Tophaceous Pseudotumors in Polynesian Patients with Gout

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Gout is common in Polynesians, affecting 15% of New Zealand Maori men, and it seems to be increasing[1]. Its frequency is the result of an underlying genetic predisposition, possibly encoding a defective renal urate channel, that is shared by all Polynesian groups including the Aboriginal tribes of Taiwan, and is exacerbated by the calorie and purine-rich contemporary Western diet[2-4]. In New Zealand Maori and Pacific Island patients our impression is that gout is not only more common but is in many respects more severe, with a younger onset and a high prevalence of polyarticular and tophaceous disease at presentation. Tophi can have unusual presentations and adverse clinical outcomes.

Case 1. A 45-year-old part-Maori man was referred for management of severe gout. His first attack was at age 34 years with classical podagra, which had progressed to frequent polyarticular flares 2 years before this presentation. Acute flares had been treated with nonsteroidal antiinflammatory drugs (NSAID). His general practitioner had attempted hypouricemic treatment with allopurinol 300 mg daily. Compliance had been poor, in part because of perceived inefficacy in the light of ongoing acute attacks, and the patient had only taken the medication on an intermittent basis for periods of up to 3 months. Current medication included low dose aspirin for ischemic heart disease. He denied excessive alcohol intake. He also had chronic renal impairment [creatinine 130 µM (1.7 mg/dl)], but no history of symptomatic renal calculi and no known family history of gout.

He had previously been evaluated by an otolaryngologist for a slowly enlarging nasal mass (Figure 1A), for which a positive diagnosis had not been reached, but which on clinical grounds was felt to be a benign lesion. Clinical examination showed no active synovitis, but multiple peripheral subcutaneous tophi of up to 1.5 cm. His serum urate concentration was 700 µM (11.7 mg/dl). Magnetic resonance

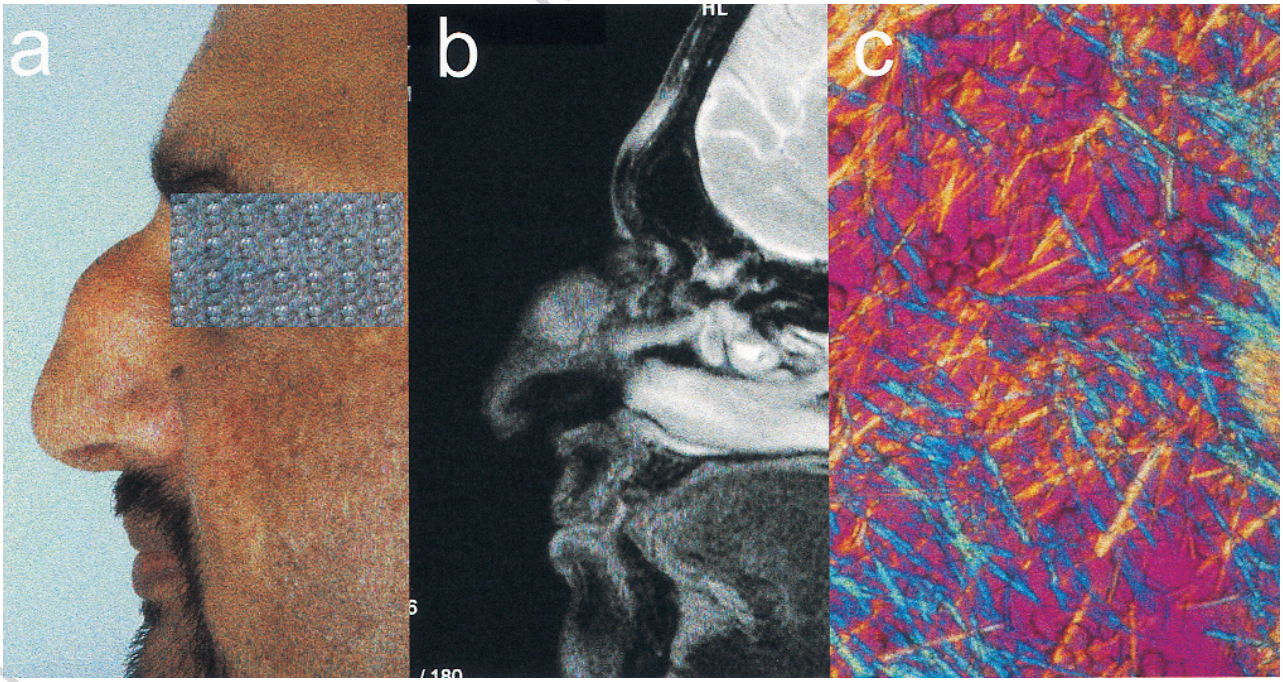

Figure 1. Case 1. a. Bulbous swelling over the bridge of the patient's nose; b. sagittal MR view; c. polarized microscopy, with 530 nm first-order compensator.

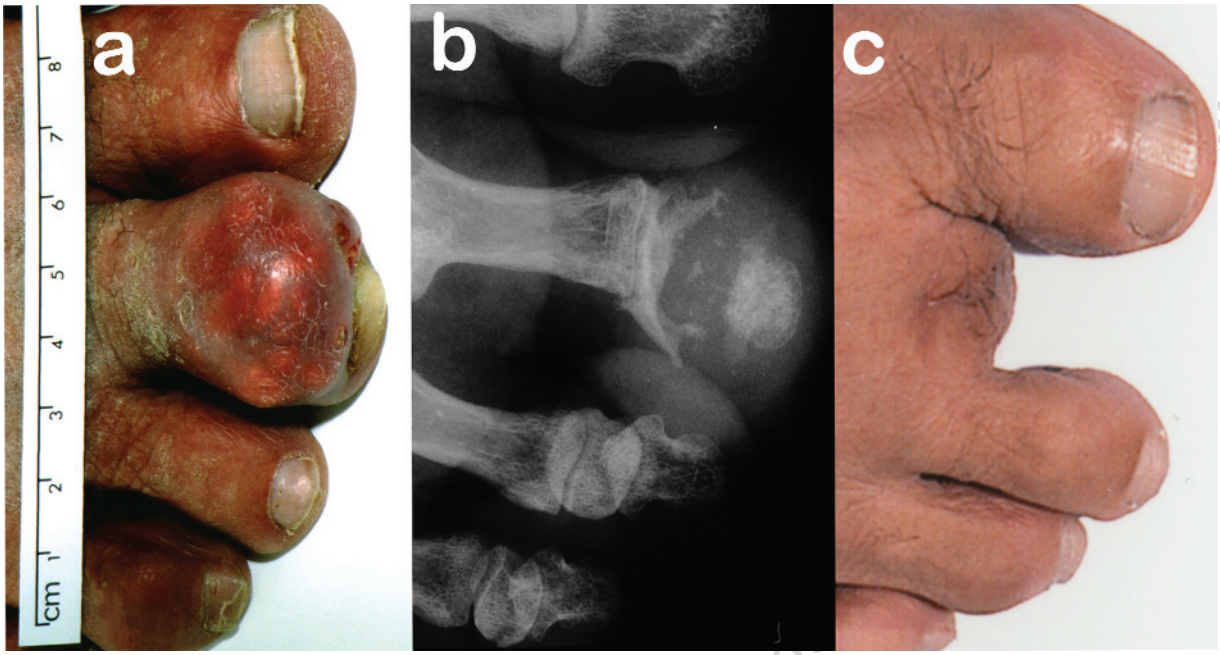

Figure 2. Case 2. a. Extensive tophaceous deposits visible through the skin overlying the middle and distal phalanges of the second toe; b. advanced destructive lesions of the phalanges; c. the eventual outcome, despite successful hypouricemic therapy.

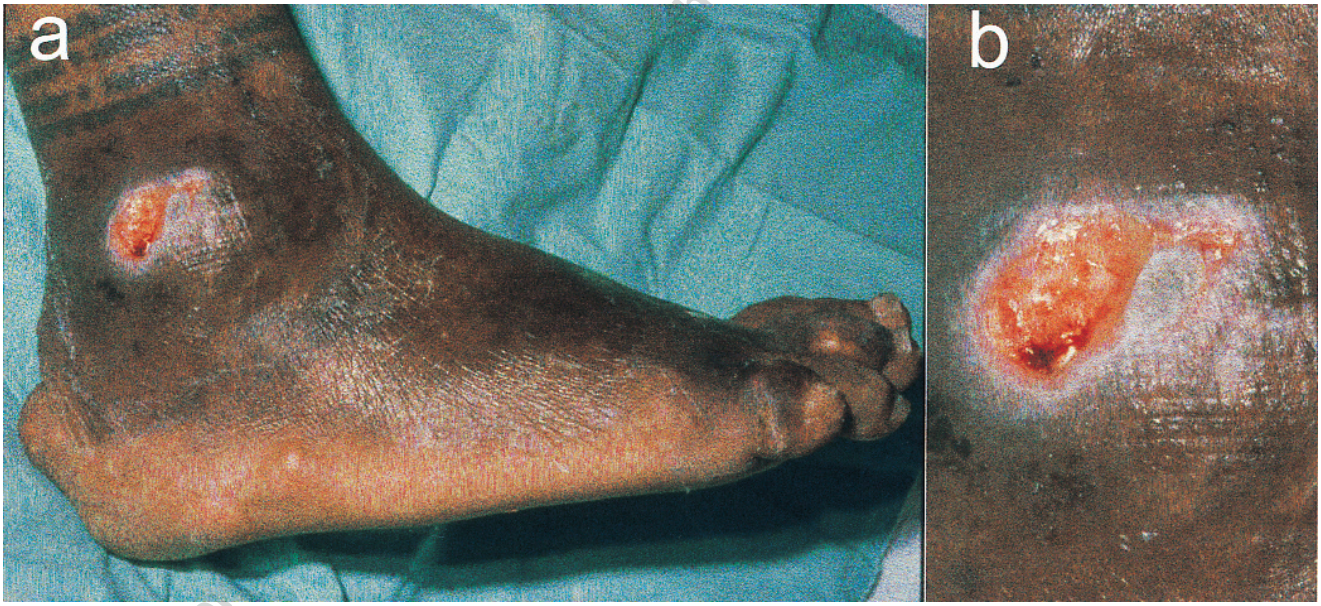

Figure 3. Case 3. a. Ulcerated tophus overlying the lateral malleolus; further large tophi visible along the lateral border of the heel, posterior to the calcaneus, and third toe; b. closeup of ulcer, with residual tophaceous material at ulcer base (sinus opening near inferior margin of ulcer, but not well visualized).

imaging (MRI) of the nasal lesion (Figure 1B) confirmed that the mass was not associated with destruction of bone or other local tissues. Fine needle aspiration and polarized light microscopy revealed classical negatively birefringent needle-shaped crystals consistent with monosodium urate. Although tophi occur in many unusual sites, there is only one prior report of a nasal lesion[5], which was treated with excisional biopsy.

Case 2. A 52-year-old man from Western Samoa had had gout since age 32 years but few acute attacks in recent years while taking oral prednisone 10–20 mg for severe asthma. Polyarticular flares resulted with attempts to taper his corti-

costeroids and had responded well to intermittent NSAID therapy on a background of regular low dose colchicine (0.6 mg bid). He was referred by his primary care practitioner after a discharging ulcer on his right second toe had failed to resolve with 2 extended courses of broad-spectrum oral antibiotics. Examination revealed typical subcutaneous and dermal tophaceous deposits (Figure 2A). The discharge was chalky in appearance, sterile to culture, and microscopy confirmed urate crystals. Radiology showed destruction of the middle and most of the distal phalanx (Figure 2B). His 24-h urate excretion was 2.7 mmol, with a fractional urate clearance of 4.8%. He remained significantly hyperuricemic (urate 630 µM, 10.5 mg/dl) despite good compliance with allopurinol 400 mg od as evidenced by a plasma oxypurinol level of 43 µM (local target > 30 µM 6–9 h postdose). With allopurinol 600 mg od and probenecid 500 mg bd his urate level decreased to 320 µM (5.3 mg/dl) and he did not have further acute attacks. However, he did not regain significant use of the right second toe and because of ongoing discomfort requested amputation (Figure 2C).

Case 3. A 36-year-old man from the Cook Islands presented with worsening ankle pain and an ulcer over the lateral malleolus (Figure 3). His first acute gout attack was at 26 years of age, polyarticular episodes beginning in his early 30s. There was a strong family history of gout. He had numerous 0.5–2 cm tophi on his hands and feet (Figure 3). His serum urate level at this presentation was 670 µM (11.2 mg/dl). A tophus near the lateral malleolus had ulcerated both to the skin and interiorly. Alkaline phosphatase was elevated at 515 U/l (normal 25–110), and his adjusted calcium was 2.90 mM (normal 2.10–2.55). MRI showed abnormal intensities in the talus, calcaneus, and distal fibula consistent with infected, infarcted bone, together with multiple sinus tracks communicating with the talus, calcaneus, posterior subtalar joint, and ankle joint. The eroded tophus had led to septic arthritis and osteomyelitis. Microbiological studies were nondiagnostic, possibly because of prior oral antibiotic courses. He presented late and his medical management had not been optimal, with no prior attempts to introduce urate-lowering therapy. He eventually required a below-knee amputation.

Gout is often regarded as an "easy" disease, with a well-understood pathogenesis, one of the few rheumatic diseases with an inexpensive remission-inducing disease modifying therapy. Certain groups of patients remain very challenging — Polynesian and Filipino ancestry, transplant patients taking cyclosporine or tacrolimus, tubulointerstitial renal syndromes including Bartters and Gitelman syndrome, and patients with a high diuretic requirement for refractory cardiac failure[4]. Gout in Polynesians is common, often begins at a young age, and is frequently polyarticular and/or tophaceous. These cases illustrate difficult management issues posed by large tophi that are in unusual locations or have caused local complications. In Case 2, it is tempting to speculate that the successful treatment of acute flares with antiinflammatory therapy (corticosteroids, colchicine, and NSAID) may have masked the ongoing progression of the tophi and bony arthropathy. Resolution of tophi requires longterm therapy with antihyperuricemic drugs in doses sufficient to maintain the plasma urate level in the lower part of the "normal" range. Despite our best attempts at patient education and encouragement, compliance is often poor and adverse structural outcomes occur.

In conclusion, gout is common and severe in Polynesians; presentation may be late, with extensive and atypical tophaceous disease; poor compliance is a common contributor to treatment failure with urate-lowering drugs; and the management of gout in Polynesian patients can be difficult.

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