Case Report

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Pathology Section

Myeloid Sarcoma Presenting as Nasal and Orbital Mass: An Initial Manifestation of an Acute Myeloid Leukaemia

AMITA JAIN GUPTA[1], SHRAMANA MANDAL[2], RICHA GUPTA[3], NITA KHURANA[4], ACHAL GULATI[5]

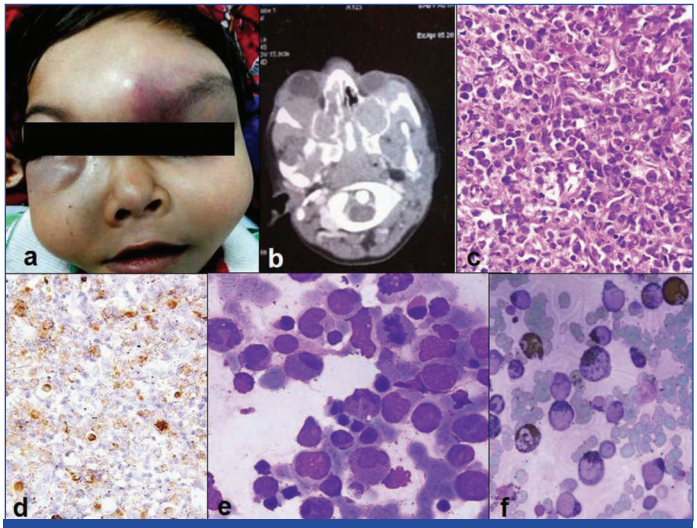
ABSTRACT

Myeloid sarcoma is an extramedullary manifestation of Acute Myeloid Leukaemia and sometimes is the only indicator of the disease. The incidence varies between 3-9.1% of acute leukaemia cases. The blast infiltration is seen most commonly in skin, lymph node, gastrointestinal tract, bone, soft tissue though can involve any body site usually as a solitary lesion and is rarely seen in nasal cavity. We present two cases of myeloid sarcoma presenting as a nasal mass in a six year old girl and other as orbital mass in 32-year-old as an initial manifestation of acute myeloid leukaemia. Histopathological examination along with immunohistochemistry clinched the diagnosis of myeloid sarcoma. Examination of bone marrow aspirate revealed blasts which fulfilled the criteria for acute leukaemia. These cases are usually misdiagnosed because often lymphoma and granulocytic sarcoma is not considered in initial list of differential diagnoses. These rare cases are being presented here as early recognition and diagnosis will ensure rapid treatment of the condition and improve the survival.

Keywords: Chloroma, Hepatosplenomegaly, Lymphocytes

CASE REPORT

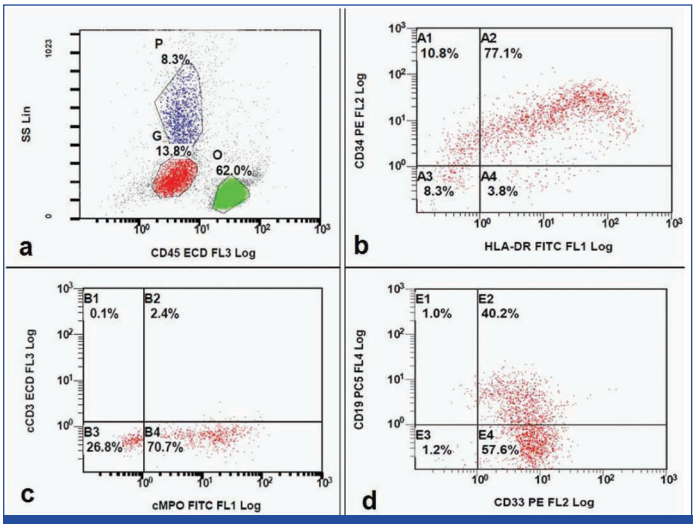
Case 1: A six-year-old girl presented with bleeding from nose since the past one month along with swelling around nose and face and blurring of vision for the past ten days. On examination, a nasal mass was present along with extension into the orbital region [Table/Fig-1a]. There was no hepatosplenomegaly. There was no history of abscess, infection, underlying malignancy and prolonged drug intake. Axial CECT showed an enhancing soft tissue mass lesion in bilateral nasal cavities and maxillary sinus with erosion of walls of maxillary sinus, extension into the ethmoid sinuses, retroconal space of bilateral orbits and premaxillary space suggestive of granulomatous lesion of nose and paranasal sinuses [Table/Fig-1b]. A nasal biopsy was done which showed a large number of atypical cells in sheets. The cells were large in size with high nucleo-cytoplasmic ratio, prominent nucleoli and hyperchromatic nucleus [Table/Fig-1c]. Few eosinophils were also noted. On immunohistochemistry, the cells expressed positivity for Leukocyte Common Antigen (LCA) and Anti-Myeloperoxidase (MPO) and were negative for desmin, myoglobin, CD 30, EMA, CD99, Cytokeratin, CD 20 and CD 3 [Table/Fig-1d]. Thus, a diagnosis of granulocytic sarcoma was made. Peripheral smear examination with complete blood count and bone marrow was then done. Haemogram showed Pancytopenia (Haemoglobin- 7.6 g/dl, Total Leucocyte Count - 2940/mm^3 and platelet count - 89000/mm^3). Peripheral smear showed 15% atypical cells, 8% polymorphs, 76% lymphocytes and 1% eosinophil. On cytochemistry, atypical cells (Blasts) were positive for myeloperoxidase stain and negative for periodic acid Schiff and non-specific esterase. Bone marrow aspirate showed a cellular marrow with 55% Blasts with diminished erythropoiesis and megakaryopoiesis. Immature myeloid precursors along with polymorphs constituted 12% of marrow nucleated cells [Table/Fig-1e,f]. Flow cytometric analysis of peripheral blood showed 13.5% cells (Blasts) with low side scatter, dim CD 45 positive. These expressed myeloid markers Cy MPO (73.1 % cells), CD 33(97.8%). There was aberrant CD 19 expression (40.2% cells positive). Other B cell (Cy CD 79a, CD22, CD 10), T cell markers (Cy CD3) and monocytic markers (CD14) were negative [Table/Fig-2]. Patient was diagnosed as Acute Myeloid Leukaemia with aberrant CD 19 expression presenting as myeloid sarcoma.



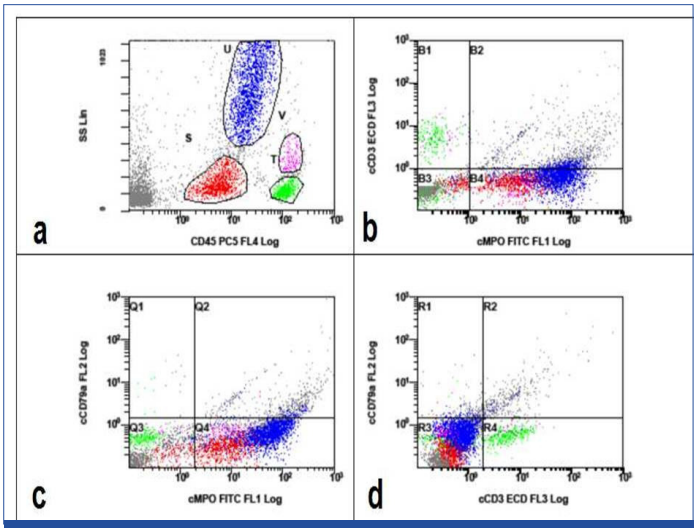
[Table/Fig-1]: a) Child with nasal mass and involvement of both the eyes; b) Axial CECT scan of nose and paranasal sinuses revealing an enhancing soft tissue mass lesion in bilateral nasal cavities and maxillary sinus; c) Nasal biopsy showing large cells with high N/C ratio, hyperchromatic nucleus, prominent nucleoli along with few eosinophils (H&E, X200); d) Photomicrograph showing blasts, immature Myeloid precursors and neutrophils expressing Anti MPO (ABP, X200); e) Bone Marrow Aspirate smear showing blasts, metamyelocytes and neutrophils (Giemsa, X400); f) Blasts in the bone marrow along with other myeloid cells are MPO positive (cytochemistry, X200).

Patient was started on induction chemotherapy (daunorubicin and cytarabine). The response to chemotherapy was awaited both on marrow and nasal mass after which patient was lost to follow up.

Case 2: A 32-year-old male presented with a diffuse supraorbital swelling, redness and inability to open the eye for the past three months. On examination a swelling was noted involving both the upper and the lower lid with mild proptosis. CECT orbit showed a mildly enhancing soft tissue lesion in extracranial compartment of right orbit extending in infratemporal fossa and right maxillary sinus with erosion of the walls and thus, a neoplastic aetiology was suggested. A biopsy of the lesion was done. Microscopy showed the features of a round cell tumour infiltrating the fibro-collagenous tissue. On immunohistochemistry, cells expressed positivity for Anti-MPO and were negative for cytokeratin, S-100, myogenin, EMA,

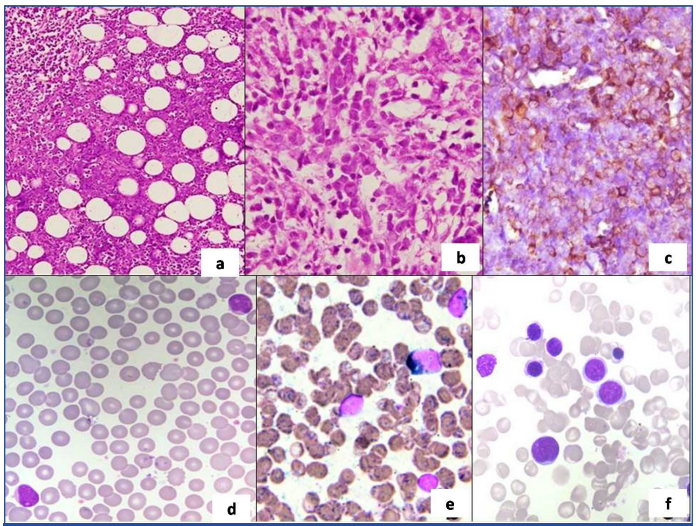


[Table/Fig-2]: a) Flow cytometry scatter plots showing blasts (Red colour), lymphocytes (green colour), immature myeloid precursors and neutrophils (Blue colour); b-d) Flow cytometry scatter plots showing blasts with expression of HLA DR, CD34, MPO, CD33 and Aberrant CD 19 expression respectively.



[Table/Fig-4]: a) Flow cytometry scatter plots showing blasts (Red colour), lymphocytes (green colour), immature myeloid precursors and neutrophils (Blue colour); b-d) Blasts express cytoplasmic MPO and are negative for cytoplasmic CD3 and CD 79a.

B cell, T-cell and HMB-45 [Table/Fig-3a-c]. A diagnosis of myeloid sarcoma was made and blood and bone marrow examination was advised. Blood examination revealed Hb 12.6 g%, TLC 7480/ mm^3 and platelet count 2.03 lac/mm^3. Peripheral smear examination revealed Blasts 20%, polymorphs 68%, lymphocytes 07%, monocytes 03%, and eosinophils 2%. Bone marrow aspirate smears examined were a diluted with peripheral blood with presence of 24% blasts. The blasts on cytochemistry expressed myeloperoxidase and were negative for Periodic Acid Schiff stain [Table/Fig-3d-f]. Flow cytometric examination on peripheral blood showed 21.3% blasts (dim CD 45 and low side scatter). Cells expressed HLA-DR (96.6%), CD 34 (99%), Cytoplasmic MPO (86.4%). The blasts did not show expression of B and T cell markers [Table/Fig-4]. Thus a diagnosis of Acute Myeloid Leukaemia was made. Patient was started on induction therapy, with daunomycin intravenous for three days and cytarabine (ara c) iv for seven days followed by consolidation with high dose ara c(HiDAC) for three doses. However, the patient relapsed after one and a half years with infiltration of bone marrow.



[Table/Fig-3]: a) Orbital mass biopsy revealed sheets of atypical cells surrounded by lymphoid cells (H&E, X100); b) Orbital mass biopsy revealed showed large atypical cells high N:C ratio, coarse chromatin and prominent nucleoli surrounded by lymphoid cells (H&E, X200); c) Shows blasts, immature myeloid precursors and neutrophils expressing Anti MPO (Avidin Biotin Stain X200); d) Peripheral smear showing blasts cells (Giemsa Stain X400); e) Blast cells express MPO in peripheral smear (cytochemistry X200); f) Bone marrow aspirate showing few blasts (Giemsa Stain X400).

DISCUSSION

Myeloid sarcoma also known as chloroma or granulocytic sarcoma is defined as the presence of proliferating myeloid blasts at an extramedullary site that disrupts the normal architecture of the organ. The mass may present along with leukaemia or may be the first manifestation of the disease process as in the present case [1]. The incidence varies between 3-9.1% of acute leukaemia cases and frequency in head and neck region is variable (12 to 48%) [2]. The blast infiltration is seen most commonly in skin, lymph node, gastrointestinal tract, bone, soft tissue though can involve any body site usually as a solitary lesion and is unusually seen in nasal cavity [1]. Very few cases of nasal chloroma have been reported in literature [1-7]. We present two cases of myeloid sarcoma presenting as a nasal mass in a six-year-old girl and other as orbital mass in 32-year-old. Myeloid sarcoma is an extramedullary manifestation of Acute Myeloid Leukaemia (AML) and sometimes is the only indicator of the disease. It can predate AML by months or years in approximately a quarter of cases, appear concomitantly with AML in 15-35% of cases, or occur after the diagnosis of AML in up to 50% of cases. It can also appear as an initial manifestation of relapse in a previously treated AML patient in remission [6]. Infiltration of any tissue by leukaemic cell is not classified as myeloid sarcoma. The term Myeloid sarcoma is used when the lesion presents as a tumour mass with effacement of tissue architecture [1]. In the present cases, the myeloid sarcoma presented as a tumour mass and as an initial manifestation of the disease process.

The origin of myeloid sarcoma has been suggested to occur in bones and periosteum as they are close to bone marrow and myeloid progenitors can thus proliferate at these sites. Haversian canal can carry these cells from bone marrow to periosteum, especially involving skull, orbit, sternum, spine, sacrum and long bones. The surrounding organs can become involved by haematogenous spread from these sites [2]. The two cases in present study may have got invaded by chloroma cells in the same manner.

The blast infiltration is common in skin, lymph node, gastrointestinal tract, bone; soft tissue though can involve any body site [1]. The disease manifestation only as a nasal swelling or as proptosis is an uncommon clinical scenario and hence leads to missed diagnosis on many occasions [3]. The most commonly considered differential diagnosis of this entity are Non-Hodgkin's lymphoma, Ewing's sarcoma/primitive neuroectodermal tumour, rhabdomyosarcoma, and neuroblastoma. In case of nasal masses, additional possibilities of esthesioneuroblastoma and small cell carcinoma should also be excluded by immunohistochemistry. Ewings sarcoma has characteristic CD 99 expression which will be absent in myeloid sarcoma. Non-Hodgkins lymphoma shows a monomorphic tumour cell population either expressing B cell or T cell, whereas rhabdomyosarcoma expresses desmin, myogenin and vimentin along with presence of rhabdoid cells. On the other hand, small

cell carcinoma shows molding and expresses cytokeratin and neuroendocrine markers. Neuroblastoma will show rosettes and may have a fibrillary material in the center of rosettes, and expresses reactivity with synaptophysin and chromogranin. Myeloid sarcomas are differentiated from all the above differential diagnosis by the expression of LCA and MPO. Isolated soft tissue lesions without overt leukaemia pose a diagnostic difficulty as it is not considered in the initial list of differential diagnoses. Hence, any case with effacement of tissue architecture by round cells with high N/C ratio, scant cytoplasm and frequent mitosis along with cells with cytoplasm showing eosinophilic granules must undergo complete haematological evaluation along with immunohistochemistry on tissue biopsy. The blasts on peripheral smear may be misrecognized as reactive lymphocytes where the platelet count and TLC are within normal limits as in the second case. Hence, a thorough peripheral smear examination is a must.

The treatment protocol for such cases is not established as it pertains to individual patients and disease in itself is uncommon in incidence and involves variable body sites and age groups. Debulking surgery (orbital decompression) and Cytarabine regimens have shown to may be helpful [3,4]. Systemic and aggressive treatment right after diagnosis, rather than localized treatment is advised as it reduces the rate of progression to acute leukaemia [4,5]. FLT 3 inhibitors, farnesyl-transferase inhibitors and, histone deacetylase inhibitors are the newer drugs which might have a potential role in these patients [6].

CONCLUSION

Myeloid sarcomas are rare and nasal/orbital chloromas are uncommon initial presentation of acute myeloid leukaemia in adults and even rarer in children. They should be considered in differential diagnosis of neoplasms where the cells have granular cytoplasm. Presence of few eosinophils and neutrophils should raise a suspicion of myeloid sarcoma.

Thus a peripheral smear and bone marrow examination is essential to confirm diagnosis of leukaemic involvement. These cases are being presented to make the clinician and the pathologist aware of existence of such lesion in nasal cavity and the orbit thus avoiding misdiagnosis and mistreatment.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Pathology, Maulana Azad Medical College, New Delhi, India.
2. Associate Professor, Department of Pathology, Maulana Azad Medical College, New Delhi, India.
3. Associate Professor, Department of Pathology, Maulana Azad Medical College, New Delhi, India.
4. Professor, Department of Pathology, Maulana Azad Medical College, New Delhi, India.
5. Professor, Department of ENT, Maulana Azad Medical College, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Shramana Mandal,
Associate Professor, Department of Pathology,
642- Pocket E, Mayur Vihar Phase II, Delhi-110091, India.
E-mail: shra_mana@hotmail.com

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