiting. Upper GI endoscopy showed duodenal bulb and posterior bulbar area and second part are hugely dilated. Large growth seen infiltrating the lateral wall of distal second part of duodenum. CT scan whole abdomen suggestive of conglomerate lymphadenopathy at pre para aortic and superior mesenteric axis invading and compressing head of pancreas and third part of duodenum. Endoscopic biopsy of duodenal growth reported at regional center as consistent with non-Hodgkin lymphoma.

CASE 8: 17 years female complained of intermenstrual bleeding and continuous bleeding per vaginum since past few months. Biopsy from cervix reported at regional center as undifferentiated carcinoma. Treated with chemotherapy at another center but with no response. Currently has anemia. White blood cells and platelet counts are normal. Bone marrow not evaluated yet.

Radiology Findings were available in only one case. CT scan – heterogeneously enhancing lobulated retroperitoneal mass left pre and para aortic region of upper abdomen partially encasing superior mesenteric artery measuring 10.2 x 6.5 x 8.9 cm. Postero-superiorly invading third part of duodenum**.** First and second parts of duodenum markedly distended.

Radiologic impression –suggestive of malignant lymphadenopathy.

Histopathology Findings:

The H&E picture was almost similar in all the cases with some variation in cell size and presence of more differentiated forms. There was effacement of the lymph nodal architecture along with sinusoidal involvement in most cases of nodal involvement. The architectural pattern was diffuse infiltration or arrangement of cells in vague aggregates. There were medium sized cells in sheets with a rare admixed small lymphocyte, except in lymph nodes where more number of lymphoid cells were admixed. The lesional cells had slightly indented to bean shaped nuclei, chromatin was dispersed and nucleoli were visible in some of the cells. Cytoplasm was scant to moderate in amount. In the more differentiated forms it was mild to moderate in amount, granular eosinophilic and nucleus was placed eccentrically in them.

Immunohistochemistry results:

The results of immunohistochemical markers performed are summarized in table--.All the cases assessed (n=8, 100%) were positive for at least one myeloid/blast marker. 7 cases assessed (n=7, 87.5%) were positive for CD34, MPO and CD117. CD15 was performed in 7 cases out which 4 (57.1%) were positive. CD68 was performed in 4 cases and it was positive in 3 (75%). CD43 was performed in 2 cases and it was positive in 01 (50%). TdT was performed in 6 cases and it was positive in 01 (16.6%). CD99 was performed in 4 cases and it was positive in 3 (75%). CD45 was performed in 4 cases and was positive in 1 (25%). Various B and T-cell markers performed were negative in all cases – CD20, CD3, CD2, PAX-5, CD79a and CD10.

OBSERVATIONS TABLE

Case No.	Cell Cytology	CD68	MPO	CD117	Other Markers
1	Medium size, moderate eosinophilic cytoplasm, moderate variability in cell size, nuclear folding and lobation, some cells granular cytoplasm	+	++	ND	-
2	Medium size, moderate eosinophilic cytoplasm, mild variability in cell size, highly folded bean shaped nucleus, some cells granular cytoplasm	+++	++		
3	Medium sized cells, some show bean shaped nucleus, moderate variability in cell size, moderate amount of eosinophilic cytoplasm in many	+	++	+	CD34+
4	Medium sized cells, folded and bean shaped nuclei, occasional lobulated nuclei	-	-	++	CD15++
5	Medium size, moderate eosinophilic cytoplasm, mild variability in cell size, highly folded bean shaped nucleus, some cells granular cytoplasm	+	+++	+++	Cd34+++
6	Medium to large sized cells, scanty cytoplasm, moderate variation in cell size, some with folded to lobated nuclei	ND	++		CD34++, CD43++
7	Medium sized cells, mild variation in cell size, moderate eosinophilic granular cytoplasm, oval to bean shaped nucleus, lobated nuclei present,	ND	++	++	CD34++, CD15++
8	Medium sized cells, mild variation in cell size, scanty cytoplasm, round to oval and many bean shaped nuclei, few lobated nuclei	ND	++	++	CD34++

DISCUSSION:

Pileri et al[1] analyzed 92 cases of myeloid sarcoma and described architectural pattern as diffuse or Indian-file when occurring at an extra-nodal site. In the lymph nodes they described a diffuse pattern when sinuses were involved or a paracortical infiltration with entrapment of residual follicles. According to immunophenotype they subdivided the cases into undifferentiated, blastic, differentiated, trilinear, with megakaryocytic differentiation, monoblastic and myelomonocytic types. They found no association between histotype and involved anatomic site with exception of monoblastic forms 50% of which occurred in the skin. Their immunohistochemical results showed majority of cases were positive for CD68, CD117, MPO and CD34. Some were also positive for TdT and CD99. In our series we found immunopositivity as CD68 (3/4) (75%), CD117 (7/8) (87.5%) and MPO (8/8) (100%).

Alexiev et al[2] analyzed 13 cases of myeloid sarcoma in which they classified lesional cells based on morphology and immunophenotype into immature granulocytic sarcoma, differentiated granulocytic sarcoma, monoblastic sarcoma, monocytic sarcoma and myelomonocytic sarcoma. In their study majority (>60%) occurred in known AML/MDS cases and they also found them to be analogous to their leukemic counterparts. In our study we had previous history of leukemia in 3 out of 08(37.5%) cases however, no previous cytological or histopathological details were available for co-relation. Majority of our cases were diagnosed without any past history 05 out of 08(62.5%) and were de novo occurrences. In our series markers of monocyte lineage were positive in 04 out of 08(50%) cases.

Zhou et al[3] analyzed 17 cases of myeloid sarcoma occurring exclusively in head and neck region. They described the architectural pattern of involvement as diffuse in soft tissues other than lymph nodes and paracortical in the lymph nodes. They also classified the lesions as granulocytic, monocytic or blastic without any maturation based on the cytological features of cells.

Campidelli[4] et al studies 25 cases of myeloid sarcoma and found architecturally a diffuse growth involvement of lymph nodes with features of sinusoidal spread. Their findings were myeloid differentiation in 3 cases (leukocyte common antigen+, CD117+/–, and MPO+), monoblastic in 2 (MPO–, CD68+/PGM1+, and lysozyme+), myelomonocytic in 1 (CD3–/+, MPO+/–, and CD68+/PGM1+), and megakaryoblastic in 1 (CD61+, linker of activated T lymphocyte–positive). They highlight multifaceted manifestation, varied histopathologic characteristics, various contexts in which MS may commonly arise and the diverse range of phenotypic and morphologic differentiation. They found myeloid sarcoma involving ileum and colon similar to our findings.

Chang et al[5] studied 17 myeloid sarcoma cases and found immunopositivity in majority of cases for CD68 and MPO. They observed CD34 expression more frequently in cases associated with CML or MDS than in those associated with AML.

Based on the unique immunophenotype (blast cell and myeloid marker expression with absence of mature lymphoid marker expression) the diagnosis of isolated myeloid sarcoma can be made accurately in most cases. The initial diagnosis is non-Hodgkin lymphoma due to high prevalence of lymph node involvement, unusual sites of involvement and because cells resemble lymphoid neoplasms – intermediate sized cells having round to oval nuclei, 1-2 nucleoli and scant cytoplasm.

The possibility of this diagnosis must be kept in mind when a clear immunophenotype of lymphoid neoplasm is not obtained whatever be the age of patient and a panel of immunohistochemical markers for myeloid differentiation should be performed. It must also be kept in mind that there is immunophenotypic overlap and some lymphoid markers can be expressed in myeloid sarcoma, therefore a broad panel of markers should be applied to reach a definitive result.

There is possibility of development of AML in myeloid sarcoma patients not given anti leukemic chemotherapy. The prognosis of isolated myeloid sarcoma is more favorable than AML without myeloid sarcoma- seer database review[6]. Anti-AML therapy is effective and now there are new cases reports of myeloid sarcoma cases where specific gene mutations are being detected with excellent response to targeted therapy[7].

CONCLUSION:

Myeloid sarcoma is a rare entity that mimics lymphoma and may involve lymph nodes or extra nodal sites. It can occur de novo, precede or coincide with AML, CML, MPN or MDS. There is overlap of some lymphoid markers with myeloid sarcoma and only if the possibility is kept in mind when immunohistochemical analysis for lymphoma does not yield clear results and a broad spectrum of markers is applied can an accurate diagnosis be made. It is treated as AML and diagnosis must be made early for successful therapy.

Figures:

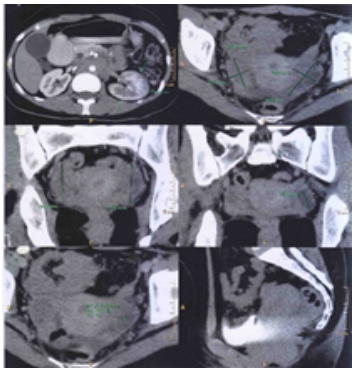

Figure 1. CT Scan: Heterogeneously enhancing lobulated retroperitoneal mass left pre & para aortic region of upper abdomen partially encasing superior mesenteric artery measuring 10.2x6.5x8.9cm. Poster superiorly invading 3rd part of duodenum. 1st & 2nd part of duodenum markedly distended. IMP-S/o Malignant lymphadenopathy.

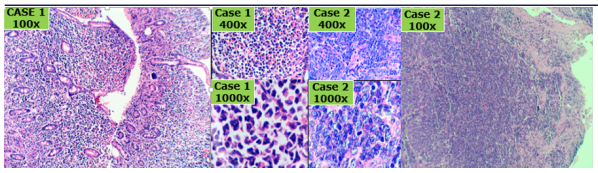

Figure 2. H&E picture was similar in all the cases. There was effacement of architecture of the lymph nodes and not just sinusoidal involvement. There were medium sized cells admixed with small lymphocytes. The lesional cells had slightly indented to bean shaped nuclei. Chromatin was dispersed & nucleoli were visible in some of the cells. Cytoplasm was scant to moderate and eccentric in some cells.

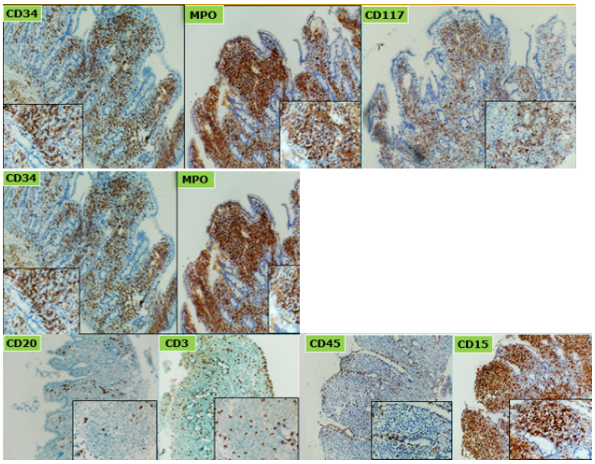

Figure 3. IHC markers of mature lymphoid differentiation (CD20, CD3, CD45) were immunonegative in the lesional cells. IHC markers for precursor lymphoid differentiation (TdT) were also immunonegative in lesional cells. The lesional cells were immunopositive for precursor/blast differentiation CD34, CD117. Many were also immunopositive for myeloid differentiation marker MPO. Proliferation index markers were moderate to markedly high.

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