

The paradox of recurrent with rare: A rare case of bilateral proptosis and facial palsy in acute myeloid leukemia with recurrent cytogenetic translocation t(8:21)

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ABSTRACT

A 13-year-old female child presented with bilateral proptosis and subconjunctival hemorrhage of 2 months duration. Subsequently, the biopsy and peripheral smears confirmed the diagnosis of acute myeloid leukemia (AML). Recurrent cytogenetic translocation t(8:21) in AML associated with extramedullary manifestation; was discovered which is a rare event. Furthermore, myeloperoxidase negative blasts and periodic acid Schiff negative blasts in AML with t(8:21) is a very rare combination to the best of our knowledge.

Key words: Acute myeloid leukemia, bilateral proptosis, cytogenetics

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INTRODUCTION

Acute myeloid leukemia (AML) accounts for nearly 15% of all leukemia in children.^[1] The leukemic cells can infiltrate any extramedullary site, tumorous accumulations within soft tissues and bones; which have been given the term granulocytic sarcomas. The incidence of extramedullary disease seems to be slightly higher in Africa^[2] and Asia.^[3] It is thought that extramedullary disease or granulocytic sarcomas originate in the bone marrow, and the cells are believed to spread via the Haversian canals to collect in the subperiosteum and form soft tissue masses.^[1] Within the head and neck, orbits are commonly affected due to active hematopoiesis.^[1] In cases where the orbital tumor is the initial manifestation, peripheral blood and bone marrow

involvement usually occurs within a year of occurrence of the orbital disease.^[4]

In this report, we describe a case of AML that presented to the ophthalmology clinic with proptosis. A diagnosis of AML was subsequently made by peripheral blood smear or incision biopsy. The patient was also diagnosed with t(8:21), however, the cytogenetic markers most frequently encountered in the translocation were found to be negative. This case emphasizes the importance of the simple tests in the diagnosis of this life threatening hematological malignancy even if the cytogenetics may be negative. The management of these patients still remains a challenge. In our patient; however, bilateral proptosis completely resolved after induction of standard chemotherapy regimen.

CASE REPORT

A 13-year-old girl presented with bilateral proptosis of eyes since 2 months. This patient was never diagnosed with any hematological malignancies. The presenting symptoms included pain in the right ear, purulent discharge, fever, and conjunctival hemorrhage involving both eyes since 2 months. The subconjunctival hemorrhage was more on the right compared to the left. It was not associated with loss of vision in either eye. The constitutional symptoms of weakness, fatigue, and anorexia; accompanied the presentation of the patient. On examination; she was febrile, pale, and

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tachycardic. Bilateral nonreducible proptosis was present; more on the right side as compared to left. Periorbital swelling was present; however, fundus showed normal disc and no retinal hemorrhages were present. Visual acuity was normal, and there was no restriction of eye movements. Pupillary reflexes were normal. Right ear examination revealed discharge; tympanic membrane was dull with a central perforation. Infranuclear right facial palsy was present along with bilateral conductive deafness. Bilateral mastoid tenderness was present. There was no lymphadenopathy. Systemic examination was normal except for mild hepatosplenomegaly.

Investigations revealed anemia with hemoglobin of 6.7 g%, hyperleukocytosis, with total leukocyte count (TLC) of 120000/cu mm; a diagnosis of AML was made by the peripheral smear which had 75% blasts. Bone marrow smear revealed a differential count with blasts predominating (92%), followed by lymphocytes (2%) and the rest was equally constituted by polymorphs, metamyelocytes, and eosinophils; which confirmed the diagnosis of acute leukemia. Blasts were negative for myeloperoxidase (MPO) and periodic acid Schiff (PAS) [Figure 1] however, positive for neuron specific enolase. Blast cells were large with moderate to abundant cytoplasm, high nucleocytoplasmic ratio, lobulated nucleus with fine chromatin with some having reniform nuclei. On cytogenetics; blast cells were positive for t(8:21) (q22, q22) in all metaphases [Figure 2]. Flow cytometry was positive for CD13, CD33, CD117, human leukocyte antigen DR, CD19 and negative for CD3, CD7, CD10, CD20, CD22, MPO. Urine examination, urine culture, blood culture, renal function, coagulation profile, liver function HIV, antinuclear antibodies, antineutrophil cytoplasmic antibody, Vitamin B12 and folate levels, and cerebrospinal fluid (CSF) studies were normal. Direct and indirect coombs test were also negative. Contrast study of head including orbit and paranasal

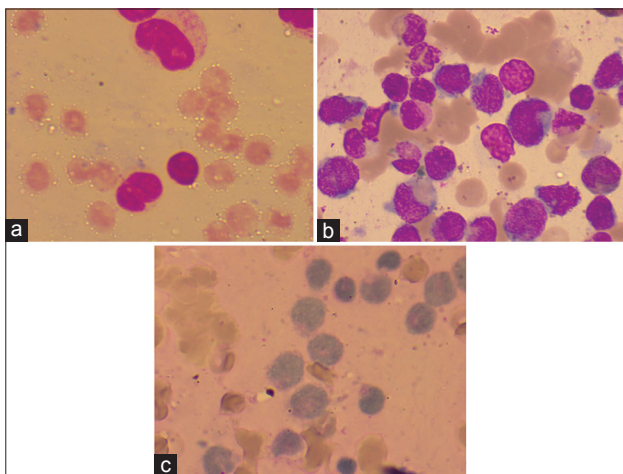


Figure 1: (a) Peripheral smear under oil immersion, (b) bone marrow smear showing blasts negative for myeloperoxidase. (c) Bone marrow blasts negative for periodic acid Schiff

sinuses demonstrated retrobulbar mass, pansinusitis with soft tissue density seen along the roof of both orbits, infiltrates were seen within the orbital isointense to muscle more pronounced on the right. Contrast study of the temporal bone revealed bilateral otitis media and granulation in both of the mastoids [Figure 3]. Further workups viz. ultrasonography abdomen suggested hepatosplenomegaly. Once the diagnosis was established the child was treated with standard chemotherapy regimen and showed improvement suggested by regression of proptosis and improvement of overall clinical status.

DISCUSSION

In children younger than 15 years, the incidence of AML is found to be seven cases per million.^[5] AML occurs from the proliferation of myeloid cells in the bone marrow; and their spillage can be detected on a peripheral blood smear. When the tumorous cells are found in the soft tissue, it is named as granulocytic sarcomas; which accounts for about 3% of cases of AML.^[6]

Acute myeloid leukemia most commonly affects children and young adults. Various Western series reported a median age of 7 years (range: 1–61 years) and some reported 8.8 years in their studies;^[6,7] and our patient was a 13 year old. Other sites affected include the skull, paranasal sinuses, spine, ribs, sacrum, and sternum; involvement being related to the active hematopoiesis at these sites;^[1] which were essentially negative in our case. Cavdar's series reports the diagnosis of leukemia 8 weeks after the orbital symptoms were reported.^[2] Our case, the systemic symptoms were reported 2 months after the onset of proptosis. The differentials include rhabdomyosarcomas, neuroblastoma, Burkitt's lymphoma, neuroblastomas, and Ewing's sarcoma.^[1] The patient usually presents to an ophthalmologist which was also true in our case.

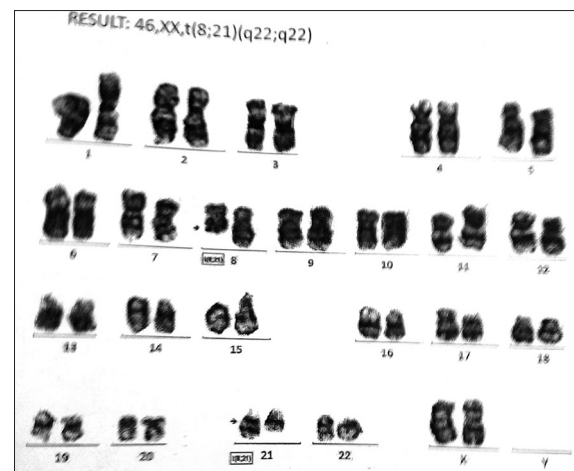


Figure 2: Blast cells positive for t(8:21) (q22, q22) in all metaphases



Figure 3: (a) Contrast showing isointense infiltrates to muscle; more pronounced on the right and bilateral proptosis (arrow). (b) Soft tissue density over the roof of both orbits (arrow). (c) Bilateral otitis media with mastoiditis with granulation tissue /cholesteatoma in the mastoid bone (arrow)

For diagnosing AML, peripheral smear is carried out; which reveals the presence of immature blast cells. The TLC is usually high with a relative neutropenia. Bone marrow examination and flow cytometry should be performed to confirm the diagnosis. The computed tomography (CT) findings have been described as a focal homogeneously enhancing lesion with well-defined margins, usually isodense to muscle^[1] Romanowsky stained (Giemsa) air-dried smears are useful in interpreting the hematologic lesions of leukemia and lymphoma. Immunocytochemistry or immunohistochemistry using an antibody against MPO could confirm the diagnosis. The esterase activity is detected using Leder stain on paraffin-stained slides; which is thought to have a 75% positivity rate.^[6]

The etiology of bilateral proptosis may be ophthalmic or nonophthalmic. The common conditions causing bilateral acute onset proptosis in children are orbital cellulitis, fungal sinusitis with extension to orbits, cavernous sinus thrombosis, bilateral optic glioma, inflammatory pseudo tumor, thyroid ophthalmopathy, rhabdomyosarcoma and neuroblastoma.^[8] Even having bilateral proptosis with facial palsy and hyper leukocytosis in a child would prompt a

clinician to think of acute lymphoblastic leukemia rather than AML.^[9] It was only after normal study of CSF and contrast-enhanced CT head along with paranasal sinuses that revealed cholesteatoma as the cause of infranuclear facial palsy that further differential diagnosis had to be thought of in our case. Further evaluation revealed t(8:21) q22:q22 a recurrent cytogenetic translocation in this case [Figure 3]. Hence, AML with t(8:21) q22:q22 with extramedullary presentation as bilateral proptosis and facial palsy in a 13-year-old girl made a rare combination.

The combination of bilateral proptosis with MPO and PAS negative blasts makes a very rare one. In children; granulocytic sarcoma with t(8:21) does seem to have a major impact on long-term mortality or rate of remission.^[10] Chemotherapy regimens will lead to an adequate remission as was seen in our case. Thus, to conclude t(8:21) can present as bilateral proptosis and even with negative special stains as described above.

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