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Two Cases of Miliarial Gout: A Rare Variant of Chronic Tophaceous Gout

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Abstract

Gout is a systemic disease characterized by recurrent arthritis associated with hyperuricemia and deposition of monosodium urate (MSU) crystals in joints, bones, and soft tissues. A rare variant is the deposition of MSU crystals in the skin. Among the variants of cutaneous gout, miliarial gout is the most unstudied and unreported due to its rarity. Two patients diagnosed with chronic tophaceous gout presented with multiple milia-like papules on the extremities. Skin biopsies revealed pale basophilic material deposited in the dermis, surrounded by an inflammatory infiltrate of lymphocytes, histiocytes, and multinucleated giant cells. Needle-shaped crystals noted correspond to uric acid crystals. These findings were consistent with miliary gout. Urate-lowering therapy is the mainstay treatment of gout. In this report, we highlight the clinical course, complications, cutaneous manifestations, laboratory abnormalities, and histopathological features of milarial gout. These cases supplement the few that have been documented in the English-language literature, in addition to higher ICU and overall hospital length of stay.

Keywords: Arthritis, joint pains, miliarial gout, tophaceous gout

Introduction

Gout is a systemic disease characterized by recurrent arthritis associated with hyperuricemia and deposition of monosodium urate crystals in joints, bones, and soft tissues. There are three clinical stages of gout: acute gouty arthritis, intercritical gout, and chronic tophaceous gout. An acute attack of gout is typically monoarticular and intensely inflammatory, occurring on the lower extremities. Upon resolution of an acute attack, the patient is said to have entered an intercritical period. Chronic tophaceous gout is characterized by collections of solid urates accompanied by chronic inflammatory

and often destructive changes in the surrounding connective tissue.[1] A rare variant of chronic tophaceous gout is the deposition of monosodium urate (MSU) crystals in the skin. There are several morphological manifestations of tophaceous gout including miliarial, bullous, fungating, nodular, ulcerative, papular, and pustular.[2] Among these variants, miliarial gout is the most unstudied and unreported case.

Case Reports

Case 1

A 49-year-old Filipino male, diagnosed with chronic tophaceous gout for more than 5 years known to self-medicate with nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids, presented with multiple milia-like papules on both upper and lower extremities. Intermittent joint pains in the hands, knees, and feet were also experienced. Two weeks prior to consultation, the patient noted multiple indurated, erythematous plaques, nodules, and milia-like papules with whitish discharge on both posterior thighs. In the interim, the patient developed cellulitis and severe joint pains, causing difficulty in ambulation. The patient had an episode of fever and deterioration in sensorium prompting consultation at the emergency room. On physical examination, there are multiple disseminated yellowish milia-like papules (Figure 1) on both upper and lower extremities occurring singly or in confluence. Some lesions were warm to touch with whitish to yellowish discharge and erythematous surrounding area suggestive of infectious cellulitis. Multiple tophi were also seen on the hands, knees, and feet (Figure 2). Some lesions discharge whitish material and leave pitted residual scars (Figure 3). Dermoscopy revealed a whitish central area and a surrounding yellowish area (Figure 4). There is also absence of vascular structures within the lesion.

Laboratory investigation showed azotemia (652.7 umol/L), hyperuricemia (16.64 mg/dL), leukocytosis (32.6x109/L) with segmenter predominance (0.91), and toxic granulations. Patient was admitted due to sepsis secondary to multiple infected tophi with cellulitis; acute kidney injury secondary to acute tubular necrosis and sepsis; chronic tophaceous gout in flare with disseminated miliary tophi. A skin biopsy, stained with Hematoxylin and eosin (H&E), of the right knee revealed pale basophilic material deposited in the dermis, surrounded by an inflammatory infiltrate of lymphocytes, histiocytes, and multinucleated giant cells (Figure 5). These findings were consistent with miliary tophi.

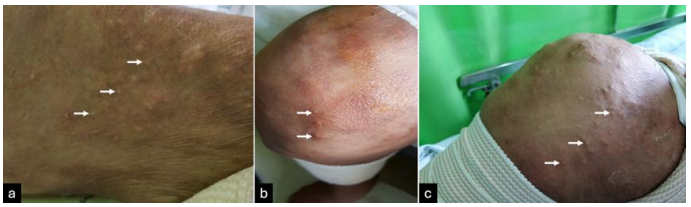

Figure 1: Milia-like lesions on the anterior left leg (a), left (b), and right (c) knees

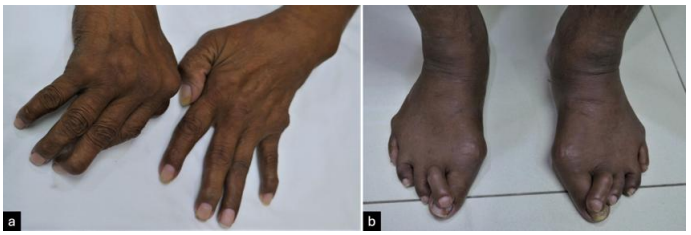

Figure 2: Multiple tophi on dorsal aspect of the left hand (a) and feet (b).

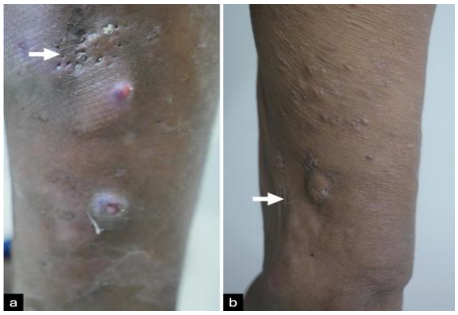

Figure 3: Pitted residual scars (a and b).

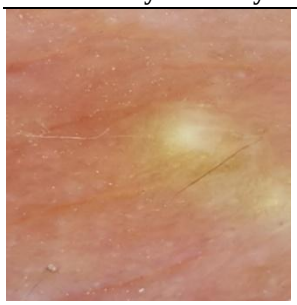

Figure 4: Whitish central area and surrounding yellowish area on dermoscopy.

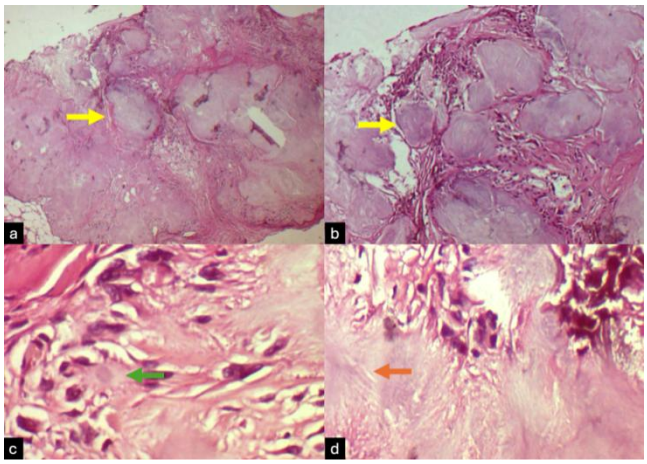

Figure 5: Histopathology showing epidermal ulceration, pale hyaline masses (a and b) surrounded by a sparse infiltrate (H&E, 200x). Histiocytes, multinucleated giant cells (c), and needle-shaped crystals (d) were also seen in the dermis (H&E, 400x).

The patient was started on broad-spectrum antibiotics (Piperacillin-Tazobactam and Vancomycin), hydrocortisone, and colchicine. He also underwent hemodialysis. Septic workup showed no growth on blood culture but revealed Citrobacter koseri on wound culture, which was sensitive to the given antibiotic. The patient's condition improved clinically and was eventually started on Febuxostat.

Case 2

A 53-year-old male presented with an 8-year history of joint pains and paresthesia. Four years prior to consultation, the patient developed skin-colored nodules and plaques on the posterior thigh. In the interim, lesions progressed into multiple skin-colored nodules that were now affecting the elbows and hands causing joint pains and stiffness. He was diagnosed with hyperuricemia and eventually experienced swelling and ulceration on the left middle finger. Three weeks prior to consult, the patient noted an abscess on the left foot associated with a tight sensation. On physical examination, classic gouty tophi (Figure 6-a) on the joints of the left foot as well as multiple milia-like lesions (Figure 6-) on the thighs were noted.

Figure 6: A case of miliary or disseminated gout presenting with both the classic gouty tophi (a) on the joints and milia-like lesions (b) on the thighs.

H&E-stained sections (Figure 7) revealed pale hyaline masses, ulceration, extrusion, and transepidermal elimination of gouty material with a dense infiltrate of histiocytes, lymphocytes, and plasma cells in the dermis. Foreign body type-multinucleated giant cells engulfed gouty material and were surrounded by a moderately dense inflammatory infiltrate of lymphocytes, histiocytes, and plasma cells.

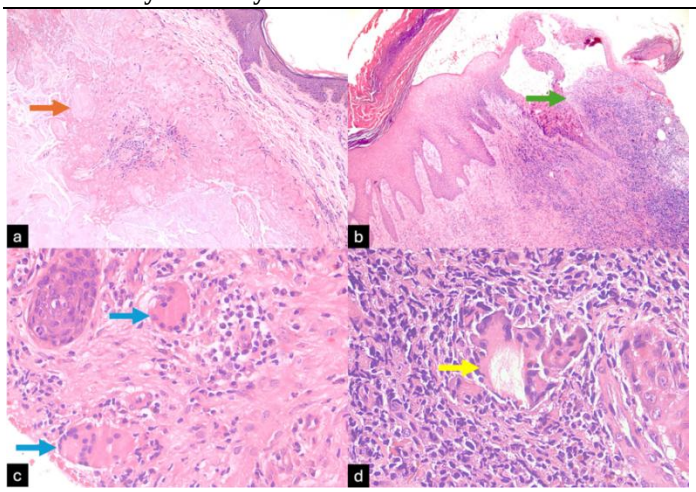

Figure 7: Histopathology showed pale hyaline masses (a), ulceration, extrusion, and transepidermal elimination (b) of gouty material with a dense infiltrate of histiocytes, lymphocytes and plasma cells in the dermis (H&E x 100x).

On higher magnification, foreign body giant cells (c and d) were observed (H&E x 400).

The patient was also known to have hypertension and diabetes mellitus and was a chronic alcoholic beverage drinker. Lesions improved after the patient was started on colchicine and allopurinol.

Discussion

Gout is a metabolic disease that most often affects middle-aged to elderly men and postmenopausal women. It is typically characterized by episodic acute arthritis or chronic arthritis caused by the deposition of MSU crystals. The metatarsophalangeal joint of the first toe is often involved, but tarsal joints, ankles, and knees also are commonly affected.

The three clinical stages of gout: acute gouty arthritis, intercritical gout, and chronic tophaceous gout can be regarded as emerging sequentially (but with some overlapping), with clinical severity that often parallels the frequency of acute gout flares and the eventual development of chronic gouty arthropathy and tophaceous gout.[1]

Chronic tophaceous gout is characterized by collections of solid urate accompanied by chronic inflammatory and often destructive changes in the surrounding connective tissue. The tophi are often visible and/or palpable and can be present on the ears or the soft tissues, including articular structures, tendons, or bursas. Tophi are typically not painful or tender. They may attenuate the skin, revealing a yellow or white color.

Shukla et al. presented the first sub-classifications and different morphologies of intradermal tophaceous gout. Among the seven classes (miliarial, bullous, fungating, nodular, ulcerative, popular, and pustular), the most unreported case is miliarial gout, which can be a sign of advanced disease such as uncontrolled hyperuricemia complicating to renal insufficiency and sepsis secondary to infected tophi with cellulitis.[2]

Since 2007, only 7 cases of miliarial gout were reported. Three cases were reported in the United States of America. One case reported in Canada 2, Spain 3, and Taiwan 4. This report describes the 2nd and 3rd cases in the Philippines but we feel the condition is just underreported.

All of the 7 reported cases of miliarial gout presented with an increase in serum uric acid levels. Three cases reported in Spain, Canada, and Taiwan developed superimposed bacterial infection on the skin leading to cellulitis, in which 1 case died of sepsis. Infection usually complicates the condition because of transepidermal elimination of the gouty material and progressive ulceration.

The studies of Shukla et al. (Canada)[2], Aguayo et al. (Spain)[3], and Hung et al. (Taiwan)[4] reported a case of miliarial gout in a middle-aged individual. These patients

developed white-yellow papules and plaques on the anterior and posterior aspects of the lower extremities. The case reported by Shukla et al and Hung et al eventually developed renal complications and the latter died of sepsis due to metabolic acidosis and multiple organ failure.[4] Three cases from the United States of America[5-7], and 1 case here in the Philippines were confirmed to have miliarial gout on skin biopsy but no complications were observed.

Lo and colleagues presented a case of a 35-year-old Filipino man with a 15-year history of gouty arthritis, and tophi formation in joints and skin. Physical examination revealed the presence of yellowish subcutaneous non-tender, movable hard nodules along the forearms, shoulders, and torso. The patient was initially given colchicine and eventually allopurinol. The lesions did not form cellulitis or infection over the tophi and were monitored as out-patient.[8]

Miliarial gout is one of the intradermal tophaceous gouts with a classic presentation of multiple small yellowish papules resembling milia. In the cases we reported, the lesions were accompanied with a secondary bacterial infection. The patient improved with the appropriate treatment of antibiotics and a short course of steroids.

The pathogenesis of intradermal gout remains unknown, although some journals proposed several mechanisms. Reduced urate solubility and enhanced crystal precipitation owing to decreased temperature in the peripheral body and enhanced crystal deposition in sites subjected to repetitive trauma have been suggested to play a role in intradermal tophi development.[9] Miliarial gout can be a sign of advanced diseases such as uncontrolled hyperuricemia and chronic renal failure. Thus, early diagnosis and treatment can decrease mortality.

Miliarial gout is one of the many sub-classifications of intradermal gout where medical management remains the mainstay. Based on the Philippines Clinical Practice Guidelines, urate-lowering therapy is still the cornerstone in the treatment of gout. Optimal serum acid levels of gout patients should be kept at ≤6mg/dl or ≤5mg/dl if with tophi.[10]

Conclusion

This report present cases of chronic tophaceous gout presenting as miliary tophi, which can be a sign of advanced disease. Although the patients presented with typical multiple tophi on the extremities, a concomitant rare manifestation of miliary tophi can also occur. Knowledge of the cutaneous manifestations of gout can lead to early diagnosis and treatment, thus preventing complications such as renal insufficiency, tophaceous deposits, superimposed bacterial skin infections, and sepsis.

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