Case Report
Gouty Panniculitis with Ulcerations in a Patient with Multiple Organ Dysfunctions

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Gouty panniculitis is a rare manifestation of gout. Clinically, it is characterized by indurated subcutaneous nodules in nonjoint areas. Pathologically, typical characteristic gouty tophi can be seen in subcutaneous tissue. It is postulated that gouty panniculitis develops as a consequence of uric acid accumulation in the body and localized inflammatory changes in subcutaneous tissue. We report a case of a 46-year-old man with a 20-year history of gout who developed multiple subcutaneous nodules over the abdomen and right groin/thigh area over a 2-year period. After a recent episode of congestive heart failure and acute renal failure, the nodules increased in size and the overlying skin became erythematous and ulcerated. Pathologic examination demonstrated typical tophi in the dermis and subcutaneous tissue. A review of the literature yielded fifteen similar cases that had been previously reported. We conclude that gouty panniculitis may be a manifestation of undertreated gout and may be exacerbated by the deterioration of other systemic functions.

1. Introduction

Gouty panniculitis is a rare manifestation of gout. It is characterized clinically by indurated, erythematous, or ulcerated subcutaneous nodules. Histologic confirmation is achieved by identification of tophaceous crystal deposition in the lobular subcutaneous tissue [1, 2]. The clinical presence of indurated subcutaneous plaques may precede, or appear subsequently to the articular clinical expression of tophaceous gout [1]. We report a case of gouty panniculitis manifesting as multiple subcutaneous nodules in different locations with and without ulceration. The recent literature related to this disease entity is also reviewed.

2. Case Report

A 46-year-old male with a 20-year history of gout presented with nontender nodules in the subcutaneous tissue of the abdomen, groin, and right thigh. The nodules had been present for two years; however, over the past three weeks, some of the nodules became erythematous and eventually ulcerated. In addition, the patient had recently been admitted for congestive heart failure and acute renal failure 3.5 weeks prior to presentation. His gout had never been treated. Furthermore, the patient’s medical history was complicated by type II diabetes and morbid obesity with a BMI of 40.6.

Physical examination revealed multiple, whitish subcutaneous nodules and 4 skin ulcers in the lower half of the abdomen, right groin, and right thigh. All ulcers measured between 1 and 3 cm; fibrinous, necrotic, and chalky whitish material covered poorly formed granulation tissue. The nonulcerated pale, white nodules with focal erythema could be palpated subcutaneously and averaged from 1.0 to 1.5 cm in diameter (Figure 1(a)). Clinically, there was also significant swelling of the right elbow and the MCP joints on the patient’s right hand.

Results of laboratory tests from the patient’s most recent admission revealed the following: uric acid 14.3 mg/dL (reference range 4–7 mg/dL), blood glucose 255 mg/dL (reference range 70–99 mg/dL), BUN 47 mg/dL (reference range...
Figure 1: Skin and subcutaneous lesion. (a) Ulcer and erythematous nodule in right groin area, 1 to 1.5 cm; (b) negative birefringence of urate crystal on fresh tissue touch imprint slide (400x); (c) and (d) subcutaneous lesion: low power picture shows subcutaneous tissue erosion with pools of pale staining or slightly eosinophilic amorphous/feathery material surrounded by collagen fibers and chronic inflammatory cells (c, 40x); high power picture shows feathery eosinophilic crystalline material converging in the center and surrounded by palisading histiocytes and multinucleated giant cells (d, 200x).

5–20 mg/dL), creatinine 1.61 mg/dL (reference range 0.8–1.4 mg/dL), and estimated GFR 46 mL/min/1.73 m² (reference range ≥59). His uric acid levels were 10.8 mg/dL and 11.2 mg/dL at the time of surgical removal of the ulcerated nodules, 3 and 4 weeks later. At that time also, his renal function and blood glucose levels were still abnormal: BUN 38 mg/dL, creatinine 1.65 mg/dL, GFR 45 mL/min/1.73 m², and blood glucose 147 mg/dL.

The patient underwent 3 excisional biopsies, including 2 from an abdominal skin lesion and 1 from the right thigh. All 3 specimens were submitted separately, over a 3-week period, for histological evaluation. Sectioning of the specimens revealed multifocal areas filled with white, chalky material. Touch imprint slides were prepared before tissue fixation. Microscopic examination under polarized light showed multiple needle-shaped crystals displaying negative birefringence (Figure 1(b)). Permanent histology slides showed pools of pale and slightly eosinophilic amorphous as well as feathery material in the dermis and subcutaneous tissue (Figures 1(c) and 1(d)). The lesions demonstrated different stages of development. The smaller lesions had a central area of feathery crystalline material surrounded by palisading histiocytes and multinucleated giant cells. The larger lesions consisted of disorganized, laminated material surrounded by collagen fibers and chronic inflammation. The lesions eroded outward to the skin surface leading to ulceration. Based on the clinical, laboratory, and histologic findings, a diagnosis of multifocal gouty tophi was made.

3. Discussion

Gout has become increasingly common in the Western world, such that the lifetime risk of acquisition is now approximately 1-2% [3, 4]. Tophi are a common clinical manifestation of gout. They contain collections of monosodium urate crystals and are commonly located in the vicinity of joints of the elbows, hands, and feet. They lead to joint destruction and chronic (long-term and continuous) joint pain and stiffness. Gouty panniculitis is characterized by inflammation of the subcutaneous fat and manifests itself clinically as nodular (lumpy) lesions on the legs and trunk, which ulcerate and ooze fluid containing monosodium urate crystals [5]. In contrast to tophi, panniculitis has been reported, thus far, only in a very small percentage of patients with gout. Thus, Webershock [2] reported one case in 2010 and reviewed 8 prior reported cases from 1977 to 2007 [2, 6–9]. Recently, however, Ochoa et al. [1] reported an additional 6 cases from
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asingleinstitutionandconcludedthatpanniculitisshouldbe
considered as one of the principal clinical manifestations of
gout. These authors also raised the question of whether this
particular manifestation has hitherto been under reported.

The pathogenesis of gouty panniculitis is currently not
well understood. Some predisposing factors may enhance the
deposition of monosodium urate crystals in the subcutaneous
tissue. As expected, hyperuricemia is present in the vast
majority of patients diagnosed with this condition [7]. A
high metabolic rate, leading to increased production of uric
acid, may lead to an oversaturation of monosodium urate
with joint deposition and deposition in the lobular sub-
cutaneous tissue [1]. In addition, preexisting subcutaneous
tissue damage is known to increase the risk of subcutaneous
panniculitis. Additional factors may include venous stasis,
varicosities, or chronic edema related to cardiac failure and
elevated serum amylase or lipase [2, 7]. Elevated serum
amylase and lipase, in patients with renal failure and end
stage renal disease, may be due to decreased renal clearance
of these enzymes [10, 11]. Hence, chronic renal insufficiency
associated with hypertensive nephropathy or other medical
conditions represents a potential risk factor for gouty pannici-
litis [1].

Ochoa et al. postulated that gouty panniculitis could be
caused by localized inflammatory changes in the lobular sub-
cutaneous tissue. This inflammation may be triggered or per-
petuated by blood supply disruption caused by monosodium
urate crystals, consequently resulting in microtrauma to the
terminal capillary walls and adipose tissues. This hypoxia
then renders the subcutaneous tissues vulnerable to further
injury [1].

More recently, uric acid has been shown to activate the
NLRP3 (NOD nucleotide-binding oligomerization domain)
like receptors, pyrin domain 3 inflammasome, which plays
a key role in innate immunity. In lipopolysaccharide (LPS)
stimulated mice, monosodium urate crystals (as well as calcium
pyrophosphate dihydrate) crystals have been shown to cause
an increase in caspase-1 activation and the secretion of IL-1β.
However, mice deficient for inflammasome components were
defective in crystal-induced IL-1β secretion [12]. Moreover,
in a peritoneal murine model of gout, monosodium urate
crystal-recruited monocytes differentiate into proinflamma-
atory M1-like macrophages producing more IL-1 along with
other cytokines and chemokines [13]. These experimental
findings support the concept that the innate immune system
may play a critical role in the triggering of crystal-induced
acute inflammation. Consonant with these findings, IL-1 inhibitors appear to be beneficial in the treatment of gout.

Our patient had a long history of untreated gout. Over
two years, he progressively developed subcutaneous nodules
over his abdomen, groin, and right thigh area. His blood uric
acid levels ranged between 10.8 mg/dL and 14.3 mg/dL during
his recent hospitalization. The subcutaneous nodules became
erythematous and ulcerated soon after the development of
congestive heart failure and acute renal failure. His renal
failure was a likely consequence of his cardiac insufficiency,
the latter providing low blood perfusion of the kidney.
In addition, this patient was diabetic and may have had
underlying diabetic nephropathy. This in turn could have
made the kidney more susceptible to impaired perfusion due
to the acute onset of heart failure. The deterioration of kidney
function and the use of the loop diuretic furosemide may have
accelerated the accumulation of uric acid in the patient's
body [14], ultimately exacerbating his gouty panniculitis.
Furthermore, the severe hyperuricemia might have led to
further deterioration of renal function. Histologically, the
newly developed small lesions, which were surrounded by
palisading histiocytes, may be indicative of the active phase
of his panniculitis. The patient's other medical conditions,
which contributed to gout development, included type II
diabetes [15] and morbid obesity [16].

The differential diagnosis of gouty panniculitis encom-
passes a wide range of disorders including sclerema neo-
torum, subcutaneous fat necrosis, pancreatic panniculitis,
poststeroid panniculitis, factitial panniculitis, hemorrhagic
panniculitis, and many others [1, 2, 7]. Although gouty
panniculitis can often demonstrate a granulomatous reaction,
the detection of feathery crystalline material, although rare,
is helpful. Since monosodium urate crystals can be dissolved
during paraffin fixation and routine hematoxylin and eosin
(H&E) staining, the feathery structures seen on permanent
histology slides actually represent empty spaces previously
occupied by the needle-shaped crystals of monosodium
urate. Thus, the direct detection of crystals using polarized
light requires either touch imprint slides prepared from fresh
tissue or the use of ethanol fixation during tissue processing.

All gouty panniculitis cases (18 in total, including the
current case) are reviewed. The average age of onset is 47.2
years old. In general, gouty panniculitis is a late clinical
manifestation of chronic gout (average 17 years). However,
the skin lesions may also be manifested before the onset of
classic gout [1]. Gouty panniculitis appears more likely to
develop in male patients, with a male to female ratio of 7:1.
Hyperuricemia (mean 9.8 mg/dL) plays an important role in
the development gouty panniculitis. Some patients, who have
a normal uric acid level at diagnosis, may have experienced
long-term hyperuricemia at an earlier time. Among all 18
cases, abnormal renal function was noted in 12 (66.7%) patients [1, 6, 8, 9, 17, 18]. Due to the lack of complete
metabolic panel (CMP) data, renal function in the remaining
6 cases could not be assessed [2, 7, 19]. Also, elevation of
erthrocyte sedimentation rate and C-reactive protein have
been noted in some cases [2, 7, 8].

With regard to gouty panniculitis, although no specific
treatment for this condition is currently available, systemic
anti-inflammatory therapy, including corticosteroids, can
to often ameliorate the symptoms [2, 7, 17]. The nonhealing
ulcerated lesions can also be surgically resected. Our patient
was treated with NSAIDs (naproxen) and prednisone with a
fair response.

4. Conclusion

Although gouty panniculitis is an uncommon symptom of
gout, the development of nodules in subcutaneous tissue
should alert the clinician to the need for a more careful moni-
toring of the patient. Uncontrolled hyperuricemia can lead to
devastating dermatopathologic consequences. Skin manifestations can be an indicator of undertreated or untreated gout, as well as the decompensation of other systemic conditions such as renal dysfunction. Further systemic workup or close clinical monitoring should be considered in such patients.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References


