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E Parano V Pavone F Di Gregorio P Pavone R R Trifiletti

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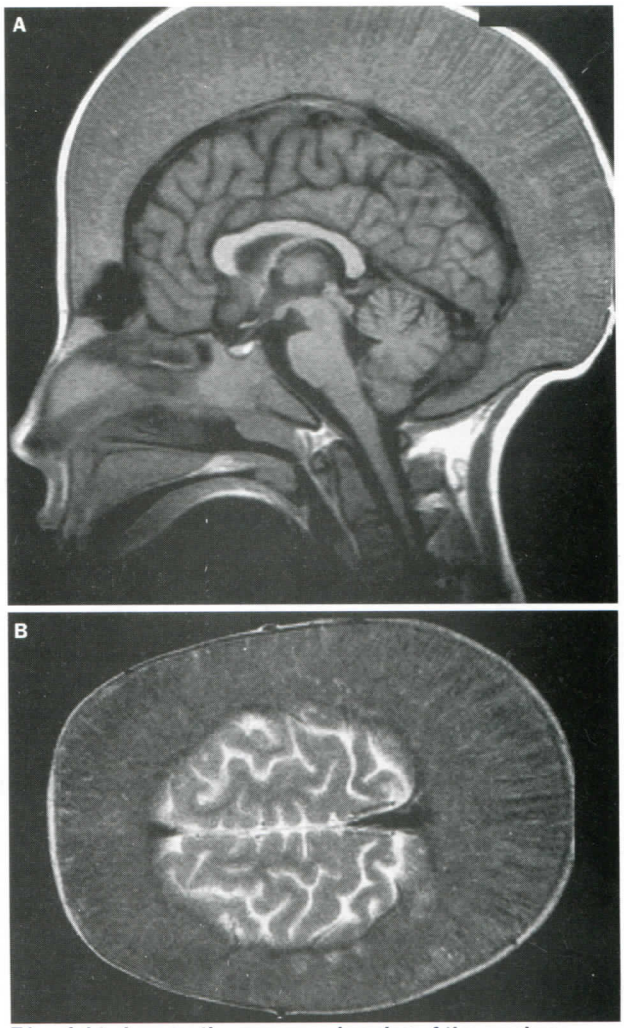
We report on a patient with thalassaemia which was refractory to blood transfusions. The clinical picture was striking, and highlights the potential severity of intrathecal bone reactions after chronic intractable haemolytic anaemia.

A Sicilian girl was born to unrelated parents known to be heterozygous for β-thalassaemia. She was first seen at age 5 years, with pallor and failure to thrive. At that time she had only mild facial abnormalities. She was anaemic, with a haemoglobin concentration of 8·0 g/dL; haemoglobin electrophoresis showed 95·0% haemoglobin F and 5·0% haemoglobin A_2. Molecular genetics analyses showed a homozygous β-039 mutation. A diagnosis of β-thalassaemia was made.

Blood transfusions were deferred until age 9, since haemoglobin remained in the range 7–9 g/dL; this finding suggested thalassaemia intermedia. Because of progressive craniofacial deformity, three attempts at blood transfusion were made, but each induced severe Coombs-positive haemolytic anaemia. Severe haemolysis ensued, and was refractory to treatment with intravenous methylprednisolone (300 mg/day), intravenous γ-globulin (1 g/kg for 5 days), and cyclosporin. Haemoglobin concentrations fell to 3–4 g/dL; after splenectomy, they rose to 6–8 g/dL. No further transfusions were attempted over the next 5 years, and her craniofacial deformities progressed. Magnetic resonance imaging was done at age 14·2 years to assess these deformities; scans revealed a massive intrathecal bone reaction with normal brain anatomy (figure). Her neurological examination remained normal. Several months later the patient suddenly developed haematemesis and epistaxis. Acute pulmonary oedema, cardiovascular collapse, and asystole ensued.

Intrathecal bone reactions were commonly seen in patients with β-thalassaemia and other severe anaemias before the introduction of long-term hypertransfusion protocols in the 1960s, and before the availability of modern cranial imaging.[1–3] Among the several hundred patients with β-thalassaemia seen at the University of Catania over the past 30 years, only a small number have developed intrathecal bone reactions, and none has had a reaction as severe as that in this child. β-thalassaemia intermedia is a form of homozygous β-thalassaemia characterised by mild haemolytic anaemia (haemoglobin concentrations of 7–9 g/dL) which usually does not require blood transfusion. Our patient developed progressive craniofacial deformities, which led to several attempts at blood transfusion despite stable haemoglobin concentrations. Because of severe alloimmune haemolytic reactions, however, such transfusions had to be aborted. We believe that the severe, intractable haemolytic anaemia accelerated the bone reaction and led to the massive skull thickening evident at age 14.

The images show an extreme example of the greatly widened diploic space, and a "hair-on-end" appearance of the skull bone. There is pronounced expansion of the skull base and maxilla, associated with severe orthodontic deformities. The skull is very osteopenic, particularly in the frontal area. In contrast to the severe bone deformities, the brain, dwarfed by its bony cradle, remains normal in size and structure.



T1-weighted magnetic resonance imaging of the cranium
A, sagittal view; B, axial view. Note massive enlargement of all skull bones.

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1 Reimann F, Gökmen E. The brush skull: a review on occurrence, radiology, anatomy, course and meaning of this symptom—V, changes in the skeleton in severe blood diseases. *Blut* 1969; **19:** 423–37.
2 Reimann F, Kuran S. Cause, origin and nature of the "brush-like" symptom on the skull in severe blood disorders: VI, studies on the alterations of the skeletal system in severe blood diseases. *Virchows Arch A Pathol Anat* 1973; **358:** 173–91.
3 Orzincolo C, Castaldi G, Scutellari PN, Franceschini F. The "lamellated" skull in beta-thalassaemia. *Skeletal Radiol* 1989; **18:** 373–76.

Department of Neurology and Neuroscience, Cornell University Medical College, New York, NY, USA (E Parano MD, R R Trifiletti MD); **Institute of Bioimaging and Physiopathology of the Central Nervous System, National Research Council of Italy** (E Parano); **and Orthopaedic Clinic** (V Pavone MD) **and Paediatric Clinic, University of Catania, Catania, Italy** (F Di Gregorio MD, P Pavone MD)

Correspondence to: Dr Enrico Parano, Clinica Pediatrica, Università di Catania, Viale Andrea Doria 6, 95125 Catania, Italy
(e-mail: parano@mbox.unict.it)

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