

## Letters to the Editor

### First report of osteonecrosis of the calcaneum in a young Kuwaiti female with hemoglobin E/ $\beta$ thalassemia

Sirs,

The occurrence of osteonecrosis in the setting of sickle cell anemia is well known (1), whereas its occurrence in patients with  $\beta$ -thalassemia is decidedly rare (2, 3). Osteonecrosis occurring in patients with hemoglobin E/ $\beta$ -thalassemia has not been described so far in the world literature.

A 28-year-old unmarried Kuwaiti woman, born of a second-cousin marriage within the Al-Shatti tribe of Kuwait, and under treatment for  $\beta$ -thalassemia major, presented with excruciating pain around the left heel. Clinically she was jaundiced, and had moderate hepatomegaly with typical bronzed facies. The left calcaneum was acutely tender.

Results of hematological investigations (with normal values in brackets) showed normal ESR, hemoglobin 109 g/L (115-165), hematocrit 0.350 L/L (0.37-0.47), MCV 86.2 fL (76-98), MCH 27.4 pg (27-31), MCHC 308 g/l (310-350), and platelets  $428 \times 10^9/L$  (150-400). The WBC count was markedly elevated ( $113 \times 10^9/L$ ) due to the presence of circulating normoblasts. Corrected WBC count was  $4.0 \times 10^9/L$ . The blood film showed abundant circulating normoblasts, polychromatic cells, target cells and Howell-Jolly bodies.

MRI of the left ankle (Fig. 1) showed heterogeneous signals with coarse trabeculation in keeping with the changes of thalassaemia. Two well-defined bony lesions



**Fig 1.** T2 WI fat saturated MRI image of the left ankle showing two well defined bony lesions at the anterior aspect of the calcaneum: one just posterior to the cubo-calcaneal joint and measuring 11 x 9 mm, and the second posterior to it measuring 13 x 7 mm.

were noted at the anterior aspect of the calcaneum, one measuring 11 x 9 mm, and the second posterior to it measuring 13 x 7 mm. Both lesions were consistent with avascular necrosis, having high signal intensity in T2 WI fat saturated images in keeping with fluid containing lesions with thin sclerotic margins. Three-phase bone scan showed a photon-deficient defect in the left calcaneum, corresponding anatomically with the lesions demonstrated by MRI, and "cold" in all 3 phases.

Hemoglobin electrophoresis showed an elevated level (35.2%) of fetal hemoglobin (HbF). An additional band amounting to 32% of the total hemoglobin was identified as HbE. High levels of hemoglobin A were also present. Based on previous electrophoretic findings, the patient was diagnosed as having double heterozygosity for Hb E disease and  $\beta$ -thalassemia. These results were confirmed by high performance liquid chromatography. The parents of the index case were also investigated. The father was found to be carrying the beta-thalassaemia trait while the mother was shown to have the HbE trait.

Osteonecrosis in sickle cell disease is presumably due to the plugging of introsseous vessels by sickled erythrocytes (4). Contrary to the situation in sickle cell disease, however, standard textbook teaching states that osteonecrosis is not a feature of thalassaemia because there is no sickling of the red cells and hence no thrombosis leading to bone infarction (5). However, osteonecrosis of the femoral head was described in 1986 in 4 patients with homozygous  $\beta$ -thalassaemia. (6) Osteonecrosis of the femoral head and distal femur was again described in two patients with  $\beta$ -thalassaemia major in 1994. (3) A case report of osteonecrosis of the femoral head occurring in a patient with thalassaemia minor has also been published (7).

Nevertheless, there have thus far been no reported cases of osteonecrosis in the setting of HbE/ $\beta$ -thalassaemia. The latter genotype, characterized by compound heterozygosity for the HbE and  $\beta$ -thalassaemia genes, can phenotypically present as  $\beta$ -thalassaemia intermedia or  $\beta$ -thalassaemia major, depending on the severity of the co-inherited thalassaemic gene. The presentation in our patient was that of  $\beta$ -thalassaemia major. The site of involvement in our patient is also peculiar since all the six previously described cases (3, 6) were localized to the femur. It can be speculated that the high numbers of circulating normoblasts in our patient, perhaps coupled with dehydration, contributed to a hyperviscosity state, causing thrombosis in the calcaneal vessels with resultant multiple foci of osteonecrosis.

It is noteworthy that both sickle cell anemia

(8) and thalassaemia (9) are common in Kuwait. Consanguinity is probably the reason why this problem is common here, as exemplified by the fact that approximately 80% of 129 beta-thalassaemia major patients analyzed were the offspring of first- or second-cousin marriages (9).

The present case is unique in several respects. It is the first report of osteonecrosis in a patient with HbE/ $\beta$ -thalassaemia. It is also the first description of calcaneal osteonecrosis in the setting of thalassaemia major, and the first report of osteonecrosis in thalassaemia from Kuwait.

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### References

1. MILLER PF, KRAUS AP, SEBES JI *et al.*: Sickle cell disease as a cause of osteonecrosis of the femoral head. *N Engl J Med* 1991; 325: 1476-81.
2. ORZINCOLO C, SCUTELLARI PN, BARIANI L, PINCA A, BECCARI G, CASTALDI G: Aseptic necrosis of the head of the femur in Cooley's disease. *Radiol Med (Torino)* 1986; 72: 102-4.
3. KATZ K, HOREV G, GOSHEN J, TAMARY H: The pattern of bone disease in transfusion-dependent thalassaemia major patients. *Isr J Med Sci* 1994; 30: 577-80.
4. SMITH JA: Bone disorders in sickle cell disease. *Hematol Oncol Clin North Am* 1996; 10: 1345-56.
5. GILLILAND BC: Relapsing polychondritis and other arthritides. In BRAUNWALD E, FAUCI AS, KASPER DL *et al.* (Eds.): *Harrison's Principle's of Internal Medicine*, 5th ed., New York, McGraw Hill 2001; 2005-16.
6. ORZINCOLO C, CASTALDI G, SCUTELLARI PN, BARIANI L, PINCA A: Aseptic necrosis of femoral head complicating thalassaemia. *Skeletal Radiol* 1986; 15: 541-4.
7. RIZK NN, NASR FW, FRAYHA RA: Aseptic necrosis in thalassaemia minor. *Arthritis Rheum* 1977; 20: 1147-8.
8. ADEKILEAD: Sickle cell disease in Kuwait. *Hemoglobin* 2001; 25: 219-25.
9. AL FUZAE L, ABOOLBACKER KC, AL SALEH Q: Beta-thalassaemia major in Kuwait. *J Trop Pediatr* 1998; 44: 311-2.