Case Report

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AML's Hidden Footprint: Autopsy Pathology Uncovers Extensive Extramedullary Involvement

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ABSTRACT

Background: Extramedullary Involvement (EMI) in acute leukemia refers to the infiltration of leukemic cells into organs or tissues outside of the blood or bone marrow compartments. This phenomenon manifests in various locations such as the skin, bones, and lymph nodes.

Case report: We present an uncommon occurrence involving a 46-year-old male, wherein extensive myeloid infiltrates were identified during autopsy examination.

Literature review: EMI is believed to manifest in approximately 3-8% of adults diagnosed with Acute Myeloid Leukemia (AML).[1]

Clinical relevance: It highlights the diagnostic complexity of AML and emphasizes the need for meticulous gross and microscopic examination during autopsy with clinicopathological correlation and utilization of special tests like immunohistochemistry in diagnosing such rare entities.

Keywords: Extramedullary Involvement; Autopsy; Acute myeloid leukemia; Myeloid sarcoma.

Introduction

Myeloid neoplasms originate from hematopoietic progenitor cells and predominantly affect the bone marrow, as well as secondary hematopoietic organs such as the spleen, liver, and lymph nodes. These neoplasms are broadly categorized into three main groups: acute myelogenous leukemias, myelodysplastic syndromes, and chronic myeloproliferative disorders.[2]

Extramedullary Involvement (EMI) in leukemia denotes the infiltration of leukemic cells into organs or tissues beyond the blood or bone marrow compartments. This phenomenon is estimated to arise in 3-8% of adults diagnosed with AML. Myeloid sarcomas, also known as granulocytic sarcomas, according to WHO classification, represent extramedullary tumors comprised of myeloid blasts, forming masses that disrupt normal tissue architecture in AML patients. Extramedullary disease, in a broader sense, encompasses leukemic manifestations outside the bone marrow and peripheral blood.[3]

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The prevalent locations for EMI include bones, periosteum, and internal organs such as the peritoneum, pericardium, mediastinum, kidneys, and lungs. In the head and neck region, common sites encompass the soft palate, nasopharynx, orbit, scalp, and face.[2]

It can manifest concurrently, after, or preceding bone marrow involvement. EMI is often linked with specific molecular mutations such as MLL rearrangement and FLT3 mutations, as well as distinctive flow cytometry markers like CD56, CD2, CD4, and CD7. Additionally, it exhibits characteristic myelomonocytic or monocytic morphology.

Factors contributing to the risk of EMI encompass subtypes M4 or M5 according to the French–American–British classification, presence of myeloblasts expressing specific T-cell markers CD13 and CD14, elevated peripheral total leukocyte count, and the occurrence of chromosomal abnormalities such as t(8;21) or inv(16).[4]

The prognosis for individuals with isolated or synchronous EMI in AML remains a topic of debate. Initial evaluations suggested that EMI could be associated with poorer outcomes, but larger studies have presented conflicting findings. Additionally, emerging data suggest potential variability in prognosis based on the specific organ site affected by EMI.[5]

This case report highlights the intricate diagnostic hurdles encountered in AML, elucidated through the presentation of a rare instance involving extensive myeloid infiltrates in a 46-year-old male.

Case report

We present a case involving a 46-year-old male patient discovered deceased in a bathroom. The brain, both lungs, part of liver, spleen, both kidneys and heart were sent to the pathology department for autopsy examination.

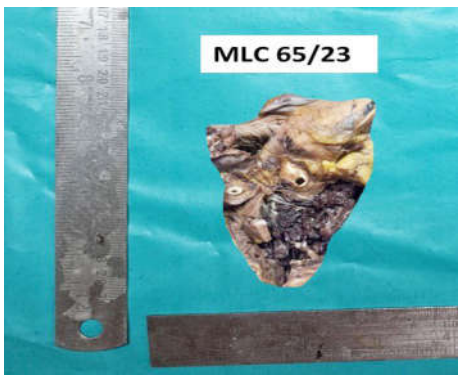

Fig. 1: Heart showing mural clot in the left ventricular cavity

Gross examination: Spleen was enlarged with red pulp expansion (fig. 2). The heart appeared hypertrophied with a visible mural clot in the left ventricular cavity (fig. 1). Cerebrum, cerebellum, bilateral lungs, kidneys, and liver were unremarkable grossly.

Fig. 2: Splenomegaly

Microscopy: Multiple sections from different organs - cerebrum and cerebellum, lungs, liver, spleen, kidneys, myocardium and epicardial vessels showed neoplastic infiltration by large cells resembling immature myeloid precursors (fig. 3,4,5,7,8,9). The blastoid cells were 1.5 to 2 times the size of small lymphocytes and exhibited cleaved nuclei, clumped chromatin, and moderate cytoplasm (fig. 6).

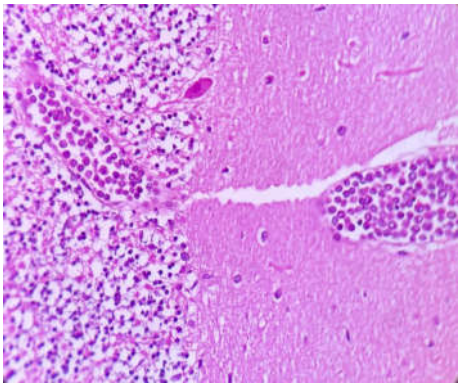

Fig. 3: Cerebellum with neoplastic cells in the blood vessels (H&E,10X)

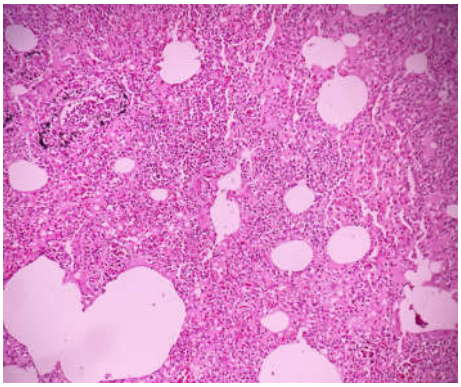

Fig. 4: Lung interstitial infiltrates of neoplastic cells (H&E, 10X)

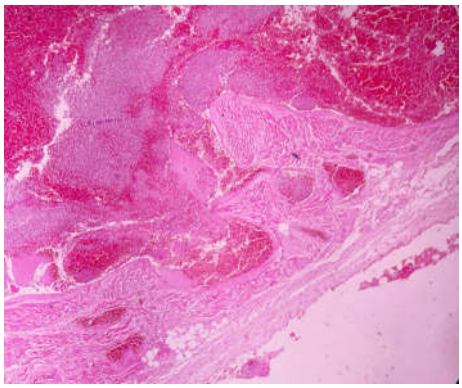

Fig. 5: Mural thrombus with adjacent myocardium (H&E, 40X)

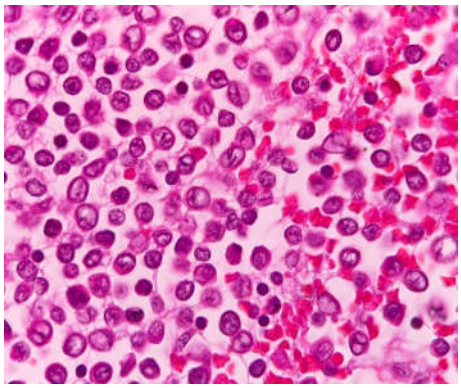

Fig. 6: Blastoid cells exhibiting cleaved nuclei and clumped chromatin (H&E, 100X)

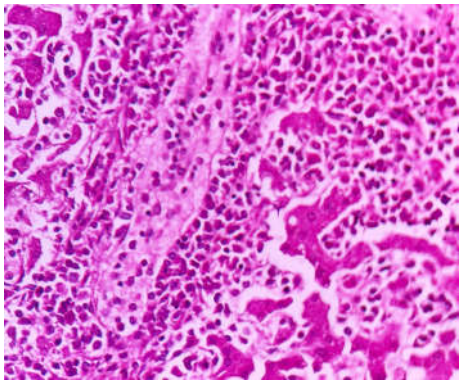

Fig. 7: Liver sinusoids distended and filled with neoplastic cells (H&E,40X)

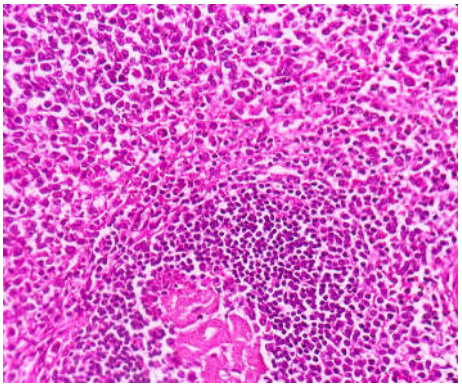

Fig. 8: Spleen with white pulp compressed by surrounding neoplastic infiltrates (H&E, 40X)

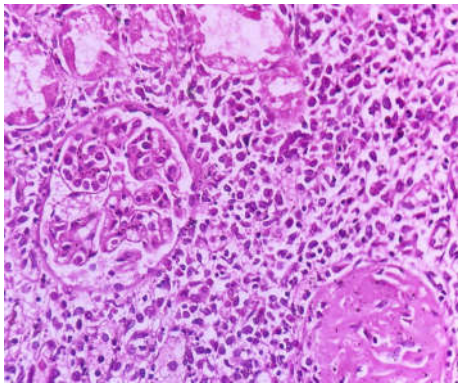

Fig. 9: Kidney showing interstitial neoplastic infiltrate (H&E, 40X)

After identifying the neoplastic infiltration, a detailed history was obtained. This revealed that the deceased had a recent history of fever, elevated WBC count (1.4 Lakh/cumm), marked thrombocytopenia (20 thousand/cumm) and he was provisionally diagnosed to have acute leukemia. Correlating histopathology with clinical details a provisional diagnosis of Hematolymphoid malignancy with extensive extramedullary involvement was made. IHC was performed with MPO, CD20 and CD3. The neoplastic cells showed diffuse strong granular cytoplasmic positivity for MPO (fig. 10) and were negative for CD20 and CD3, confirming the diagnosis of Acute Myeloid Leukemia with extensive extramedullary involvement.

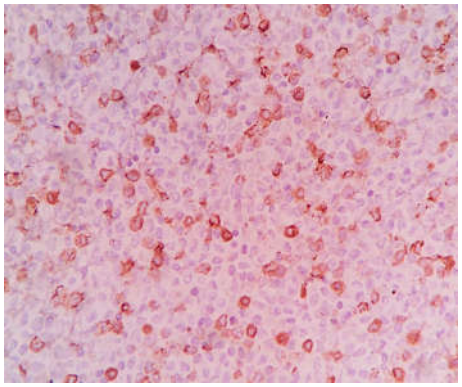

Fig. 10: Neoplastic cells showing diffuse strong granular cytoplasmic positivity for MPO (H&E, 40X)

Discussion

Leukemic cell infiltration to extramedullary sites is encountered in both acute and chronic leukemia with presentation at the diagnosis or during illness, after complete bone marrow remission or as an incidental autopsy finding. In acute leukemias, although commonly seen in ALL, EMI in AML accounts to an incidence of 2.5-9.1%.[6] The incidence of hematolymphoid malignancies at autopsy is 0.98%, with AML cases

being 14% of it and those with diffuse EMI to multiple organs is 2-10%, marking its incidence as low as 0.02-0.1%.[7] Primary diagnosis of AML with EMI made at the autopsy is highly unusual and this enlightens the role of pathologists and diagnostic autopsy.

Association of EMI with numerous factors like chromosomal abnormalities [trisomy 8, t(8,21), inv 16], expression of cell surface markers (CD56+ & CD117-), subtypes (Myelomonoblastic and monoblastic), total leukocyte counts are in the scope of study in recent years.[1] No organ or tissue is exempted from infiltration and the cases usually present with a single or dual organ involvement with a higher incidence among males in the age group of 30-50 years.[1,8] Concomitant multi organ involvement by leukemic infiltrates has an extremely rare incidence. Reviewing the literature from the available multiple online data bases, only a single case report with similar presentation in an adolescent girl is found to be reported previously.[9]

Leukemic infiltrates to myocardium in AML are often encountered. Arson SF and Lewy E, in their study on ECG changes in acute leukemia found 34% of cases with myocardial infiltrates at autopsy, clinically misdiagnosed and treated as RHD, coronary disease, AV block and CHF.[10] In our case, the representative bits from left ventricular wall myocardium showed leukemic blasts, which could have attributed to a conduction block, but no previous ECG to substantiate the same was available.

Angiocentric and angiodestructive infiltrative pattern observed commonly in CD56 positive AML cases results in microscopic and clinical changes in organs like lungs, kidneys and brain.[11] Previous studies show perivascular, alveolar and interstitial infiltrates of leukemic cells and the resultant pulmonary edema as the common lung findings and are concordant with the findings in our case.[12] Similarly, peritubular and glomerular capillary occlusion by the large blast cells account to the changes in renal parenchyma as observed in the current case. Although renal involvement is commonly presented as nephromegaly and AKI with a variable incidence of 4-47%, no such changes were present in this case.[13] Thrombosis of small cerebral and cerebellar vessels by blast cells along with leukemic infiltrates are the common CNS findings, although the latter was absent in our case.[14]

As observed by Waghmare TP et al in the autopsy study of hematolymphoid malignancies, 61.2% cases had hepatosplenomegaly at autopsy. Diffuse red pulp expansion with the leukemic cells is the common finding in spleen as observed in our case.[7] In 41% of AML cases solitary or concomitant involvement of liver is seen along with other organs with a cholestatic picture microscopically.[15]

Immunohistochemistry has aided in the final definitive diagnosis as NHL was a close morphologic diagnosis and the most common hematolymphoid malignancy presenting with diffuse multiorgan infiltrates (48.9%).[7] High total leukocyte count, low platelet count, thrombosis of small vessels by blast cells and leukemic infiltrates in all the vital organs substantiates the fulminant clinical course and early demise of the patient.

Conclusion

This case exemplifies the unforeseen consequences of AML. It underscores the invaluable role of clinicopathological correlation, autopsy examination and IHC in deciphering diagnostic enigmas and expanding our understanding of this exceptionally rare entity.

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