Subcutaneous Tophaceous Nodule Formation Due to Deposition of Cholesterol Crystals

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Subcutaneous nodules commonly occur in many rheumatic and systemic diseases and may contain various crystals including monosodium urate (MSU), calcium pyrophosphate dihydrate, hydroxyapatite, and calcium oxalate[1-5]. To our knowledge only 6 patients with subcutaneous nodules resembling tophi containing cholesterol crystals have been described[6-9].

A 75-year-old man was referred to the rheumatology clinic due to a 2 year history of nodular swelling over his left elbow. The history was significant for hypertension, controlled with hydrochlorothiazide 25 mg per day. He had no history of rheumatic disease and review of systems was negative. Examination revealed a nontender subcutaneous nodule over the left elbow region with no involvement of the olecranon bursa or elbow joint (Figure 1). There was no evidence of erythema, warmth, or tenderness. The remainder of the examination was unremarkable. Laboratory evaluation included normal complete blood

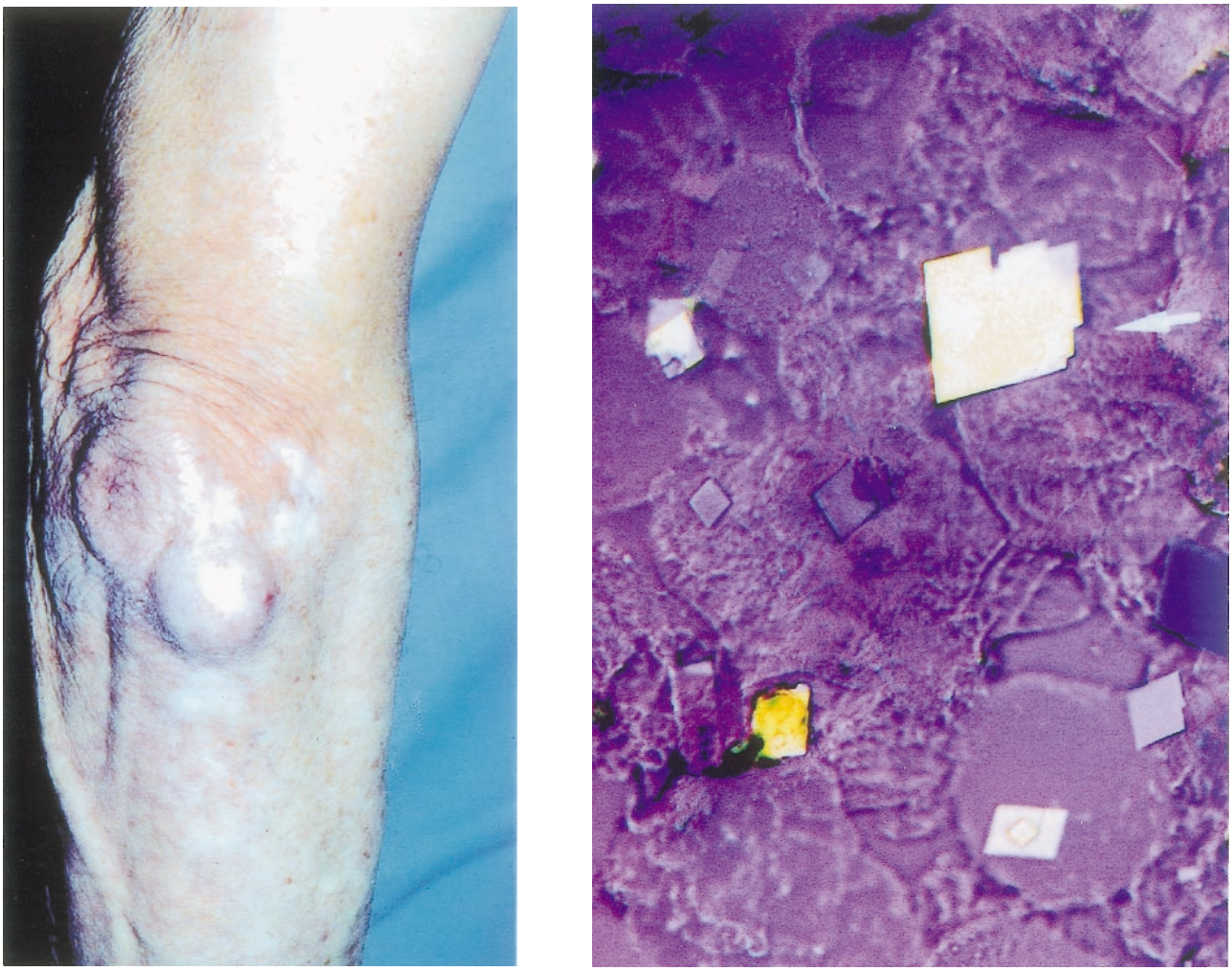

Figure 1. A. Subcutaneous nodule over the left elbow region. B. Aspirated material with typical flat, rectangular crystals with notched corners (arrow).

count, serum chemistries, and serum lipid profile. Serum uric acid was elevated at 8.0 mg/dl (normal 2.4–7.0 mg/dl). Rheumatoid factor (RF) was negative. Aspiration biopsy of the nodule was performed and thick creamy-white material was obtained. Examination under polarized light microscopy revealed noninflammatory fluid with many cholesterol crystals in clumps resembling tophi, both rod shaped and typical flat, rectangular crystals with notched corners (Figure 1B). At followup 3 months later, the nodule was stable in size.

Cholesterol crystals are occasionally detected in chronic rheumatoid, osteoarthritis, or bursal effusions[10,11], but have not been commonly described as tophaceous deposits. Although subcutaneous nodules may occur in many diseases, such as systemic lupus erythematosus, lupus profundus, scleroderma, rheumatic fever, pancreatic disease, various vasculitides, amyloidosis, necrobiosis lipoidica diabeticorum, multicentric reticulohistiocytosis, and some bacterial, viral and fungal infections[1], subcutaneous olecranon nodules are most commonly seen in association with rheumatoid arthritis and gout. The factors that lead to cholesterol crystal deposition in subcutaneous tissue are unclear; however, it has been speculated that repeated microtrauma to the skin can result in release of cholesterol molecules from destroyed cell membrane lipids, leading to cholesterol tophus formation[7]. Local biosynthesis can also be a factor in cholesterol accumulation[9,12]. The inflammatory capacity of cholesterol crystals is probably minimal, although synovitis has been observed in rabbits when cholesterol crystals are injected intraarticularly[10,11,13,14]. Neither our patient nor the reported cases had a systemic lipid disorder, and indeed the presence of synovial fluid cholesterol crystals does not seem to bear a relationship to serum lipoprotein abnormalities[10].

Local factors possibly played a role in our patient and the previously described cases. Fam, *et al* reported 2 patients with nodules, one at the lateral malleolus and one near the 5th metatarsophalangeal joint. Chronic trauma from boots possibly contributed to the nodules in both patients by causing local tissue breakdown[6,7]. One of the patients developed the nodule only a few months after beginning to wear heavy safety boots and experienced resolution of the nodule after changing footwear[7]. Szachnowske and Bridges described 2 men with nodules over the extensor forearms and felt the nodule distribution was consistent with repeated injury, given their farming occupation[8]. Lanting, *et al* described 2 patients with subcutaneous nodules[9]. The first developed a nodule on her 5th finger while using crutches and eventually had a nodule excision. The 2nd patient developed nodules on his elbow and both feet. The elbow location was felt to be a usual site for mechanical pressure, and footwear was felt to be a contributing factor for the forefoot nodules. He experienced resolution of his nodule after changing footwear. Our patient developed a nodule over the left elbow region after working for many years as a crane operator in a steel mill. The olecranon area is susceptible to repeated microtrauma and we suspect our patient experienced chronic trauma due to his occupation operating heavy machinery.

Both MSU and cholesterol crystals may be rod shaped, and we did not perform a chemical analysis on the aspirated material, such as uricase digestion, nor did we use DeGalantha stain. Despite this, we are confident the rod shaped crystals are not MSU, given the cystic nature of the tophus, lack of clumping of rods, as would be expected in a gouty tophus, and abundance of typical plate-like cholesterol crystals. Joint, bursa, and nodule/tophus aspiration with a careful analysis of the aspirated material remains a most useful and often diagnostic procedure in the evaluation of patients with rheumatological conditions.

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