An 18-year-old male presented to the emergency department of Khoo Teck Puat Hospital with knee pain and swelling while playing basketball. He was unable to bear weight. He had a surgical history of combined liver and kidney transplant 3 years ago.

What do the radiographs of the left knee (Figs. 1A and 1B) and previous skeletal survey radiographs (Figs. 2A and 2B) show? What is the diagnosis?
A. Renal osteodystrophy
B. Lead poisoning
C. Osteopetrosis
D. Hyperoxaluria
E. Treated leukaemia

Findings and Diagnosis

Frontal and lateral radiographs of the left knee show an avulsion fracture involving the inferior pole of the patella (Figs. 1A and 1B). The bones were diffusely osteopenic with lucent metaphyseal bands involving proximal tibia, fibula and distal end of femur with adjacent dense sclerotic bands. The previously done skeletal survey revealed end-plate sclerosis of lumbar vertebral bodies (Fig. 2A) and lucent metaphyseal bands in distal radius, ulna and small tubular bones of hands with subjacent dense sclerotic bands (Fig. 2B). The patient also had bilateral renal cortical nephrocalcinosis (Fig. 3). Subsequent investigations included: serum creatinine 841ul/L (65 to 125), 24-hour urine oxalate 1.89 mmol/day and parathyroid hormonal levels 31.0 pmol/L (1.3 to 7.6). Renal biopsy was done which revealed oxalate calcifications within the tubular lumens with moderate to marked tubular atrophy consistent with renal tubular oxalosis. Genetic analysis revealed mutation of the alanine-glyoxylate amino transferase (AGXT) gene.

The diagnosis was primary hyperoxaluria.

Discussion

Primary hyperoxaluria (PH) is an uncommon autosomal recessive disease which occurs in 1 in 60,000 to 120,000 live births and affects glyoxylate metabolism.1-3 It is classified into 3 types: PH1, seen in 80% of patients, occurs due to mutation of the AGT gene resulting in deficiency of the enzyme alpha-ketoglutarate/glyoxylate carboligase present in the hepatocyte peroxisomes. PH2 represents 10% of cases and results from deficiency of glyoxlate reductase enzyme, and PH3 occurs in 10% of cases due to mutation of HOGA1 gene causing deficiency of hydroxyl-oxoglutarate aldolase enzyme.1,4,5 In PH1 and PH2 presentations, patients develop
end-stage renal disease due to increased levels of oxalate and glycolate in the circulation. In PH3, although there is urinary oxalate elimination, progression to end-stage renal disease has not been reported.

Patients with PH typically present in childhood, with median age being 5 years. Children commonly present with symptoms of recurrent nephrolithiasis. Eventually, patients develop renal failure due to nephrocalcinosis, secondary interstitial fibrosis and infection secondary to urolithiasis. PH affects renal function resulting in deposition of highly insoluble calcium oxalate crystals in extra-renal tissue. These crystals then incite an inflammatory reaction and cause tissue damage. Although oxalate deposition can occur in various organs like blood vessels, central nervous system, eyes, skin, peripheral nerves and even the intestine, imaging is useful for detecting renal and musculoskeletal involvement.

For early diagnosis and to prevent end-stage renal disease in patients with suspected PH, it is essential to get a thorough family history along with oxaluria tests like 24-hour urine glycolate and oxalaemia. In uncertain cases, histological studies, especially renal biopsies, which can demonstrate oxalate crystals, are very useful. Genetic analysis is required to categorise the mutational variant and confirm the diagnosis.

In the musculoskeletal system, the radiographic spectrum of PH is influenced by factors affecting bone metabolism and includes high levels of calcium oxalate, secondary hyperparathyroidism and renal osteodystrophy. The earliest radiographic features are dense metaphyseal bands affecting the extremities of long bones. In contrast to renal osteodystrophy, dense metaphyseal bands of oxalosis develop rapidly, are homogeneous and of greater density. This is due to dense oxalate crystals superimposing on already increased bone density of secondary hyperparathyroidism. With disease progression, oxalate crystals deposited in the metaphyseal band incite an inflammatory reaction. This inflammatory reaction causes bone resorption; as a result, bones later develop wide translucent metaphyseal zones adjacent to or within previously seen dense metaphyseal bands. Other radiologic features which may be seen in patients with PH are diffuse osteosclerosis, rugger jersey spine, subperiosteal bone resorption, acro-osteolysis, vascular and soft tissue calcification. These findings are primarily due to secondary hyperparathyroidism and renal osteodystrophy. Other skeletal manifestations in paediatric patients are delayed skeletal maturation, pathological fractures and epiphyseal injuries which can affect their growth and development.

Another organ that is commonly affected is the kidney. Any young child presenting with recurrent urolithiasis and bilateral cortical nephrocalcinosis should be investigated further for possible PH. Renal damage occurs due to recurrent nephrolithiasis, infection secondary to urolithiasis, nephrocalcinosis and interstitial fibrosis. Conventional radiographs and ultrasound imaging together can help identify cortical nephrocalcinosis, renal or ureteric stones and complications like hydronephrosis and pyelonephritis. The only curative treatment for PH is combined kidney-liver transplantation.

**Conclusion**

It is important to be aware of skeletal and other systemic imaging manifestations of PH for early diagnosis, as patients with this condition can now benefit from longer survival due to newer treatment methods such as combined kidney-liver transplantation.

**REFERENCES**


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