



MYELOID METAPLASIA IN PAEDIATRIC AXILLARY LYMPH NODES: A RARE PRESENTATION OF INFANTILE OSTEOPETROSIS

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Article Info	ABSTRACT
<p>Received 03/09/2015 Revised 17/09/2015 Accepted 22/09/2015</p> <p>Key words: Osteopetrosis, Myeloid metaplasia, Axillary lymphadenopathy.</p>	<p>Osteopetrosis is a rare congenital, heterogeneous group of genetic disorders characterized by increased bone density due to impaired bone resorption by osteoclasts. Abnormal osteoclast activity paired with normal bone formation by osteoblasts leads to the development of densely sclerotic fragile bones. A seven month old male child presented with bilateral axillary lymphadenopathy of two months duration. On examination small palpable 0.5 cms lymph nodes were found bilaterally. On FNAC these lymph nodes showed features of myeloid metaplasia (extra medullary haematopoiesis). Peripheral smear of the patient showed anemia, thrombocytopenia with features of leukoerythroblastosis. Ultrasound showed hepatosplenomegaly. On X ray patient showed generalised thickening of bones. Bone marrow aspiration attempted was unsuccessful. Final diagnosis of Osteopetrosis with extra-medullary haematopoiesis was established. Myeloid metaplasia in lymph node aspirates of a patient presenting with lymphadenopathy and hepatosplenomegaly should raise strong suspicion of Osteopetrosis, which needs to be confirmed on radiology.</p>

CASE HISTORY

A seven months old male child of a non-consanguineous married couple was brought to the paediatric outpatient department for swellings in both arm pits. These swellings were noted by parents two months ago. There was no history of fever or any other respiratory tract symptoms. Child was born normally and had uneventful post natal history. Child had achieved head control and was not able to stand at the time of presentation. On examination he weighed 5.2 kilograms and measured 85 centimetres in length. There was prominent frontal bossing and wide open anterior fontanel. Single axillary lymph node was palpable on both sides measuring 1.5 and 1.2 centimetres in maximum diameter on right and left sides respectively. Cervical, inguinal and epitrochlear lymph nodes were not palpable. Per abdomen examination was unremarkable. No neurological abnormality was found. Vision and hearing were normal.

MATERIALS AND METHOD

Patient was subjected to fine needle aspiration cytology of the axillary lymph nodes to find out the cause of lymphadenopathy. Cytosmears from both the swellings showed similar findings comprising of polymorphous lymphoid cell population admixed with hematopoietic cells (figure1). Myeloid lineage was represented by many promyelocytes, myelocytes, metamyelocytes and band forms. The cells were cytomorphologically unremarkable. Erythroid lineage was represented by many early, intermediate and late erythroblasts showing normoblastic reaction. A few scattered megakaryocytes were also noted. Cytological diagnosis of myeloid metaplasia in both axillary lymph nodes was given and further investigations were suggested. Hence, the first investigative clue towards the diagnosis was provided by the cytopathologist. Other investigations revealed: Hb: 8.6 gm/dl, ESR: 26 mm in 1st hr, TLC: 30,000/cumm, Neutrophils-24%, Lymphocytes-51%, Monocytes-02%, Eosinophils-04%, Band forms: 03%, Myelocytes: 03%, Metamyelocytes: 02%, Promyelocytes: 05%, Blast cell- 0%. Blood film showed



moderate anisopoikilocytosis of red blood cells, mostly macrocytic. Nucleated red blood cells were also noticed (20/100 WBCs). A fair number of tear drop cells were seen. Platelets were adequate. No hemoparasite was found on peripheral smear. Peripheral smear suggestive of leuko-erythroblastosis was reported and still further investigations were advised. Bone marrow examination to find the cause of leuko-erythroblastosis was done. However, bone marrow aspiration was unsuccessful yielding hemorrhagic smears only.

Further biochemical evaluation showed Serum calcium: 8.7 mg/dL, Serum inorganic phosphate: 4.2mg/dL. Serum electrolytes showed Sodium: 141 mmol /L, Potassium: 4.1 mmol /L, Chloride: 106.4 mmol /L, Total CO₂: 24 mmol /L, Serum Creatinine: 1.6 mg/ dl,

serum alkaline phosphatase: 260 U/L.

Ultrasonographical evaluation showed mild hepato-splenomegaly. Antero-posterior view and lateral view digital radiographs showed increased density of diaphysis of ribs, femurs, body of vertebrae and pelvic bones (figure 2). Also, there was loss of cortico-medullary differentiation with bone in bone appearance (endobone). Hence, a diagnosis of osteopetrosis was made on radiology.

In view of cytological, peripheral smear and radiological findings, a final diagnosis of infantile osteopetrosis with leuko-erythroblastosis and myeloid metaplasia in axillary lymph nodes was given. Patient was referred to higher centre for chemotherapy and is doing well till follow up period of 8 months.

Fig 1. Cytological smear showing polymorphous lymphoid population admixed with precursor myeloid cells and a megakaryocyte.

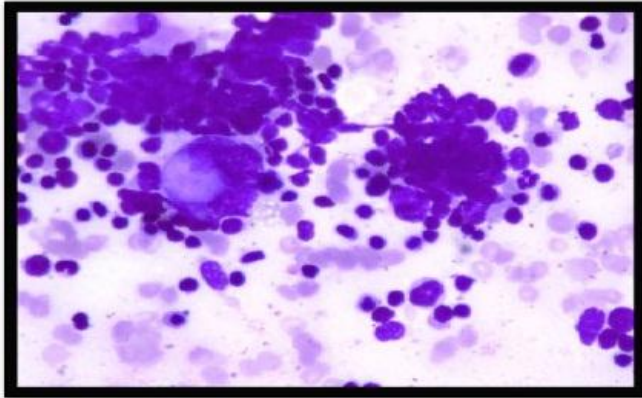
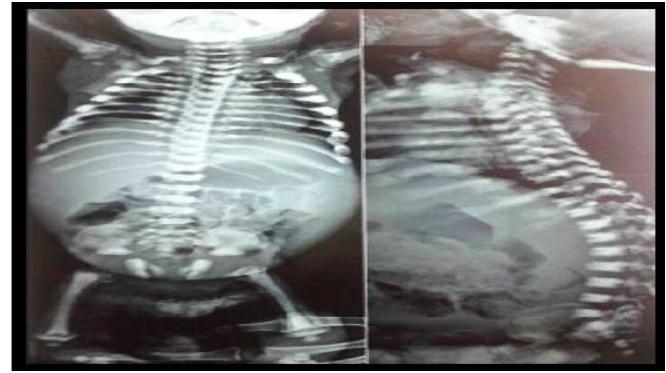


Fig 2. Digital radiograph showing generalised increase in bone density and loss of cortico-medullary differentiation with hand of child's mother showing remarkable contrast



RESULTS AND DISCUSSION

Development and growth of hematopoietic tissue outside of the bone marrow is termed myeloid metaplasia or extramedullary haematopoiesis (EMH). Although essential in fetal life, its occurrence after birth is usually considered abnormal [1]. Common sites are liver, spleen and lymph nodes. It can occur due to primary haematological conditions like myelofibrosis, secondary conditions involving bone marrow like metastasis and conditions leading to ineffective erythropoiesis like thalassaemia [2].

Osteopetrosis is rare developmental bone abnormality characterized radiologically by a generalized increase in density of the bones and failure of tubulation. It was first described by Albers-Schonberg who called it marble bones and later Karshner (1926) designated it as Osteopetrosis which is the term most widely used today [3]. It usually presents as pathological fractures in adults and fever or failure to thrive in infants. Other clinical features include anaemia, optic atrophy and hepato-splenomegaly.

Extramedullary hematopoiesis (EMH), occurring as a compensatory mechanism for bone marrow dysfunction, is almost always associated with hemoglobinopathies,

including thalassemias, sickle cell disease and hereditary spherocytosis (HS), and myelofibrosis, as well as other bone marrow disorders [4]. This case highlights the need to consider skeletal disorders under differential diagnosis while evaluating cases with extramedullary hematopoiesis. The first clue to the diagnosis in our case was the presence of extramedullary hematopoiesis in cytological smears from axillary lymph nodes.

Osteopetrosis, characterised by generalised bone density can occur as autosomal recessive and autosomal dominant disorder, both these forms are congenital abnormalities with localised chromosomal defects. Autosomal recessive osteopetrosis, the more severe form tends to present earlier. Hence, it is referred to as "infantile" and "malignant" compared to its autosomal dominant mate. In osteopetrosis, there is defective osteoclast function and overgrowth of bone: which become thick, dense and sclerotic. However, their increased size does not improve their strength. Instead, their disordered architecture, results in weak and brittle bones that results in multiple fractures with poor healing.

In autosomal recessive osteopetrosis, the defect is located on chromosome 11q13. Presentation may be at birth or children may be still-born. Those who survive,



present with general failure to thrive or bone marrow failure. The present case however did not show features of failure to thrive and was attaining developmental milestones on time.

Other [5] clinical features include cranial nerve entrapment, snuffling (nasal sinus architecture abnormalities), hypercalcaemia, pancytopenia, hepatosplenomegaly, intracerebral haemorrhage, premature senile facies and dental caries. One of the commonest presentations is with ocular disturbance: failure to establish fixation, nystagmus or strabismus. The cause of these symptoms is compression of the optic nerve roots because of foramina overgrowth. This case has unusual presentation as the only complain was axillary swellings.

Differential diagnosis of Osteopetrosis includes conditions, which produce general increase in bone density like fluorosis, myelosclerosis, Engelmann's disease, and sclerosing form of Paget's disease, melorheostosis, lymphoma and osteoblastic cancer metastasis [3]. These differentials however occur in characteristic clinical settings and are relatively easy to exclude.

The prognosis for untreated patients of infantile osteopetrosis is poor, especially in children who have early visual and haematologic impairment [6]. Not infrequently, children are stillborn and most of the remainder have a very poor quality of life with death resulting by the age of ten. Death is secondary to bone marrow failure with recurrent infections, massive haemorrhage or transformation to leukaemia and its sequel. Our case highlights a subset of such cases that do well if diagnosed early.

It is usually unnecessary to treat EMH, with the exception of symptomatic patients. Since extramedullary

hematopoietic tissue is highly radiosensitive at relatively small doses, radiotherapy has been indicated to be an effective method for controlling chronic compression symptoms, while surgical treatment is reserved for immediate symptomatic relief. It has also been reported that the surgical resection of EMH may cause further deterioration of anaemia and promote hematopoietic behaviour in other areas. Therefore, it is important to determine a correct pre-operative diagnosis to avoid unnecessary surgical trauma and improve prognosis.

To the best of our literature search, this is the first case report of infantile osteopetrosis presenting as axillary lymphadenopathy. This case highlights not only a unique presentation of infantile osteopetrosis but also emphasises the need to consider skeletal disorders while evaluating extramedullary hematopoiesis in lymph node by a cytopathologist.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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