CASE REPORT

Myeloid Sarcoma: A Mediastinal Masquerader

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ABSTRACT

Mediastinal Myeloid Sarcoma is a rare entity. Here we present a case of a 28-year-old gentleman, who first presented with a mediastinal mass and was clinically considered lymphoblastic lymphoma. He was diagnosed initially as having T lymphoblastic lymphoma on a mediastinal trucut biopsy. After one month patient was diagnosed with Acute myeloid leukemia on peripheral smear and bone marrow examination and was confirmed with the help of flow cytometry. The biopsy slides from the mediastinal mass were reviewed and based on the smear findings additional immunohistochemical markers were added and diagnosed as Myeloid Sarcoma.

KEY WORDS: Myeloid sarcoma, Mediastinum, Acute myeloid leukemia.

Introduction

Myeloid sarcoma (MS) is an uncommon neoplastic condition.[1]It consists of immature myeloid cells occurring at an extramedullary site like the bone, skin, or lymph node, although any part of the body may be affected.[1] Primary mediastinal myeloid sarcoma can be misdiagnosed as lymphoma if this differential is not kept in mind. The age-adjusted incidence rate of isolated MS is 0.9% with a median age of 59 years.[2] Isolated myeloid sarcoma (MS) is an extramedullary tumor mass composed of malignant myeloid precursor cells without any evidence of leukemic cells in the peripheral blood and bone marrow.[3] The incidence of mediastinal myeloid sarcoma was around 0.03%.[4]

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Case History

A 28-year-old gentleman presented with difficulty in breathing. The laboratory investigations showed hemoglobin 11.8 gm/dl, WBC: 4500/ cumm, and platelet: 2,52,000/ cumm. No records of any peripheral smear study were available. CT scan revealed a heterogeneously enhancing multiloculated soft tissue density lesion measuring 95x66x43 mm3 in the anterior superior mediastinum. Few enlarged pretracheal and hilar nodes were seen. Moderate pericardial effusion and mild pleural effusion were present. A possibility of lymphoma was suggested in the scan report. A diagnosis of Malignant round cell neoplasm was suggested elsewhere on mediastinal biopsy. A diagnosis favoring T Lymphoblastic Lymphoma was given following immunohistochemistry. The patient was referred to our institute after one month.

We initially received a trucut biopsy from the mediastinal mass for review. It was a suboptimal biopsy with an extensive crushing artifact. Biopsy showed a neoplasm composed of small to medium-sized cells, with scant to moderate eosinophilic cytoplasm, mild to moderately pleomorphic cells with an irregular nuclear outline, finely dispersed chromatin, and some showing nucleoli.

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(Figure 1) No sclerosis was noted. Histopathological diagnosis was given as small round cell tumor – mediastinal? Non-Hodgkin Lymphoma? Other round cell tumor. Immunohistochemistry was done. The panel included Terminal deoxynucleotidyl transferase (Tdt), CD 79a, CD 3, PAX 5, CD 10, AE1, Vimentin, CD99, CD 2, CD 8, CD 34, and CD 4, all of which came negative except for CD 34 (Figure 2) and CD 4 which was positive. MIB 1 was around 80%. Simultaneously we received peripheral blood and bone marrow sample from the same patient in the hematology department. Lab investigations showed hemoglobin 11.9 gm/dl, WBC: 9000/ cumm, and platelet: 1,20,000 / cumm. Peripheral blood had 58% blasts. Bone marrow showed around 60% blasts. Blasts were medium-sized with moderate to abundant vacuolated cytoplasm, some showing granules, round/ oval nuclei, and dispersed chromatin. (Figure 3) Special stains were done. Sudan black was positive and Periodic acid–Schiff stain (PAS) was negative. Marrow report was given as marrow involved by Acute Myeloblastic Leukemia (AML). Flow cytometry was done for confirmation. In the bone marrow sample, 64% of blasts were gated using CD 45 V 500C vs side scatter. The blasts mainly expressed myeloid markers Myeloperoxidase (MPO), CD 13, CD 33, and CD 117 along with CD 34. All T cell markers were negative (cCD 3, CD 7, sCD 3, CD 4, CD 5, CD 2, CD 8, Tdt)

Correlating with peripheral blood and marrow findings an additional panel was performed on the biopsy which included MPO (Figure 4) and CD 117 and both came as strong positive suggesting myeloid sarcoma infiltrating mediastinum. Molecular studies were also performed. FISH results which showed normal chromosome 16, negative for RUNX1-RUNX1T1 fusion, and FLT3 negative. Patient was on Daunorubicin, Vincristine, Methotrexate and Cytarabine. Post-induction marrow was in morphological remission and showed 1% blasts with an absolute neutrophil count of 2236 cells/mm3.

Discussion

Granulocytic sarcoma was first described by Burns in 1811.[5] Myeloid Sarcoma most commonly consists of myeloblasts, with or without features of promyelocytic or neutrophilic maturation, that partially or completely efface the tissue architecture. Sometimes it displays myelomonocytic or pure monoblastic morphologic features. Tumors with all three lineages or predominantly erythroid precursors or megakaryoblasts are rare. Myeloid

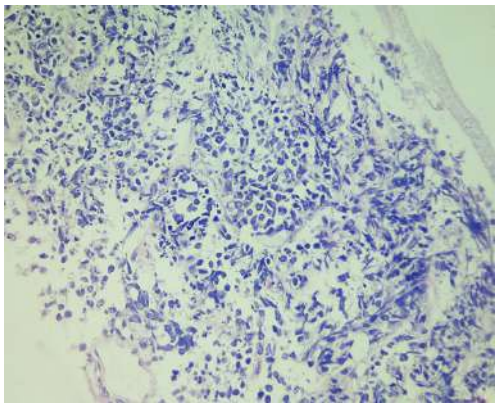

Figure 1: Mediastinal biopsy showing sheets of myeloblasts (x10 Hematoxylin and Eosin stain)

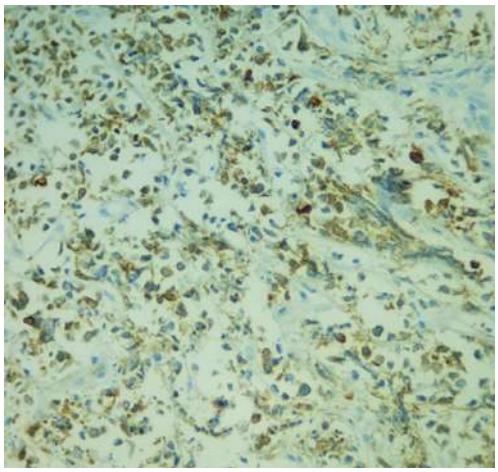

Figure 2: CD 34 Immunohistochemistry – Positive membranous staining (x10)

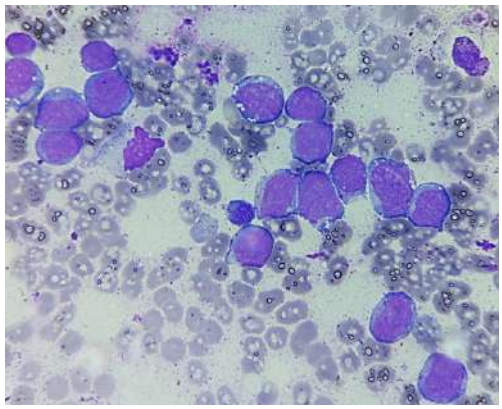

Figure 3: Bone marrow aspirate smears showing myeloblasts (x100 Wright stain)

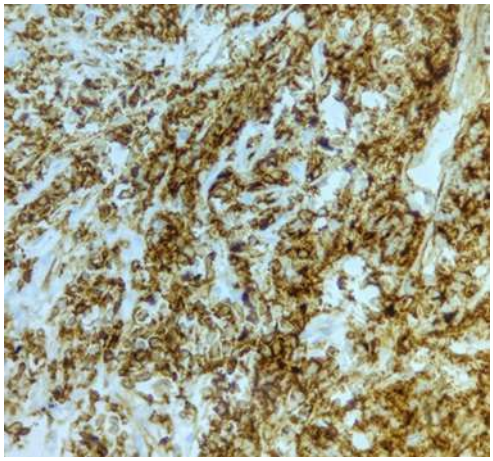

Figure 4: Myeloperoxidase (MPO) Immunohistochemistry - Positive cytoplasmic stain (x40)

Sarcoma may develop de novo or in association with Acute myeloid leukemia (AML), Myeloproliferative neoplasm (MPN), or Myelodysplastic syndrome (MDS).[6]

Myeloid sarcoma may present as the first manifestation of AML or any other hematological malignancy, preceding it for months or even years.[7] In such cases, it can be confused with lymphoma as in our case. Myeloid sarcoma occurs rarely in the mediastinum and clinically it can mimic lymphoma. Even in the immunohistochemical step, they can be confused with lymphoma as both express certain common leukocyte antigens. The increased diagnostic error rate could be due to this lesion's rarity and the low index of suspicion.[7] In a study by Muss et al, the incidence of MS in AML has been reported as 3 to 8%.[8] A careful morphological study in search of features of myeloid differentiation and a well-directed immunohistochemical study (anti-myeloperoxidase, anti-lysozyme, anti-CD15, anti-CD68), will eliminate the diagnosis of lymphoma. The exact diagnosis is important as the treatment is completely different in myeloid sarcoma and lymphoma.

In immunohistochemistry for Myeloid Sarcoma CD68-KP1 is usually expressed followed by myeloperoxidase (MPO), CD117, CD99, CD68/PG-M1, lysozyme, CD34, terminal deoxynucleotidyl transferase (TdT), CD56, CD61/linker of activated T lymphocyte/factor VIII–related antigen, CD30, glycophorin A, and CD4.[9] Acute Myeloid Leukemia can show clonal T-cell receptor rearrangements and/or express T-cell antigens, such as CD7 or CD4 (particularly in monocytic leukemias), all of which can create confusion while attempting to distinguish T-cell lymphoma from AML.[10] Myeloid sarcoma also exhibits aberrant antigenic markers like cytokeratins, and B- or T-cell markers. Cytogenetically, Myeloid Sarcoma has been found to occur in association with a variety of chromosomal abnormalities, in particular, t (8;21), inv (16), and an extra chromosome 8.[11]

This case report stresses the approach to the diagnosis of a mediastinal mass. With the age, size, and morphological picture, the differentials to be considered are Myeloid sarcoma, Lymphoblastic lymphoma, Primary Mediastinal large B cell lymphoma, and Hodgkin lymphoma.[12] Lymphoblastic lymphoma will have medium-sized cells and tumor cells will be positive for CD34, Tdt, and T or B cell markers. A small fraction of lymphoblastic lymphoma can show negative Tdt. These cases should be thoroughly evaluated by correlating with clinical and blood pictures including peripheral smear and bone marrow. Primary mediastinal large B cell lymphoma has intermediate to large-sized cells with prominent sclerosis. Sclerosis was absent in our case. Tumor cells will be positive for CD 20, CD 19, CD79a, PAX 5, and CD 30. Hodgkin lymphoma shows Reed Sternberg cells and will be positive for CD 15, CD 30, MUM1, and weak PAX 5 positivity.

Here in our study the presence of blasts in the peripheral smear helped to clinch the diagnosis although Myeloid sarcoma doesn't need to always present with a leukemic phase. A complete hematological workup should include a thorough peripheral smear examination, bone marrow study if necessary, and other ancillary techniques.

Conclusion

Myeloid Sarcoma occurring in a young patient with a mediastinal mass, pericardial effusion, and pleural effusion is indeed rare. These features are usually observed in precursor T-lymphoblastic leukemia/lymphoma or classical Hodgkin lymphoma. Hence a high index of suspicion, a thorough study of the morphology including peripheral smear examination, selected immunohistochemistry panel and clinical correlation is required to arrive at the correct diagnosis.

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