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An Unusual Presentation of Acute Lymphoblastic Leukemia as an Orbito-Sino Nasal Mass

I. V. Renuka[1], SK. Rizwana[2], B. Amulya[3], M. Atchyuta[3], I. V. Renuka[4], SK. Rizwana[5], B. Amulya[6], M. Atchyuta[7]

Abstract: ***Introduction: Orbital extramedullary leukemic infiltration (termed "orbital chloroma") is an uncommon, but a well described manifestation of Acute Myeloid Leukemia (AML). However, such a presentation is infrequent in acute lymphoblastic Leukemia (ALL) with less than 25 cases described in the literature. We describe the clinico-radiological, haematological and histopathological characteristics of a child with proptosis, with an eventual diagnosis of ALL. We will be discussing the differential diagnosis and also review the relevant literature. Case Report: A 7-year-old girl, presented with progressive proptosis and vision loss in the right eye. CECT PNS showed infiltrative soft tissue masses in the bilateral orbits (right > left) with trans-osseous spread to the bilateral basi-frontal dura and right ethmoidal sinuses. Presence of trans-osseous spread without intervening bone destruction raised an imaging differential diagnosis of histiocytosis, lympho-reticular malignancy and metastatic neuroblastoma. Ultrasonography showed additional lesions in the pancreatic head and kidneys. Trans-nasal ethmoidal biopsy showed small round blue cells with scant cytoplasm, hence a possibility of non-Hodgkin's lymphoma/Chloroma was considered. Immunohistochemical markers Neuron Specific Enolase (NSE), CD20 and Desmin were negative. Peripheral smear showed few atypical lymphocytes. Bone marrow aspiration showed rich cellularity with predominantly medium to large lymphoblasts with convoluted nuclei, 1 to 2 prominent nucleoli and scant basophilic cytoplasm, establishing a diagnosis of ALL-L2. Flow cytometry confirmed the diagnosis by CD38, CD19, HLA DR, CD22-Positive, CD34, CD20, CD7, CD56, CD2, CD36, CD64, CD 15, CD13, CD33, CD117, MPO, CD3 were negative. CD 10 was variable showing CALLA positivity (B cell lymphoblasticleukemia). Conclusion: Paediatric lymphoid orbital deposits ought to raise a suspicion of a systemic leukemia. Although AML is still the first differential in such cases, ALL should always be considered with a high index of suspicion owing to a significant difference in management.***

Keywords: Acute Myeloid Leukemia (AML), Acute lymphoblastic leukemia (ALL), Immunohistochemistry-IHC

1. Introduction

We present a case of a 7-year-old female child presenting with a mass over left nasal bone with proptosis and swelling of eyelids which is rapidly progressive and with decreased vision of both the eyes for one month.

2. Case History

Acute lymphoblastic lymphoma presenting at the Sino nasal location is rare. The frequency of the head and neck region varies, according to the literature, between 12% and 48%. In this region, the most frequently affected sites are the soft palate, orbit, salivary glands, scalp and face.[1]

Tumor mass consisting of immature granulocytic cells at an anatomic site other than the bone marrow is Myeloid sarcoma or Chloroma. The Sino nasal area may be a site of isolated Chloroma contributing to 20% of Sino nasal Myeloid Sarcoma cases. Myeloid Sarcoma has a wide age distribution and paediatric population is a preference age group. Due to its rarity, the diagnosis of Myeloid Sarcoma could be highly challenging.[2]

Early detection of extra-medullary granulocytic sarcomas and lymphomas would benefit the patient management and hence prognosis of these rare neoplasms.[1]

Results and Laboratory investigations:

Clinical diagnosis was Hodgkins / NonHodgkinslymphoma.

CT scan findings showed a nill-defined, homogenous intensely enhancing dural based soft tissue lesions in frontotemporal lobes extending across the calvarium. (Figure1A, 1B)

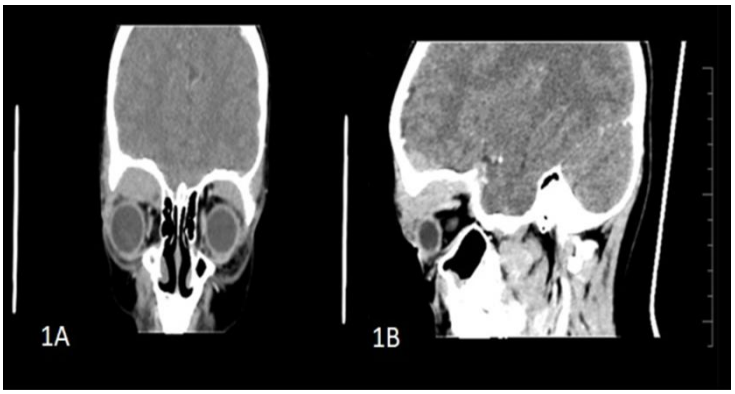

Figure 1A, 1B: CT showing homogenous intensely enhancing dural based soft tissue lesions in frontotemporal lobes extending across the calvarium

CECT: Suggestive of a Lymphoma.

Ultrasound shows focal lesions in both kidneys and a lesion at the peripancreatic head suggestive of a Lymphoma.

Peripheral Smear:

RBC: normocytic normochromic cells with haemoglobin 10.6gm/dl, WBC shows Total count as 3600cells/cumm with leukopenia, showing shift to left and few atypical lymphocytes (61%) with neutrophils (32%) (Figure2B).

Platelets: showed thrombocytopenia with a count of 40, 000 lakhs/cumm no haemoparasites were seen.

Bone marrow aspiration from iliac crest: BM-11/21 smears studied showed rich cellularity with predominantly medium to large lymphoblasts (70%) which have convoluted nuclei and 1 to 2 prominent nucleoli. The cytoplasm was scant and basophilic. The cells were admixed with mature lymphocytes and few mature neutrophils. Erythroid and granulocytic series were suppressed. Megakaryocytes were not seen. (Figure 2A, 2C)

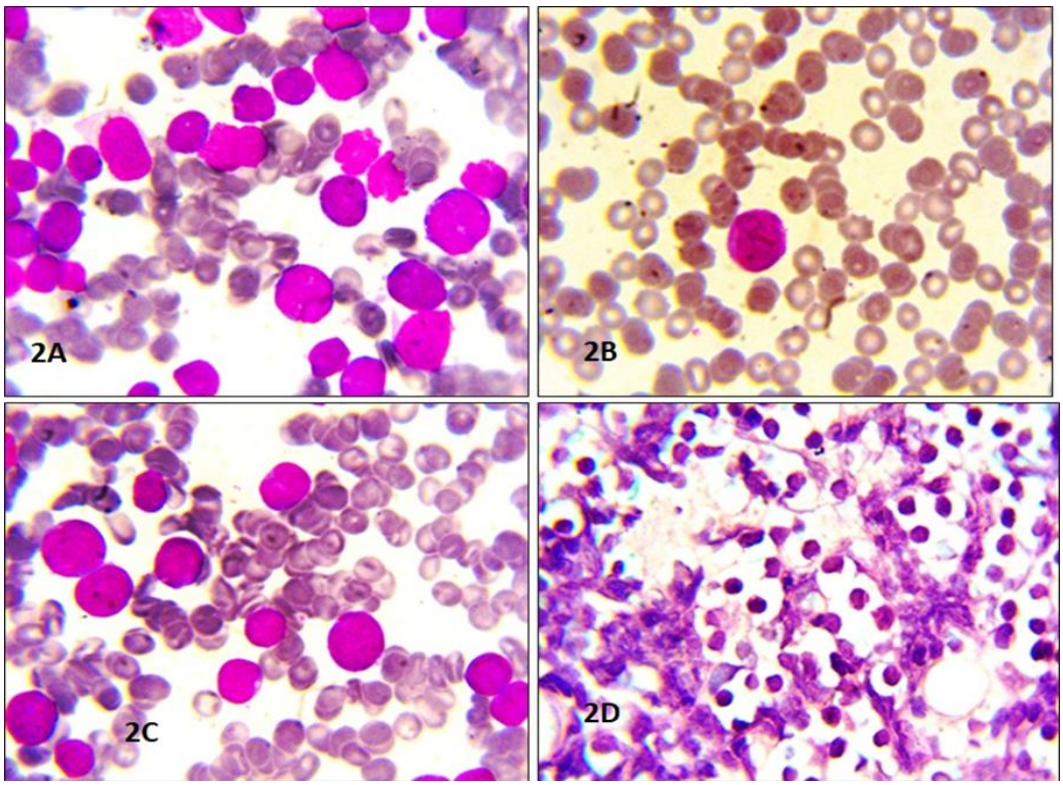

Figure 2A: Bone marrow aspiration showing highly cellular marrow with medium to large lymphoblasts (70%) with convoluted nuclei, 1-2nucleolii and scant basophilic cytoplasm admixed with few lymphocytes. (Leishman's stain 400x)
Figure 2B: Peripheral smear with leucopenia and few atypical lymphocytes (Leishman's stain 400x)
Figure 2C: Bone marrow aspiration with medium to large lymphoblasts with convoluted nuclei, 1-2 nucleolii. (Leishman's stain 400x)
Figure 2D: shows small blue round cells in sheets and clusters separated by fibrous tissue. (H& E 400x)

Diagnosis: Acute Lymphoblastic Leukemia (ALL) L2 type

Gross: We received a biopsy of the nasopharyngeal mass by number S-254/21 as multiple grey-white tissue bits altogether measuring 1x1cms. All the tissue was totally embedded.

Histopathology of sinonasal mass: Sections studied showed a tumour composed of small blue round cells in sheets and clusters separated by fibrous tissue. Focal vague rosette patterns were seen. Individual cells were small round to oval with scant cytoplasm and monomorphic hyperchromatic nuclei. Focal areas showed smudging of the cells. Differential diagnoses suggested were NonHodgkin's Lymphoma/ Chloroma. (Figure 2D)

The advised Immunohistochemical (IHC) markers were CD 3 and CD 20 along with Peripheral Smear, Bone marrow examination and flow cytometric study.

IHC showed NSE: negative (Figure 3A), CD20: negative (Figure 3B), Desmin: negative (Figure 3C), Cd 20: negative (Figure 3D).

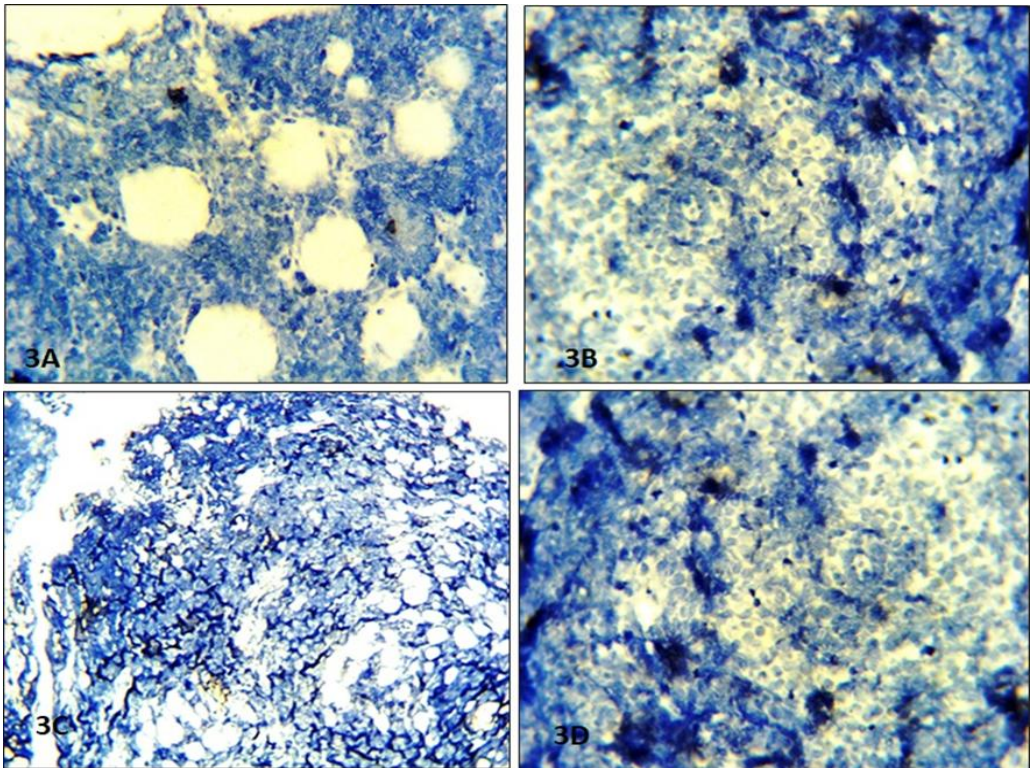

Figure 3A, 3B, 3C, 3D: IHC400x showing NSE: negative, CD 20: negative, Desmin: negative, CD3: negative

Flow cytometric analysis showed: CD38, CD19, HLA DR, CD22-Positive, CD34, CD20, CD7, CD56, CD2, CD36, CD64, CD 15, CD13, CD33, CD117, MPO, CD3-Negative. CD 10-variable showing CALLA positive (B cell lymphoblastic leukemia. (Figure 4).

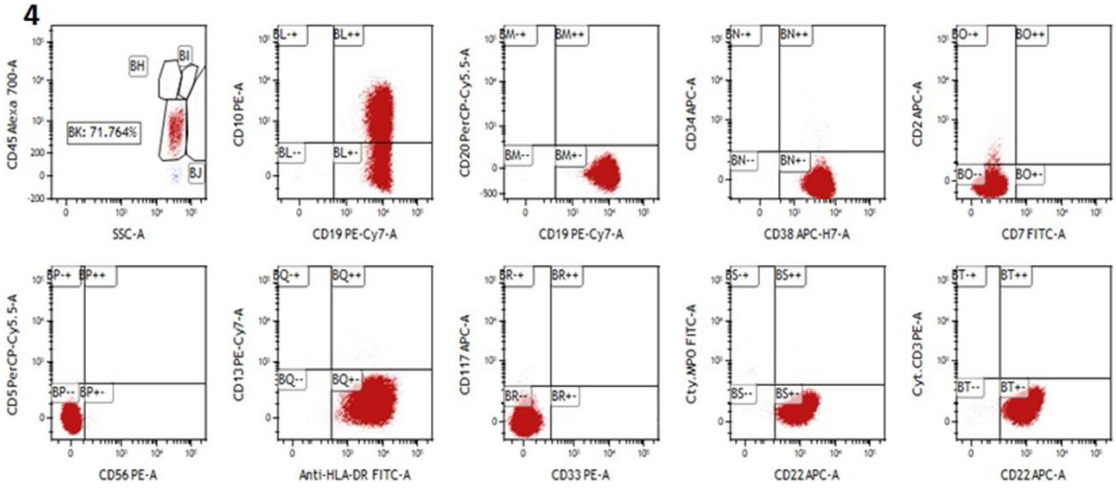

Figure 4: FLOW CYTOMETRY showing CD19, CD38, CD38, HLADR, CD22-positive. CD20, CD34, CD7, CD2, CD5, CD56, CD13, CD33, CD117, MPO, CD3- negative, CD 10- variable

3. Discussion

ALL presenting as Sino nasal masses are infrequent tumours with an aggressive clinical course. They morphologically mimic small round blue cell tumours. A clinical suspicion will only arise if there is a known haematological malignancy. These masses cause non-specific symptoms such as nasal obstruction, headache and tumour mass effects including facial swelling, proptosis and visual disturbances.

CT scan enables evaluation of size and location of the tumour and could distinguish tumour from other lesions, such as hematomas or abscesses, but definite diagnosis is dependent on biopsy of the tumour and immunohistochemical staining.

Acute lymphoblastic leukemia (ALL) is the most common malignancy in childhood. It can either be of B-cell or T-cell lineages. Common manifestations of ALL are fever, anemia, bleeding manifestations, bone pain, lymphadenopathy or hepatosplenomegaly. Among the other extramedullary sites to get involved in cases of childhoodALL at presentation or at the time of relapse, include the central nervous system, heart, lungs, ovaries, pancreas, urinary bladder, gastrointestinal tract, kidneys, skin and subcutaneous tissue,

breast, maxillary sinus, parotid gland, and bone and joints including vertebrae. Extramedullary manifestations pose diagnostic difficulties and are known to delay in treatment in childhood leukemias.[2]

Extramedullary myeloid cell tumors (also known as granulocytic sarcoma, chloroma, or myeloblastoma) are the most common form of leukemic infiltration involving the orbit.3Orbital chloromas may occur in various forms, especially in children. Focal masses may arise intraconally or extraconally and may be bilateral.4The diagnosis of leukemia is known, but as with leukemic masses elsewhere, they may precede the onset of systemic disease.[4]

The majority of head and neck or orbital masses secondary to leukemia are of the myeloid lineage. McManaway JW etal[5] found leukemic infiltration of orbit secondary to ALL in a six month old child; orbital involvement was diffuse with intraocular (choroidal) involvement.[5]

Myeloid Sarcomas are rare localised extramedullary myeloid tumors with an incidence between 3% and 4.7% of Myeloproliferative diseases and in 2–8% of patients with Acute Myeloid Leukemias.[6]

Suzuki et al summarized 10 Sino nasal Myeloid Sarcoma cases that had been reported between 2000 and 2018, including 9 adults and 1 child.[7]

Holsinger et al found 2 paediatric Sino nasal Myeloid Sarcoma cases recorded between 1955 and 1999 at a university-based, tertiary care referral centre in Houston.[8]

Bita Esmaeli et al reported a case of 40-year-old woman with an orbital mass and diffuse infiltration of paranasal sinuses secondary to precursor T-cell ALL. The radiologic findings in this patient were not typical for the previously described features of orbital chloroma, but were more consistent with an orbital abscess. Examination of orbital and ethmoid sinus biopsy specimens revealed relapse of precursor T-cell acute lymphoblastic leukemia. Although orbital involvement by granulocytic sarcoma (also known as extramedullary myeloid cell tumor and chloroma) with or without concurrent acute myeloid leukemia is well described in the literature, similar presence of acute lymphoblastic leukemia of either precursor T-cell or B-cell lineage is rare.9The diagnosis is further complicated by the lack of clinical suspicion in patients with no known hematological disorder.[10]

4. Conclusion

ALL presenting as a Sino nasal masses are very rare tumors with an aggressive clinical course. Morphologically, they can mimic a variety of tumors which fall broadly under the category of small round cell tumors. In Paediatric lymphoid orbital tumors, ALL should always be considered in the differential diagnosis due to a significant difference in management. A delay in the diagnosis may result in unwarranted fatality particularly so in paediatric patients. Early detection and antileukemic treatment are necessarily important for a favourable prognosis.

Ethical clearance: The manuscript has been given ethical clearance by the institution ethics committee and patient consent has been taken.

Conflict of interest: there are no conflicts of interest.

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