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YOUR DIAGNOSIS

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Painful hand and foot swelling in a 6-month-old girl

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Clinical information

A 6-month-old female baby was admitted to our hospital because of an acute painful swelling in her left hand and foot. Her parents and three brothers were African in origin but the baby was born in Italy. The family history was unremarkable for rheumatic or auto-immune diseases. In the past medical history there was prolonged neonatal jaundice due to glucose-6-phosphate dehydrogenase (G6PDH) deficiency. No recent trauma was referred. One month before our observation the mother noticed a slight swelling on both hands and feet, interpreted as insect bites which spontaneously disappeared after a few days.

On admission the clinical examination revealed a nice, well-nourished girl in good clinical condition with a painful swelling on the dorsal aspect of the left hand and foot. Ankle and wrists were mobile with no signs of inflammation. The skin was intact with normal colour and temperature. Fever (38.5°C) and concomitant upper airway infection were also present. The growth and the psychomotor development were adequate for age. Laboratory studies showed: normocytic anaemia (RBC 3600000/mm^3, Hb 8.5 g/dl, haematocrit 27.2%, MCV 75.6 fl, reticulocytes 11.7%), WBC 11400/mm^3, platelets 289000/mm^3 and indirect hyperbilirubinaemia (2.11 mg/dl). ESR, CRP, liver and renal function tests, serum immunoglobulins (IgG, IgA, IgM), protein electrophoresis and complement fractions (C3, C4) were normal for age. Direct and indirect Coombs tests were negative. Blood culture, Mantoux and VDRL tests and serology for the main respiratory virus were also negative. Urinalysis was unremarkable. Standard X-ray films of both hands and feet revealed no bone lesions.

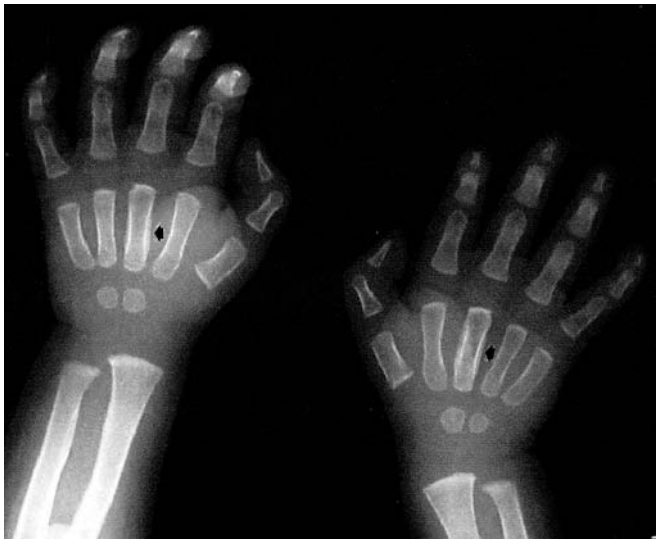

Fig. 1 Standard X-ray film of the hands 3 weeks after onset of symptoms. Periosteal apposition is visible in the third right and left metacarpal bones (*arrow*)

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Diagnosis: hand-foot syndrome in sickle cell anaemia

Normocytic anaemia, with reticulocytosis, indirect hyperbilirubinaemia and negative Coombs test suggested a haemolytic non-autoimmune process. The peripheral blood smear showed sickle RBC and the sickle testing was positive. The diagnosis was confirmed by haemoglobin electrophoresis showing a percentage of HbS as high as 75%. Both her parents were found to be heterozygotes for sickle cell anaemia (SCA) and G6PDH deficiency. The painful swelling of hands and feet was interpretated as "hand-foot syndrome", an acute dactylitis, which occurs in infants and young children with SCA between 6 months and 2 years of age.

Treatment was symptomatic, including oral and parenteral hydration, analgesics (acetaminophen), a course of oral antibiotic and a blood transfusion to dilute the circulating sickle red cells and improve the microvascular perfusion. Two weeks later the standard X-ray film of the hands showed evidence of periosteal repair reaction in the third left and right metacarpal bones (Fig. 1).

Discussion

Main signs and symptoms pointing to the diagnosis of SCA are normocytic anaemia, reticulocytosis and increased indirect bilirubinaemia in a black child. Sickle testing and haemoglobin electrophoresis confirm the suspicion. Differential diagnosis of a sudden, contemporary painful swelling of hands and feet in a 6-month-old girl also includes various causes.

In our patient, the medical history and normal standard X-ray film on admission ruled out a traumatic lesion. Normal acute phase reactants (ESR, CRP and protein electrophoresis), leukocyte count, Mantoux and VDRL tests and culture for virus and bacteria excluded an infectious process such as septic arthritis, osteomyelitis, tuberculosis or syphilis. Radiological and haematological findings and the normal LDH and ferritin values, made a tumour and leukaemia unlikely. Storage diseases were improbable because they are usually accompanied by general symptoms (stunted growth, psychomotor development delay, etc) other than osteoarticular complaints [3].

Among the various kinds of haemoglobinopathies, homozygous sickle cell disease is a frequent cause of musculoskeletal symptoms [1, 4,6]. It is found mainly in black individuals living or coming from regions where *P. Falciparum* malaria is endemic (Equatorial Africa, India, USA, Caribbean Islands and Brazil). Association with G6PDH deficiency is not rare, but does not modify the course of the disease [2,5]. Characteristic of the sickle haemoglobin (HbS) is the substitution of glutamic acid at the 6th position of its β-chains by valine [4,6]. This haemoglobin, in deoxygenated conditions, polymerises with subsequent damage of the erythrocytes [4,6]. Polymerisation is also dependent on fetal haemoglobin concentration, body temperature, acidosis or dehydration. Sickle cells aggregate and interact with the vascular endothelium causing occlusion of small and, sometimes, large blood vessels with various types of ischaemic manifestations [4,6].

Musculoskeletal symptoms in SCA include acute arthritis, osteonecrosis, particularly of the femoral head, *Salmonella* septic arthritis and, as in our patient, the so called "hand-foot syndrome" [1,4]. This is, essentially, a dactylitis due to an ischaemic necrosis caused by the rapidly expanding bone marrow that chokes the blood supply. It is, frequently, the first manifestation of SCA in infants, since affected newborns are usually asymptomatic [1,4]. The clinical picture is characterised by acute painful swelling of one or more extremities, accompanied by fever and leukocytosis. As in our patient, the standard X-ray film is initially negative; 2–3 weeks later, areas of bony destruction with periosteal reaction may appear. The episodes are usually self-limiting but tend to recur [1, 4,6]. The treatment is symptomatic including oral and parenteral hydration, analgesics, antibiotics and blood transfusion. As far as the general treatment of SCA is concerned, new therapeutic approaches include the use of hydroxyurea to induce HbF synthesis, sodium cromoglycate for its antisickling activity and, most important, bone marrow transplantation [1, 4,7].

SCA, rare in Europe a few years ago, is now more and more common because of the higher influx of populations from Equatorial Africa and India. This condition should be considered in the differential diagnosis, as a cause of painful limbs in young children, particularly when they belong to an ethnic group at risk for this disease.

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