

Headache and Scalp Edema in Sickle Cell Disease

Giovanna Pari and Hyman M. Schipper

ABSTRACT: *Background:* Major neurological complications of sickle cell disease include cerebral infarction and intracranial hemorrhages. *Methods:* We describe the case of a 25-year-old man with sickle cell disease who developed a severe headache of acute onset, located at the vertex. There was associated pitting edema of the scalp. *Results:* Technetium and gallium bone imaging showed focal decreased uptake of the tracers, consistent with a recent fronto-parietal skull infarction. Management included intravenous hydration and analgesic medication. *Conclusions:* In addition to the more common intracranial vaso-occlusive complications, skull infarction should be considered as a cause of new-onset headache in patients with sickle cell disease, especially if scalp edema is present.

RÉSUMÉ: *Anémie falciforme: céphalée et oedème du cuir chevelu.* *Introduction:* Les infarctus cérébraux et les hémorragies intracrâniennes constituent les principales complications neurologiques de l'anémie falciforme. *Méthodes:* Nous présentons le cas d'un homme de 25 ans avec anémie falciforme qui a développé une céphalée intense, d'apparition soudaine, localisée au vertex ainsi qu'un oedème local. *Résultats:* Des scintigraphies au technétium et au gallium ont démontré une hypcaptation de la région du vertex, suggérant la présence d'un infarctus du crâne. Le traitement a consisté en une hydratation par voie intraveineuse et une analgésie. *Conclusions:* Nous concluons que l'infarctus crânien doit être considéré dans le diagnostic différentiel des céphalées aiguës chez les patients avec anémie falciforme, en particulier s'il y a un oedème du cuir chevelu.

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Sickle cell disease is known to have multiple neurological complications related to vascular occlusion. The latter are a major source of mortality and morbidity in up to 26% of affected individuals.¹ Neurological complications of sickle cell disease include cerebral infarctions, intracerebral and subarachnoid hemorrhages, meningitis, and fat emboli.¹⁻³ A syndrome of headache, proptosis, and unilateral lid edema secondary to orbital bone infarction has been rarely reported.⁴

We report a patient with sickle cell anemia presenting with a severe headache and the unusual finding of pitting edema of the scalp.

CASE REPORT

A 25-year-old East-African man with known sickle cell anemia presented with a 3 day history of severe headache and scalp swelling. Since childhood, he has had several admissions for painful crises each year and required at least twenty transfusions in the last ten years while in Zaire. The patient also has a history of previously treated malaria, glucose-6-phosphate dehydrogenase deficiency, and osteomyelitis of the left tibia in 1991. The patient had a negative test for the human immunodeficiency virus in 1993. There is no history of chest syndrome or previous neurological, renal, or ocular complications of sickle cell disease.

Three days prior to admission, the patient was awakened by a severe, throbbing headache located bilaterally at the vertex. He felt generally weak and diaphoretic. On the day prior to admission, he noted non-painful swelling over the forehead and scalp. The headache was exacerbated when the patient was in an upright position, and it was not relieved by codeine. There was no associated nausea or vomiting, photophobia, sonophobia, visual change, or focal sensory-motor symptoms. Concomitant with the headache, there was left shoulder and elbow pain, which was typical of many prior crises.

On examination, the patient appeared in moderate distress with a temperature of 37.5°C, arterial blood pressure of 115/70 mm Hg, and a regular heart rate of 84/min. Head examination was remarkable for pitting edema of the vertex and forehead which was more marked on the right side. No meningeal signs were present. Conjunctivae were pale. Cardiac auscultation revealed a grade II/VI systolic ejection murmur at the left lower sternal border. Chest and abdominal examinations were normal. There was a small area of tenderness over the left scapula and shoulder. There were several scars from previous osteomyelitis over the left tibia. On neurological examination, the patient was alert and fully oriented. Cranial nerve, motor, sensory and coordination testing was entirely normal. Reflexes were 2+ and symmetrical, and plantar responses were flexor.

Laboratory studies showed a normocytic anemia with a hemoglobin level of 6.4 g/dl, hematocrit of 19.4, white blood cell count of 15 500/mm³ and a normal platelet count. Blood smears showed anisocytosis and poikilocytosis, with sickle, fragmented, and target cells. Prothrombin and partial thromboplastin times were normal. Serum iron and total iron binding capacity were 6 µmol/l (normal values: 7-32 µmol/l) and 54 µmol/l (normal values: 45-73 µmol/l) respectively, with an iron saturation of 0.11 (normal values: 0.20-0.55). The serum ferritin was increased at 2324 µg/l. Folate level was above normal; vitamin B₁₂ level was normal. Biochemical tests were normal with the exception of increased serum lactate dehydrogenase and alkaline phosphatase at 455 u/l and 234 u/l, respectively. Human immunodeficiency virus and blood malaria tests were negative. A lumbar puncture showed normal

From the Department of Neurology, Jewish General Hospital, McGill University, Montreal.

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Presented in part, at the 7th International Headache Congress, September 16 - 20, 1995. Reprint requests to: Dr. Hyman M. Schipper, Department of Neurology, Jewish General Hospital, 3755 Cote St. Catherine Road, Montreal, Quebec, Canada H3T 1E2

cerebrospinal fluid glucose, protein, and cell count. Cerebrospinal fluid culture and cryptococcus latex antigen were negative.

A brain computed tomography (CT) scan demonstrated normal brain parenchyma with marked extracranial soft tissue swelling in the right, and to a lesser extent in the left, fronto-parietal region (Figure 1a). Bone windows showed widening of the skull's diploic space characteristic of sickle cell anemia (Figure 1b). Skull roentgenographs showed similar diploic thickening as well as thinning of the cortical bone outer table (not shown). Doppler ultrasound revealed patent jugular veins bilaterally.

A radionuclide bone imaging study was performed two hours after the administration of 25 mCi of technetium 99m methylene diphosphate (^{99m}Tc] MDP). A flow study of the head demonstrated diffuse hyperemia of the calvarium with the exception of a focal area with marked decreased flow in the midline parietal region (Figure 2a). Delayed bone tracer images of the skull showed the same area of decreased uptake in the midline parietal region, consistent with bone infarction (Figures 2b, 2c). Gallium imaging also demonstrated decreased uptake in this region (Figure 3) thereby excluding osteomyelitis. Images of the remainder of the skeleton showed evidence of recent bone infarcts in the left humeral head and proximal right femur. Areas of increased uptake in the right humeral head, left hip and right sacroiliac joint regions were consistent with healing infarcts.

The course in hospital was uncomplicated and hematological parameters remained stable. The patient received intramuscular meperidine analgesia and intravenous hydration. After seven days in hospital, he was discharged with decreased swelling of the scalp and headache severity.

DISCUSSION

We presented the case of a young man with a severe throbbing headache and sickle cell anemia. Bone and gallium scans showed a focal area of decreased uptake of the radionuclide, consistent with a fronto-parietal skull infarction. In bone infarctions, there is typically decreased uptake during the first several

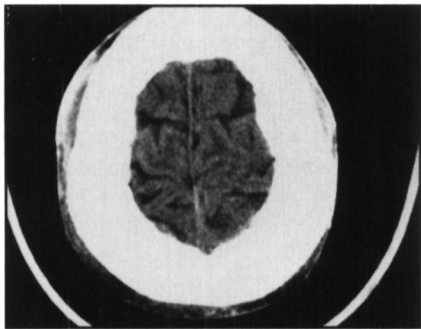


Figure 1a: A CT scan of the head shows extracranial soft tissue swelling, with normal brain parenchyma.

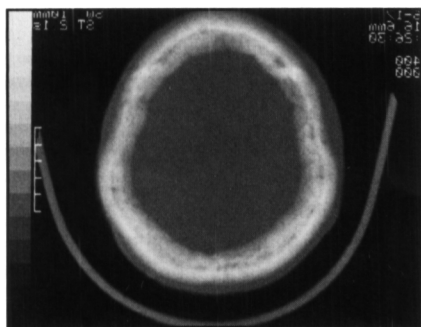


Figure 1b: Bone windows show widening of the diploic space of the skull, consistent with sickle cell anemia.

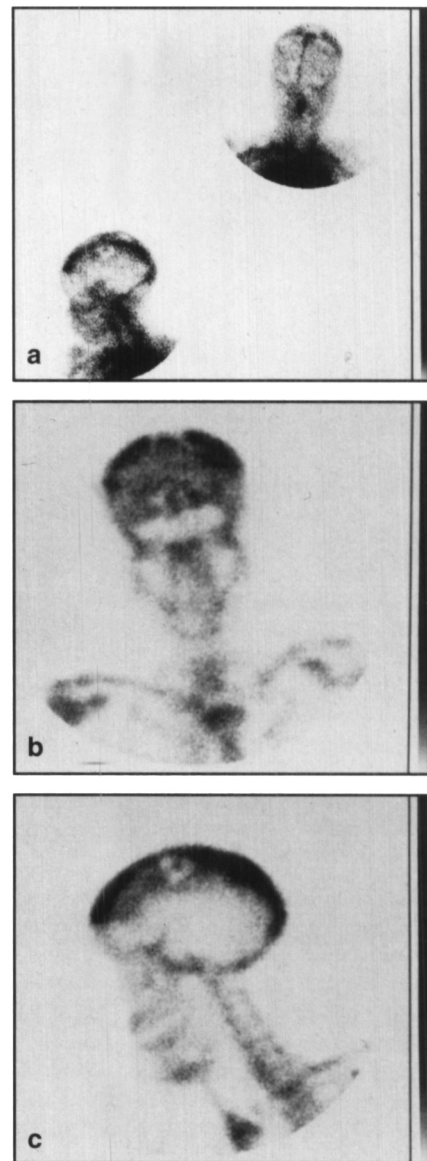


Figure 2: Technetium bone scan. Anterior and left lateral blood pool images (a) taken one minute after injection of 25 mCi of ^{99m}Tc -MDP. Bone tracer demonstrates diffuse hyperemia in the thickened calvarium and a focal area of decreased flow in the midline parietal region. Anterior (b) and left lateral (c) delayed bone tracer images demonstrate a focal area of decreased uptake in the midline parietal region indicating a recent focal infarction. Diffuse increased uptake in the calvarium is also present, consistent with bone marrow expansion related to hemolytic anemia.

days after the acute injury, followed by increased uptake as reactive hyperemia and new bone formation progress. Painful crisis in sickle cell anemia most frequently presents with pain in the lumbosacral spine, ribs, femur or abdomen.⁵ These crises are due to sludging of sickled erythrocytes, increased blood viscosity, and deposition of fibrin and platelets. These rheological changes lead to occlusion of the microcirculation, and consequently infarction and bone marrow necrosis. Painful symptoms occur in areas where marrow is present, and appear to result from increased intramedullary pressure and from the acute inflammatory response to bone marrow necrosis.⁵ Infarctions occur more frequently in long bones such as the femur, tibia,

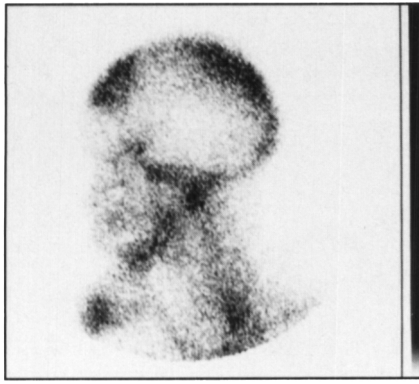


Figure 3: A left lateral 48 hour gallium-67 citrate image demonstrates decreased uptake in the parietal abnormality, thereby excluding the presence of osteomyelitis.

and humerus. Calvarial infarcts have been rarely documented.⁶⁻⁸ This infrequent occurrence may relate to the abundant blood perfusion of the skull via multiple nutrient vessels, or to the relative paucity of active bone marrow in the skull. Skull pain has been observed in 5.5% of subjects in a prospective study of 183 painful crises.⁵ However in only one case of documented calvarial infarction was headache a prominent symptom.⁶ The precise incidence of skull infarction in sickle cell patients with headache has not, to our knowledge, been delineated.

A major concern in sickle cell patients presenting with severe, acute onset headache is cerebral infarction or hemorrhage. Parenchymal as well as subarachnoid hemorrhages secondary to aneurysmal rupture have been amply documented.^{9,10} Stroke in patients with sickle cell disease has been associated with headache in up to 14% of cases in one study.¹¹ Although CT scans of the brain and cerebrospinal fluid studies are usually necessary to confirm the diagnosis of stroke or hemorrhage in these patients, the presence of pitting scalp edema, as illustrated by the present case, indicates involvement of extraparenchymal tissues.

Headache in calvarial infarction may originate from pain sensitive structures such as the skull, dura, periosteum, and extracranial arteries. The presence of scalp edema noted in this

patient is likely secondary to the inflammatory response to marrow necrosis within the infarcted calvarium and fluid extravasation into the overlying tissues.

In patients with sickle cell disease who present with acute-onset headache, the presence of pitting scalp edema is a useful clinical sign differentiating relatively benign skull bone infarction from the more ominous cerebral infarctions and hemorrhages commonly seen in this condition. Radionuclide scanning is useful in confirming the diagnosis and excluding complicating osteomyelitis. Transfusion of red cells may not be necessary if hematological parameters are stable. Fluids and analgesics may be sufficient for the management of uncomplicated skull infarction in patients with sickle cell anemia.

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