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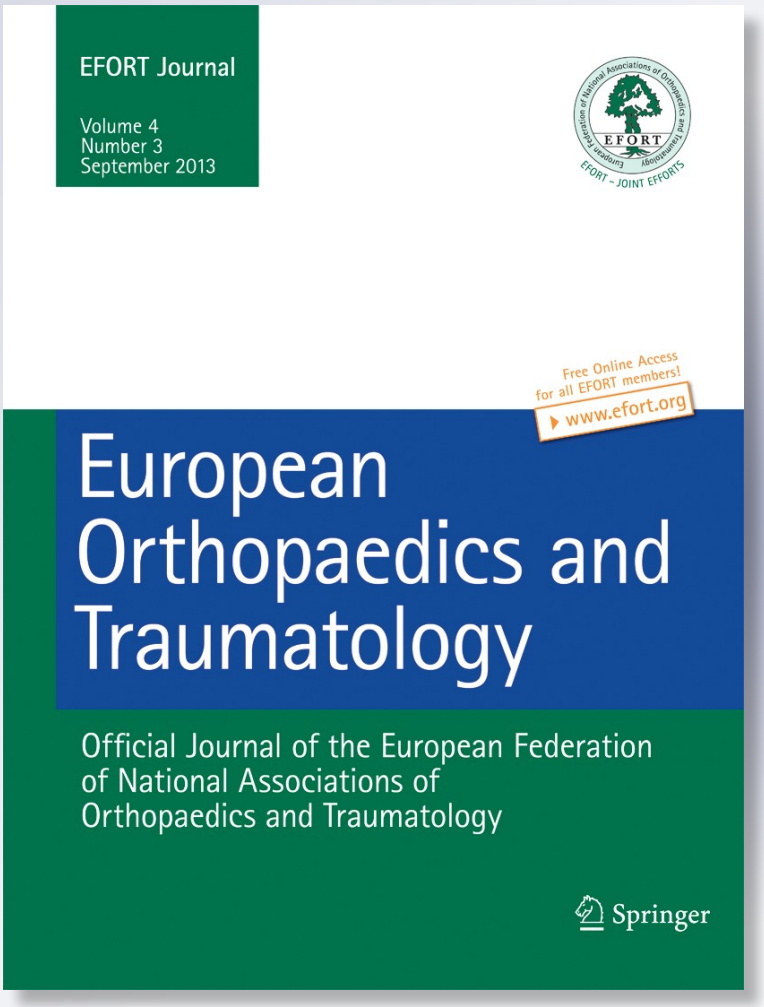

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CASE REPORT

Femoral bowing and consequent stress fracture in an adolescent with glucose-6-phosphatase dehydrogenase deficiency: first reported case

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Background

Lower extremity bowing in children is common and a frequent cause of orthopaedic referral. The role of the orthopaedic surgeon is to determine if the bowing is physiological or pathological. Recognition of the underlying pathology is of paramount importance as it enables one to differentiate between those that will resolve spontaneously and those that require treatment [1, 2]. Physiological bowing is a common condition that causes exaggeration of normal age-related angulation at the knee joint. It is normal for neonates and infants to have a varus angulation of the lower limbs and this is thought to be secondary to neonatal moulding. In most cases, correction of femoral bowing begins as the child starts walking and is considered abnormal if it persists after the age of 2. Symmetrical bowing of the long bones is a constant feature of certain skeletal dysplasias (Campomelic dysplasia, Stüve–Wiedemann syndrome and kyphomelic dysplasia), although it is also common to certain metabolic diseases (rickets, hypophosphataemia and osteogenesis imperfecta), other haemolytic diseases, neoplasia and post-trauma.

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G6PD deficiency is the most common human enzyme defect, affecting more than 400 million people worldwide, mostly in people of African, Middle Eastern or South Asian descent. It is an X-linked recessive disease characterised by abnormally low levels of glucose-6-phosphate dehydrogenase, an enzyme involved in red blood cell metabolism. All mutations that cause G6PD deficiency are found on the long arm of the X chromosome, on band Xq28. Sufferers may exhibit non-immune haemolytic anaemia in response to a number of causes, most commonly infection or exposure to certain medications. The majority of individuals are however asymptomatic. Symptomatic patients are almost exclusively male, due to the X-linked pattern of inheritance, but female carriers can be clinically affected due to unfavourable lyonization. Clinical manifestations are essentially those of acute haemolysis such as anaemia (fatigue and heart failure), jaundice and acute renal failure. The World Health Organization classifies G6PD genetic variants into five classes, from increased enzyme activity with no clinical sequelae to severe deficiency with chronic haemolytic anaemia. The most important measure is prevention of haemolysis by avoidance of certain medications and nutritional elements that could precipitate an attack [3]. There are currently no documented links between G6PD and bone abnormalities.

Case

A 15-year-old Afro-Caribbean male presented to Accident & Emergency complaining of intermittent right hip and thigh pain without any preceding history of trauma. Examination was normal and the physician attending the patent as well the reporting radiologist deemed the AP pelvic radiograph to be normal (Fig. 1). As a consequence, the patient

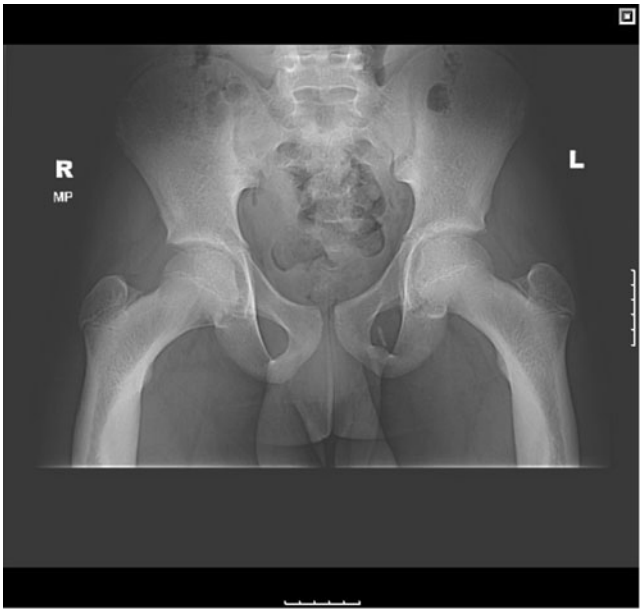

Fig. 1 Plain AP radiograph of the pelvis which does not show an obvious fracture. However on closer inspection there is bowing of both proximal femora

was reassured and discharged without referral to the orthopaedic team or any follow-up. He re-presented 4 months later complaining of severe constant right hip pain after slipping on ice and landing on his right side. His only other medical problems were mild asthma and G6PD deficiency. This condition had been diagnosed at birth after he had developed severe neonatal jaundice and was admitted to the special care neonatal unit for treatment. Beyond infancy he did not receive any specific treatment or follow-up for this condition, although he did have an extensive list of forbidden medications and nutritional elements found in specific type of food that may precipitate acute haemolysis.

He was otherwise fit and well having reached all developmental milestones at appropriate intervals. On examination, he had normal facies and stature (5 ft 8 in. in height and 60 kg in weight). He had bowing of both thighs, with shortening and external rotation of the right lower limb. Although he was unable to stand, he had correctible bilateral pes planus, with no evidence of muscle atrophy in the legs. Right hip and knee movements were limited by pain, with normal muscle power and no evidence of spinal deformity. There was no neurological or vascular deficit.

Plain radiographs showed significant bilateral lateral bowing of the femur with thickening of the medial cortex and a displaced transverse fracture of the proximal femoral shaft (Fig. 2). He was placed in skin traction and given appropriate analgesia. He subsequently underwent open reduction on a traction table under general anaesthetic and the fracture was stabilised with a large fragment plate (Fig. 3). He made an

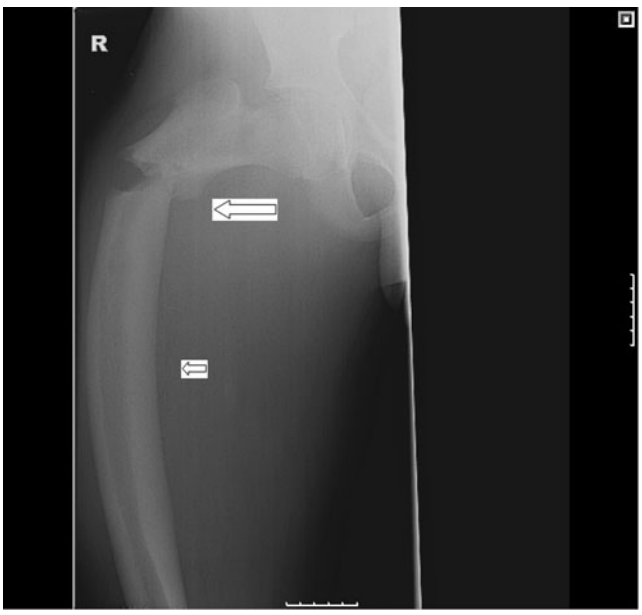

Fig. 2 Plain AP radiograph of the right femur showing lateral bowing, thickening of medial cortex (*short arrow*) and a transverse fracture in the proximal femur at the maximal point of compressive forces (*long arrow*)

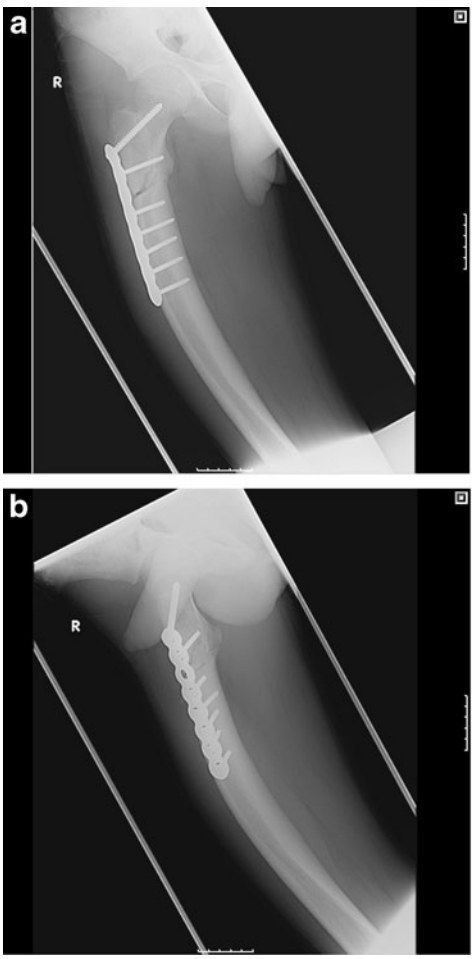

Fig. 3 **a**, **b** AP and lateral post-operative radiograph of the right figure showing operative stabilisation of the fracture

uneventful recovery immediately after the surgery. We had planned to follow him up until full skeletal maturity.

Discussion

There are currently no documented links between G6PD and bone abnormalities. It is, however, possible that a micro-deletion on the X chromosome affecting the G6PD locus could also affect other nearby genes which are relevant to bone pathology. Furthermore, re-arrangements of the X chromosome could also potentially produce such effects. An example of this is loss of one copy of the SHOX gene on the X chromosome in patients with Turners syndrome which is thought to be responsible for short stature and skeletal dysplasia in these patients [4]. The proximity of the G6PD locus to genes responsible for bony development such as the SHOX gene may have a similar effect on skeletal development.

To our knowledge, this is the first reported case of bilateral femoral bowing and consequent stress fracture in a patient with G6PD deficiency. This link therefore requires further genetic investigation. Until then, we suggest that a local protocol is put in place by haematologists and orthopaedic surgeons so that all children suffering with G6PD deficiency undergo screening radiography prior to skeletal maturity. Those found to have lower extremity bowing who may be at risk for stress fractures should be referred to an orthopaedic surgeon with an interest in skeletal dysplasia who should follow the patient up till skeletal maturity. In the acute setting, these patients may present with atraumatic pain due to the forces passing through the abnormally shaped bone causing an abnormal stress reaction or an occult fracture. Such patients should therefore undergo MRI or CT of the limb. If any abnormality is identified, then the patients weight bearing status can be reduced and the bone monitored with serial imaging to pre-empt a formal fracture and avoid the need for operative stabilisation.

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Conflict of interest The author(s) declare that they have no competing interests.

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