Case Report

Intracranial extramedullary hematopoiesis in a thalassemic girl: A Case report

Arpita Varshney, Vikas Barwa, Lalit Saini, Preeti Lamba, Rohtas K Yadav

From, the Department of Radiodiagnosis, PGIMS Rohtak, Haryana, India.

Correspondence to: Dr Arpita Varshney, PG resident, Department of Radiodiagnosis, PGIMS Rohtak, Haryana 124001, India. Email: varshneyarpita@gmail.com

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ABSTRACT

Beta-thalassemia is a haemolytic disorder with ineffective erythropoiesis and red blood cell destruction. Extramedullary hematopoiesis is one of the complications associated with beta-thalassemia. Extramedullary hematopoiesis is the ectopic production of blood cells outside the marrow in liver, spleen, lymph nodes and many other sites. Intracranial involvement is extremely rare. We report a case of 17-year-old girl with thalassemia major and intracranial extramedullary hematopoiesis who came with the complaints of seizure, headache and generalised weakness. Imaging and blood profile leads to the final diagnosis with MRI playing a key role and patient was managed successfully. With this report, we discuss the imaging findings of intracranial extramedullary hematopoiesis in details.

Keywords: Beta-thalassemia, Extramedullary hematopoiesis, Intracranial.

Extramedullary hematopoiesis is production of erythroid, myeloid and megakaryocytic cells outside the usual hematopoietic sites of adults i.e. bone marrow of long bones, ribs and vertebrae [1]. It is a rare compensatory phenomenon occurring in response to chronic bone marrow dysfunction and mostly occurs in liver, lymph nodes and spleen but intracranial occurrence is very rare [2]. Only few cases of intracranial involvement by extramedullary hematopoiesis have been reported so far; however, thalassemia (50%) and myelofibrosis (31%) account for the majority of cases [3]. Extramedullary hematopoiesis can occur in many hematologic disorders and 15% of total cases of beta-thalassemia [3]. Beta-thalassemia is a haemolytic disorder caused by genetic defect in the synthesis of beta globin chain of haemoglobin in red blood cells which causes ineffective erythropoiesis and haemolysis resulting in chronic anaemia. We are presenting a rare case of beta thalassemia with intracranial extramedullary hematopoiesis in a 17-year-old girl.

CASE REPORT

A 17-year-old girl with thalassaemia major on regular treatment and blood transfusion since last 12 years came to our hospital with chief complaints of headache, generalised weakness, shortness of breath for five days and single episode of generalised tonic clonic seizure. Patient had the treatment history of blood transfusion every month. She had no history of any recent illness, intake of medication or illicit drugs, recent head injury, any chemical or toxin exposures and no history of epilepsy or febrile seizures in family. She had a family history of thalassemia with both her parents being thalassaemic minor and her brother being thalassaemic major.

On examination, patient was conscious and well oriented and had blood pressure of 106 mmHg, pulse rate of 120/min and body temperature of 36 degree Celsius. Pallor and icterus was present and massive

hepatosplenomegaly on per abdomen examination. Patient was afebrile, had no signs of raised intracranial pressure. Nuchal rigidity and other signs of meningismus were absent. CNS examination was within normal limits with no focal neurological deficit, normal muscle power, gait and reflexes. Sensory functions and cranial nerves were normal. Other systemic examinations were also normal.

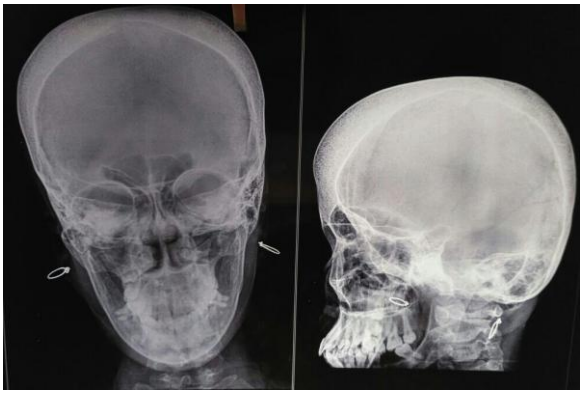


Fig 1 - X-ray skull showing thickened skull bones and hair-on-end appearance.

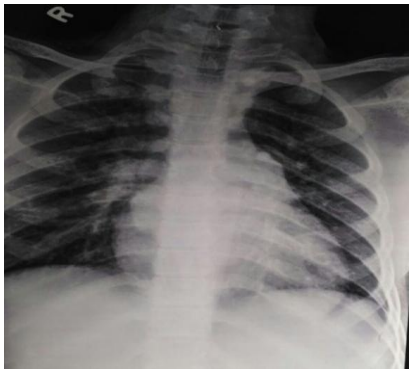


Fig 2 - Chest X-ray PA view shows mediastinal widening and osteopenic ribs.

On admission, her blood sample was sent for laboratory investigations. She had low haemoglobin levels (2.5gm), pancytopenia with low TLC (2100/uL), low RBC count (1 million/uL), low platelet count (20000/uL), low MCV (75fl/red cell), low MCH (26pg/cell), low MCHC (29g/dL), low RDW, dimorphic picture on peripheral blood smear with poikilocytosis and anisocytosis. She had iron overload with high serum iron (630 ug/L), high ferritin levels (178 ug/L), low TIBC (230 ug/L) and transferrin saturation (76%). HPLC results showed HbF 90.7%, HbA2 4.4% and HbA0 5.5%. Laboratory values were diagnostic for thalassemia major with pancytopenia and iron overload. Blood levels of glucose, electrolytes, calcium and magnesium were within normal limits. KFT and LFT were within normal limits with low albumin to globulin ratio. Blood culture was sterile. No abnormality was depicted in EEG.

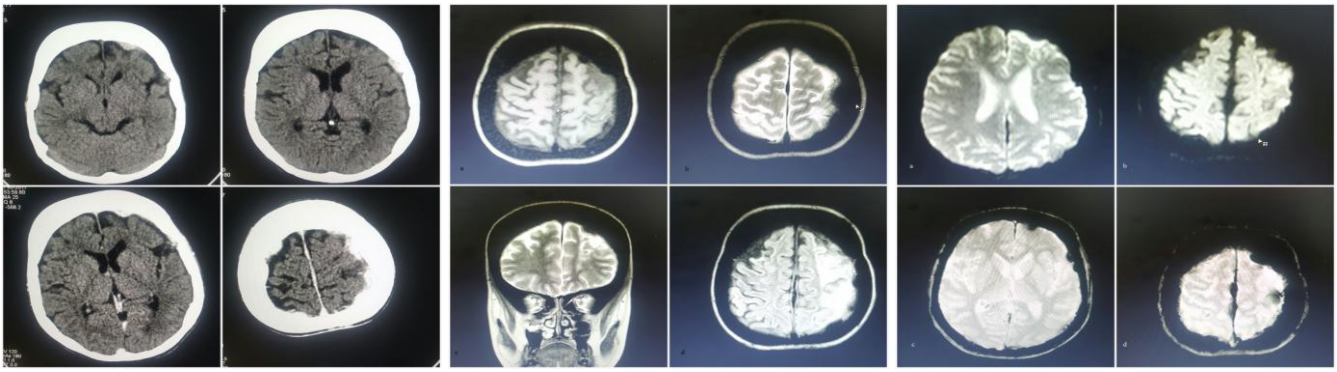
X-ray skull showed thickened calvaria and hair on end appearance (**Fig 1**). X-ray chest showed osteopenic changes in ribs and slight mediastinal widening (**Fig 2**). On ultrasonography, liver was 16.7 cm and spleen was 15.5 cm. CT showed multiple extradural lesions of higher attenuation with density of 62 hounsfield unit in left high frontal and parietal region which showed contrast enhancement with increase in density to 106 hounsfield unit following contrast study and thickened skull bones (**Fig 3**).

MRI examination showed thickened skull bones and few extradural lesions hypointense to grey matter on T1 and hypointense on T2 and FLAIR sequences (Fig 4), hypointense on DWI and blooming on T2* GRE (Fig 5). Imaging findings were consistent with intracranial extramedullary hematopoiesis. However, diagnosis was confirmed by sulfur colloid isotope scan which showed increased uptake in the intracranial lesions and paraspinal location in chest. Biopsy was taken from paraspinal location which was more feasible than intracranial lesions through CT guided procedure.

The specimen showed erythroblasts, megakaryocytes and myeloid cells on histopathological examination suggesting extramedullary hematopoiesis. In this way, final diagnosis of intracranial extramedullary hematopoiesis was made based on blood profile and imaging findings. Patient was managed by regular blood transfusion, splenectomy and low dose radiation therapy for foci of extramedullary hematopoiesis.

DISCUSSION

Beta-thalassemia are a group of genetic hematologic disorders caused by reduced or absent synthesis beta globin chains of hemoglobin and this imbalance result in hemolysis and impaired erythropoiesis [4]. It occurs in three forms thalassemia minor, thalassemia intermedia and thalassemia major among which the major one is most severe form and blood transfusion dependent. Thalassemia major is associated with several complications like iron overload, growth retardation, predisposition towards infections like HIV, hepatitis B and extramedullary hematopoiesis [4].



Figures: Fig 3 - NCCT (upper images) shows extradural hyperdense mass lesions in left frontal and parietal region showing contrast enhancement on CECT (lower images) and thickened skull bones. Fig 4 - MRI showing hypointense extradural mass lesions in left frontal and parietal region on T1 (a), T2 (b & c) and FLAIR (d) sequences Fig 5 - MRI showing low ADC (a), hypointensity on DWI (b) and blooming on T2 GRE (d) in the lesions.

Extramedullary hematopoiesis is a term which is used to describe hematopoiesis outside the bone marrow. It is the compensatory proliferation of pluripotent stem cells outside the bone marrow to meet the body's demand for anemia [5]. Mostly it occurs in liver, spleen and paraspinal region but has been reported in abdominal visceras, pleura, lymph nodes, adrenal glands, breast, thymus, kidneys, gastrointestinal tract and intracranial structures [2]. Extramedullary hematopoiesis occurs in two forms. In one form, there is paraosseous mass that occurs due to rupture of medullary tissue of bone in paraosseous tissue and in other form there is extraosseous soft tissue mass due to proliferation of multipotent stem cells in them. First form occurs in haemolytic disorders like thalassaemia with active bone marrow while the second form occurs in myelofibrosis with inactive bone marrow [6]. Beta-thalassemia accounts for 15% of total cases of extramedullary hematopoiesis. Intracranial involvement is very rare. Intracranially this has been reported in choroid plexus, falxcerebri, optic nerve sheaths, diploic space of skull [2,5,7]. In our case of thalassemia major, extramedullary hematopoiesis was seen in high frontoparietal region over cerebral convexity a rare site.

Intracranial extramedullary hematopoiesis can be an incidental finding or may present with raised intracranial pressure, vision disturbance, sensory and motor deficit, seizures, altered sensorium etc. In this case, patient presented with seizure and headache. Diagnosis can be made by imaging alone in a patient with blood dyscrasia. MRI plays an important role [8]. Laund and Aldridge first described it as extradural mass of higher attenuation as compared to grey matter and showing enhancement after contrast administration [9]. On MRI it is hypo to isointense on T1, hypointense on T2, hypointense on DWI and drop in signal on ADC which mainly occurs due to hemosiderin [8].

Management of such cases mainly include regular blood transfusion and low dose radiation therapy with surgery limited to those cases in which diagnosis is uncertain as there is high risk of bleeding with surgery [1,6]. Differentials to be considered while making diagnosis includes meningioma, neuroblastoma, chloroma, meningeal metastasis, extradural hematoma, granulomatous disease like tuberculosis and sarcoidosis [2,6]. All these differentials can mimic extramedullary hematopoiesis but later mostly occur in the setting of chronic anemia. Meningioma is mostly found in middle age group and has characteristic MR finding of T1 hypointensity, T2 hyperintensity, low intensity on DWI and strong contrast enhancement [6].

Extradural hematoma mostly occurs due to trauma or some coagulation abnormality but never shows enhancement on contrast studies in comparison to hematopoietic lesions. Chloroma occurs in patients of acute myeloid leukaemia in pediatric age group and is iso to hypointense on T1& T2, hyperintense on DWI and shows homogenous contrast enhancement [10]. Meningeal metastases occur in adult population with some primary and are T1 isointense, hyperintense on T2 and DWI and shows contrast enhancement. Granulomas are more hypointense as compared to extramedullary hematopoiesis on T2 and are mostly associated with granulomatous diseases like tuberculosis and sarcoidosis [6].

CONCLUSION

With this case report, we conclude that although rare intracranial extramedullary hematopoiesis should be kept in mind while diagnosing an intracranial mass lesion in a thalassemic patient with neurological symptoms as a simple diagnosis can help in better management of patient.

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