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Skeletal Radiology

Case report 599

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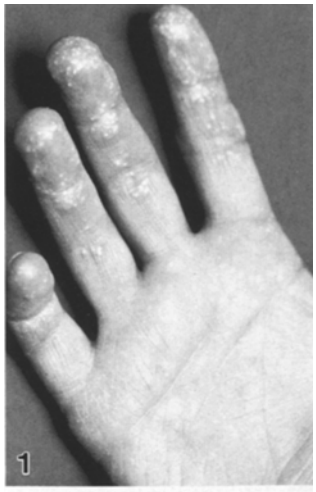
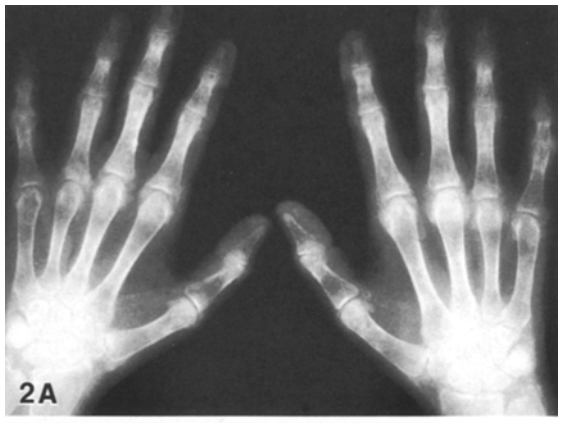
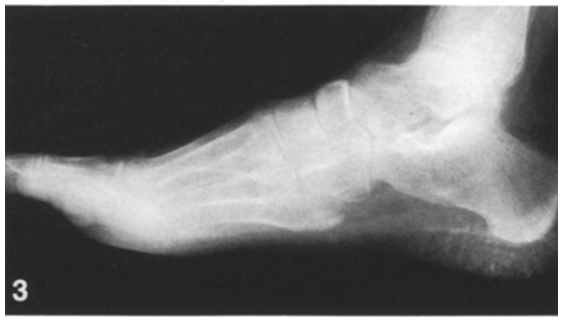
Radiological features







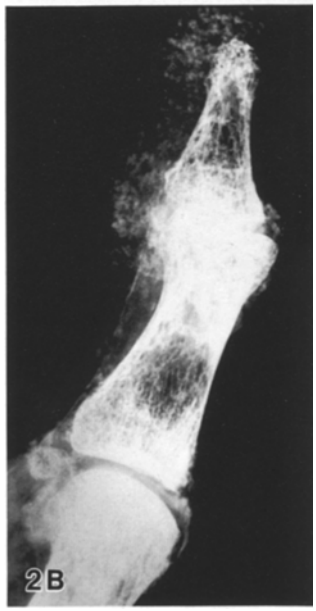


Fig. 1. Photograph of the right hand showing multiple punctate white calcific deposits in the skin on the flexor surfaces of the phalanges

Fig. 2. **A** Anteroposterior radiograph of the hands and **B** magnified view of left thumb show diffuse, punctate calcification of the soft tissues, predominantly on the flexor surfaces, and calcification of flexor tendon sheaths

Fig. 3. Lateral view of the right ankle shows calcification in the heel pad

Clinical information

A 31-year-old man with chronic renal failure from membranoproliferative glomerulonephritis who had been on hemodialysis for 9 years presented with numerous, hard, painful spots on the skin of his hands, feet, and earlobes. He also complained of episodic joint pains and symptoms of biventricular heart failure. He had two failed kidney transplants, and a successful parathyroidectomy 8 years previously. The serum calcium at the time of presentation was low at 8.0 mg/dL (normal, 8.8–10.4 mg/dL) and the alkaline phosphatase and phosphate levels were both elevated being 524 IU/L (normal, 30–130 IU/L) and 6.1 mg/dL (normal, 2.5–4.9 mg/dL) respectively. The serum creatinine was 14.0 mg/dL and the urea 92 mg/dL.

Films of the hands (Fig. 2) and ankle (Fig. 3) demonstrated soft tissue calcification.

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Diagnosis: Secondary oxalosis complicating chronic renal failure (oxalate gout [9])

The serum oxalate level in this patient was 8.8 mg/L (level in normal volunteer, <0.4 mg/L).

Histological studies of the skin (Fig. 4) showed rhomboidal, strongly birefringent crystals in the upper reticular dermis, without an accompanying inflammatory reaction, fully consistent with calcium oxalate deposition.

Many other causes of soft tissue calcification in the hands and feet, including gout, hyperparathyroidism, sarcoidosis, and calcinosis universalis do not cause diffuse punctate calcification as is seen in this case, but tend to cause dense masses of calcification around the joints. In myositis ossificans, muscles around the larger joints, particularly the hip, are involved by sheets of ossification, so this is not a diagnostic possibility here.

Calcium pyrophosphates accumulate in articular tissues, but are not found diffusely in the skin as in this case. While they are rhomboidal in shape, they are not so strongly birefringent as calcium oxalate. Furthermore, in the present case, the crystals failed to stain with alizarin red S, as crystals of calcium pyrophosphate do [1].

Urate deposits are typically birefringent, but the crystals are needle-shaped and are usually associated with a conspicuous giant-celled tissue reaction. Also, the present skin biopsy material was fixed in formalin and processed routinely in aqueous and alcoholic solutions in which urate, but not calcium oxalate, readily dissolves [1].

Discussion

A striking similarity exists between this case and one of the four cases with oxalosis secondary to end-stage renal failure shown and described by Reginato et al. [6]. In the patient he described, there was miliary deposition of calcium oxalate crystals in the flexor tendon sheaths of the fingers and in skin predominantly in the hands and also around joints. Clinical manifestations in their four patients, who had been on long-term hemodialysis, included podagra, tenosynovitis, olecranon bursitis, and acute or chronic synovitis of both large and small joints. Skin deposits were visible in the fingers and ears, as in the case here reported, and in the nose.

Acquired oxalosis is a rare disorder usually observed in association with renal failure. It should not be confused with primary oxalosis which is a hereditary metabolic defect resulting in hyperoxalemia, renal deposition of oxalate, and progressive renal failure. Oxalate is a nonmetabolizable end product of glycine and ascorbic acid metabolism and virtually all of it is normally excreted by the kidneys. Deposition of oxalate in the kidney, thyroid, and myocardium, and less commonly in the lungs and spleen, can be shown by histological studies at post mortem in patients with renal failure [2]. Deposition in bone has also been reported [4]. Hoffman has shown that chondrocalcinosis occurring in renal failure is sometimes caused by oxalate deposition and that oxalate deposition in joints can cause synovitis [3]. Deposition of oxalate occurs when the production of oxalate from endogenous or exogenous processes exceeds the solubility product of calcium oxalate.

Generally, oxalosis may occur as a result of increased intake, usually from ingesting large quantities of rhubarb; increased production following ingestion or use of glycols, xylitol, or methoxyflurane; increased uptake from the gut in patients with extensive inflammatory bowel disease; and from problems with excretion in renal failure [1]. Oxalosis complicating renal failure is due in part to renal retention of oxalate. The

Pathological features

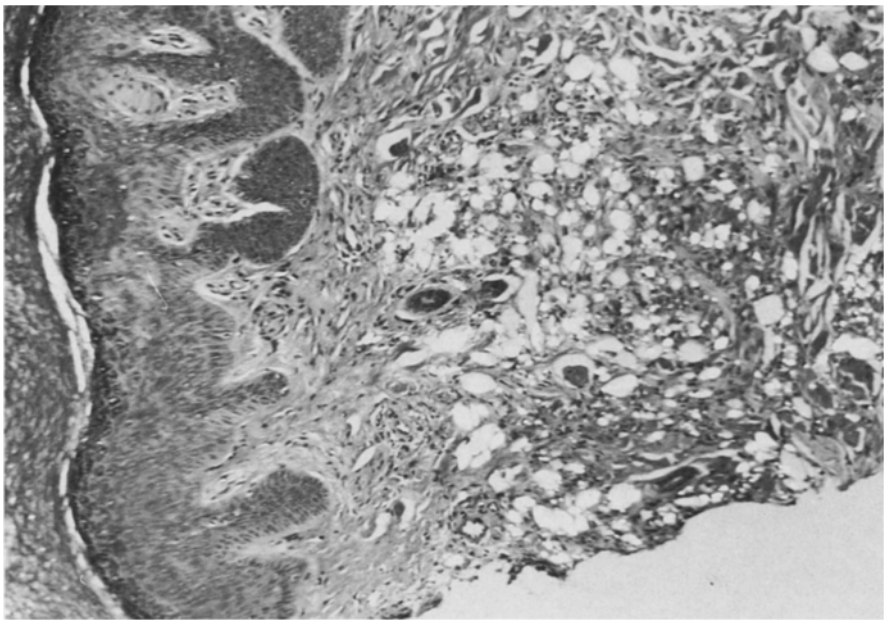

Fig. 4. Photomicrograph of a histologic section of skin from a finger (HE, $\times 200$, polarized light microscope) shows dermal, rhomboidal, birefringent crystals

plasma oxalate levels are often high in renal failure and reflect the plasma urea level, so that levels of both are high immediately before, and low immediately after, a period of dialysis [9]. Oxalate deposition tends to be more severe in patients who have been in renal failure for longer periods [2].

Previous reports of secondary oxalosis producing symptoms are similar to this one in that the patients, with a single exception [7], were ingesting large doses of vitamin C [3, 6]. The elevation of serum vitamin C levels in patients taking supplemental vitamin C tablets on dialysis has been shown to correlate with serum oxalate and is one of the metabolic precursors of oxalate, although the exact pathway is not fully known [5].

In the patient shown here, it is interesting that the skin calcification occurred in areas such as the heel pad and the flexor surfaces of the fingers which are frequently subjected to pressure.

The diagnosis was first made by a radiologist who noted the similarity of the diffuse synovial and skin calcification to that reported by Reginato et al. [6]. We believe the radiologists should be aware of this rare complication of long-term hemodialysis as the diagnosis may be more obvious radiologically than clinically. The condition can then be treated by ceasing oral intake of vitamin C and removing it from the dialysate in order to reduce endogenous oxalate production.

The term *oxalate gout* has been suggested for the occurrence of joint involvement and symptoms in secondary oxalosis [8], acknowledging its first use by Loeper in 1932.

The histological characteristics of oxalate have been thoroughly reviewed by Chaplin [1]. Distinguishing oxalate from other calcium salts depends on its optical properties (birefringence), its solubility (it is insoluble in water, alkalis, alcohol, and other organic solvents), and its staining characteristics. Microincineration techniques have also been shown to be valuable.

In *summary* a case is presented of a 31-year-old man with renal failure who developed miliary calcification in the skin and the synovium. Clinically, radiologically, and histologically the findings were typical of secondary oxalosis. It was emphasized in this article that acquired oxalosis is rare in association with renal failure. Acquired oxalosis must not be confused with primary oxalosis – a hereditary metabolic defect. It was stressed that chondrocalcinosis occurring in renal failure may be caused by deposition of oxalates which can produce synovitis. The causes of oxalosis have been reviewed and it is stressed that oxalosis complicating renal failure may occur in part due to renal retention of oxalate. The literature was reviewed concerning secondary oxalosis, and the relationship of oxalosis to the level of serum vitamin C in dialysis patients ingesting supplemental vitamin C tablets has been described. Secondary oxalosis, as in this patient, can be treated by removing vitamin C from the dialysate. The histological characteristics of oxalosis have been considered.

References

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