Abstract:
We report unusual case of 4 year old female child with right orbital swelling, right cerebellar space occupying (SOL) lesion, midline frontal SOL and hydrocephalus. Initially, right ventriculoperitoneal (VP) shunt and biopsy from the orbital swelling done, which was reported as non-Hodgkins lymphoma (NHL) but IHC and further haematological evaluations were found to be negative for NHL. As patient deteriorated further because of posterior fossa SOL, occipital craniectomy and total excision of posterior fossa SOL done. Now the biopsy was reported as myeloid sarcoma with positive CD 117 and myeloperoxidase and on examining the blood and bone marrow it was found that she was having Acute Myeloid Leukaemia (AML) M 2 type. Myeloid sarcoma itself is a rare tumour. In this case it is multiple. Multiple intra cranial myeloid sarcomas are even rare among all reported cases.

Keyword: myeloid sarcoma, Acute Myeloid Leukaemia, CD 117, Myeloperoxidase

Introduction:
Myeloid sarcoma (MS), also known as chloroma (owing to its green colour attributed to the enzyme myeloperoxidase), is a pathologic diagnosis for an extra medullary proliferation of blasts of one or more of the myeloid lineages that disrupt the normal architecture of the tissue in which it is found. It has also been addressed as granulocytic sarcoma, myeloblastoma and extra medullary myeloid cell tumour. Myeloid sarcoma (MS) is included as one of the major subgroups of myeloid neoplasms and acute leukaemia in the WHO classification and is most often found either concurrently or following a previously recognized AML. It may occur as an isolated de novo leukemic tumour, precede the appearance of blood or bone marrow (BM) disease, during remission period of already diagnosed AML and sometimes occurs...
following therapeutic autologous bone marrow cell transfusion. We present here a rare case of multiple intracranial myeloid sarcomas.

**Case report:**
4 year old 2nd born female child, born of non-consanguineous marriage by full term normal delivery who cried immediately after birth, brought with the complaints of swelling in the right eye for 20 days, head ache on and off for 1 week, vomiting on and off for 1 week, without any history of double vision, blurring of vision seizure or fever.

On examination child was conscious, oriented, obeying, afebrile, pupil-equal and reacting to light, extra ocular movements-full. Child was ambulant, Fundus-bilateral papilledema, partial mechanical ptosis present in the right eye. Swelling was present in the supero lateral aspect of orbit which was firm in consistency, non-pulsatile, not reducible. Cerebellar signs (finger nose test, finger finger nose test etc…) were present in the left side.

Initial blood investigations like haemogram, renal function test was normal. Peripheral smear showed microcytic hypochromic anaemia with few atypical lymphocytes.

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**Figure 1** shows Isodense lesion seen in the supero medial aspect of right orbit.

**Figure 2** shows contrast enhancing lesion in the left occipital region.

**Figure 3** MRT BRAIN T1AXIAL – C
As there was hydrocephalus, right VP shunt done and biopsy was taken from the right orbital lesion in the same sitting. After VP shunt child was normal. But 5 days later, her conscious level deteriorated, so it was decided to excise the posterior fossa SOL. Right suboccipital craniectomy and total excision of tumour done along with the dura as the tumour was infiltrating the dura, tumour was firm in consistency, moderately vascular, greyish white in colour. Biopsy report came as NHL but IHC marker and other haematological markers for NHL found to be negative. Fig 5-POST OPERATIVE CT BRAIN-CONTRAST

Fig 5: CT showing complete excision of posterior fossa tumour.
After 4 weeks, it was noted that orbital lesion enlarged significantly, so it was also excised by Bifrontal craniotomy and orbitotomy.
This time pathologist reviewed the entire slide again and it was reported as myeloid sarcoma. Immuno histo chemistry was done, CD117 was positive and myeloperoxidase also positive which is specific for myeloid sarcoma. Now peripheral smear repeated, bone marrow aspiration was done, both confirms the acute myeloid leukaemia M2 type.

Fig 6-HPE SLIDE
Fig 6: Slide showing cellular infiltrating neoplasm with small round cells with deep staining nuclei some with prominent nucleoli. The cells seen are infiltrating the orbital fat and fibrous tissue.

Fig 7-IHC SLIDES CD-117 MYELOPEROXIDASE Fig 7 a Fig 7 b
Figure 7 a shows positive for CD 117 (brown colour), Figure 7 b shows positive for myeloperoxidase
Fig 8: Peripheral smear shows preponderance of myeloid series with increase in number of myeloblast (arrow) with high nucleus cytoplasm ratio. Some of them show prominent nucleoli.

Fig 9: Sudan Black Stain

Figure 9 shows blast cells positive for sudan black stain (arrow).

Fig 9: Bone marrow aspirate shows increase in myeloid precursors comprising predominantly myeloblasts with high nucleus cytoplasm ratio (arrow).

Discussion:
Myeloid sarcoma, also known as extramedullary myeloid tumour, is a tumor mass of myeloblasts or immature myeloid cells occurring in an extramedullary site or in bone. Myeloid sarcomas were first described in the early 19th century.
They were initially termed "chloroma" (green tumor) owing to their green gross appearance. This appearance is a result of the presence of myeloperoxidase enzymes in the immature myeloid cells. The favored name later changed to granulocytic sarcoma, following descriptions of cases that were not green and had the gross features of a sarcoma. But it is well known that not all myeloid leukemias are derived from granulocytes hence the preferred term is myeloid sarcoma. The clinical presentation of myeloid sarcomas varies and is dependent on the site of involvement. Commonly involved sites of occurrence include subperiosteal bone structures of the skull, paranasal sinuses, sternum, ribs, vertebrae and pelvis; lymph nodes and skin are also common sites. Rare sites reported in the literature include the pancreas, heart, brain, mouth, breast, gastrointestinal and biliary tract, prostate, urinary bladder and gynecologic tract and more. A single tumor or sometimes multiple nodular masses of various sizes may occur. Myeloid sarcomas may be found in one of four settings:

1. In patients with known acute myeloid leukemia (AML) in the active phase of the disease.

2 In patients with a chronic myeloproliferative disorder (CMPD) or a myelodysplastic syndrome (MDS), in whom myeloid sarcoma may be the first manifestation of blastic transformation.

3 As the first manifestation of relapse in patients previously treated for primary or secondary acute leukemia

4 De novo in healthy subjects, in whom a typical form of AML may occur after an interval of weeks, months or even years. Rarely no leukemia develops.

1. No age group is immune; however, two thirds of the cases occur before the age of 15. Grossly the neoplastic tissue usually appears firm with a fish-flesh appearance. Not all lesions will have the peculiar green color and if present it commonly disappears with exposure to air or with fixation in formalin. Larger tumors may contain necrotic and hemorrhagic areas. Microscopically there is a diffuse monotonous infiltrate that may or may not destroy underlying normal structures. Although myeloid sarcomas are cytologically variable, most often they are composed of medium-sized to large blastic cells with ovoid vesicular nuclei with medium-sized or large centrally located nucleoli and dispersed chromatin. Their cytoplasm is scant to moderate. The mitotic count can be high. There may be apoptotic bodies phagocytosed by histiocytes (tingible body macrophages) that impart a starry sky appearance. The WHO Classification of Tumours; Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues recognize three major variants defined according to the predominant cell type and their degree of maturation. These variants are:

A blastic variant with predominance of myeloblasts,

2 An immature variant with a mix of myeloblasts and promyelocytes,

3 A differentiated variant with promyelocytes and more mature granulocytes

Less common variants recognized by the WHO include monoblastic sarcoma that is composed of monoblasts and associated with acute monoblastic leukemia and also tumors with bilineage or trilineage hematopoiesis, predominant erythroid precursors or predominant megakaryocytes that may occur in...
conjunction with transformation of a CMPD. Other variants reported in the literature include a monocytic variant, a myelomonocytic variant and a variant with intracytoplasmic Auer bodies, most often associated with acute transformation of MDS. Definite diagnostic method for myeloid sarcoma is immunohistochemistry. CD 117 and MPO are specific markers for myeloid sarcoma. Giemsa or Wright/Giemsa stains on imprints are the best way to see the morphology of the blasts. Cytochemical stains such as a positive sudan black or myeloperoxidase stain are helpful if touch imprints are available to identify the myeloid lineage. Nonspecific esterase stains can be performed to assess monocytic differentiation if imprints are available and CAE to identify granulocytic differentiation. If only paraffin embedded tissue sections are available, a Naphthol-ASD-chloracetate-esterase (Leder) stain can be performed. Myeloid sarcomas with granulocytic differentiation will often be positive. Immunohistochemical stains used for myeloid sarcoma include MPO and lysozyme. MPO immunostain is positive in most myeloblastic variants (as well as in some cells myelomonocytic variants) while lysozyme is frequently expressed in monoblastic variants. CD 15 is seen in tumors with mainly mature granulocytic cells, while CD68 is more specific for the monocytic series. Megakaryoblastic cells are characterized by the expression of factor VIII, CD 61, and CD 31 while Glycophorin C and/or blood group proteins occur in the rare erythroblastic variant. A variable percentage of non-differentiated blasts may be positive for CD13, CD33, CD 34, CD117 (c-Kit), or CD99. CD 45 expression demonstrates the leukocytic origin of the neoplastic cells; however this stain is often also not expressed. Sometimes expression of aberrant markers such as B-cell-, T-cell-, or NK-associated antigens including CD30 may be seen. Reactivity of tumor cells with CD43, a T-cell marker, without coexpression of CD3 should always prompt consideration of a myeloid tumor and not be misinterpreted as a neoplasm of T-cell origin. The use of only four antibodies (MPO, CD68, Lysozyme and CD34) has been proposed to distinguish the more common variants of myeloid sarcomas. The most frequent chromosomal abnormality associated with certain myeloid sarcomas has been observed to be t(8;21) (q22;q22), an abnormality that it shares with some AMLs. The correct diagnosis of myeloid sarcoma is important so appropriate therapy can be instituted. While the diagnosis is often thought of in patients with an established history of AML, MDS or a CMPD, in other patients the diagnosis is often missed. The differential diagnosis is lengthy and includes non-Hodgkin lymphoma (including precursor B - or T-cell, Burkitt, some peripheral NK/T-cell and diffuse large B-cell lymphomas), small round cell tumors (including neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, peripheral neuroectodermal tumor and medulloblastoma), undifferentiated carcinoma or melanoma, malignant histiocytosis and malignant mastocytosis with atypical mast cells. Extramedullary localizations of chronic myeloproliferative diseases without blast crisis should also be differentiated from myeloid sarcoma. In our case initially the tumour was diagnosed as NHL by histopathology. Immunohistochemistry may aid distinguish myeloid sarcoma from malignant lymphoma, however the coexpression of some T-cell markers and staining with TdT (Terminal
deoxynucleotidyl transferase) and CD 34 can cause difficulties in interpretation. Differentiating myeloid sarcoma from others is important as the treatment is entirely different. Treatment for myeloid sarcoma is similar to that for AML, even in cases of isolated tumors with no blood or bone marrow involvement. Radiotherapy has been proposed in association with chemotherapy for patients with massive tumors or for patients with spinal cord compression.

Conclusion:
Although extramedullary disease (EMD) and Myeloid sarcoma (MS) are recognized disease entities for more than a century, the reasons for their occurrence in a small proportion of AML patients and the difference in the timing of this complication during the course of AML remain as enigmas. MS is a relatively rare phenomenon, making it difficult to study its' impact in different AML subgroups. The literature suggests that patients with isolated MS may have a better prognosis compared with AML patients without MS. MS patients treated with AML-type chemotherapy regimens seem to have comparable outcomes to AML patients. Radiotherapy may not be needed as an adjunct to chemotherapy. The current treatment recommendation for isolated MS and MS occurring in AML patients is AML-type chemotherapy.

References:
