A 78-year-old African American male presents to his primary care office with a minimally tender mass on the lateral aspect of his 2nd digit. His history was negative for fever, chills, and trauma to the area. He endorsed joint pain diffusely with multiple episodes on podagra in the past. The tender mass had started 4 weeks prior to presentation with increased swelling of a new minimally tender mass on the digit, which has since progressed to Figure 1. With growth of the mass patient now complains of slight numbness and cold sensation in the involved fingertip. The patient takes NSAIDs for joint pain that he states does relieve some of the discomfort associated with the mass. His past medical history is significant for hypertension, which he takes Losartan and hydrochlorothiazide, hyperlipidemia, osteoarthritis, and gout, for which he does not take prophylactic medication.

When palpated the joint demonstrated firmness rather than fluctuance and there was no purulent material with attempted incision and drainage. The mass was aspirated and viewed under microscopy as seen in Figure 2 and 3.

**QUESTION 1**

What is the diagnosis?

A. Lyme Disease
B. Gouty Tophi
C. Cellulitis
D. Paget’s Disease

**QUESTION 2**

A 60-year-old man presents with pain and swelling in his great toe of three days duration. He has never had these symptoms before. On physical exam he is afebrile, and has erythema over the great toe.

Which of the following laboratory or imaging results would confirm the diagnosis of acute gout in this patient?

A. Elevated serum uric acid level
B. Gouty Tophi Radiographs showing joint space narrowing of the 1st metatarsophalangeal joint and soft tissue radio-densities
C. Magnetic-resonance imaging showing increased joint fluid and T2 signal intensity in the metatarsal head
D. Arthrocentesis showing intracellular crystals that are thin, needle-shaped, and strongly negatively birefringent
E. Arthrocentesis showing intracellular crystals that are rhomboid-shaped and weakly positively birefringent
QUESTION 3
A 67-year-old male active smoker with a history of gout, congestive heart failure (ejection fraction 35%), and moderate COPD is hospitalized for a CHF exacerbation. On the third day of his hospitalization, the patient has much improved from a respiratory standpoint but has developed a warm, painful right knee. Of note, the patient’s home allopurinol was held during his hospitalization.

Which of the following joint fluid analysis results would be most consistent with a diagnosis of recurrent gout?

A. Color: yellow; Clarity: clear; WBC: 700 (15% neutrophils); Bacteria: none
B. Color: straw Clarity: cloudy; WBC: 1000 (25% neutrophils); Bacteria: none
C. Color: straw; Clarity: clear; WBC: 2000 (30% neutrophils); Bacteria: none
D. Color: yellow; Clarity: cloudy; WBC: 20000 (70% neutrophils); Bacteria: none
E. Color: grey or bloody; Clarity: turbid; WBC: 90000 (90% neutrophils); Bacteria: many

QUESTION 4
A 58-year-old male presents to the emergency department with rapid onset of severe pain and swelling in his right great toe overnight. He reports experiencing a similar episode several years ago but cannot recall the diagnosis or the medication he was given for treatment. His medical history is significant for hyperlipidemia, poorly controlled diabetes, and stage 3 chronic kidney disease. The patient’s last documented GFR estimate 2 weeks ago was 32 mL/min/1.73m^2. The interphalangeal joint of the right great toe is aspirated, with the synovial fluid aspirate showing intracellular crystals that are thin, needle-shaped, and strongly negatively birefringent.

Which of the following is the best management option for this patient?

A. Initiate long-term colchicine therapy
B. Intrarticular glucocorticoid injection
C. Oral prednisone
D. Aspirin
E. Indomethacin
DISCUSSION

Gouty tophi are nodular masses of monosodium urate crystals deposited in the soft tissues of the body. They are a late complication of hyperuricaemia and develop in more than half of patients with untreated gout. Complications of tophi include pain, soft tissue damage and deformity, joint destruction and nerve compression syndromes. Tophi can start to appear on average 12 years after the initial gout attack and have a higher prevalence in women who are on diuretic therapy. Although uncommon, it is possible for tophi to develop without previous acute gouty arthritis. Predominantly the tophi will appear on the fingers and Helix of the ear. They contain a white pasty material and can enlarge until the come to the skin surface for drainage, form small sinus tracts that can secrete the white pasty material, or alternatively form large blisters, which may erupt and leave a continuously draining ulcer. In this case the crystals accumulated in the distal interphalangeal joint to such an extent that they had neurovascular compromising effects. When aspirated and viewed under microscopy needle shaped crystals were observed. The patient was started on Allopurinol for gout. The tophus was aspirated using a 22 gauge needle for both a diagnostic and therapeutic purpose. Minimal therapeutic relief via aspiration of material is important in this case given neurovascular compromise demonstrated by numbness and cold sensation. Material is thick and hard to aspirate successfully so an incision can be made to relieve pressure or after referral to a surgeon. This patient’s tophus resolved after 4 weeks of Allopurinol. Treatment for tophaceous gout in patients with normal renal function is pharmacological with combination allopurinol and uricosuric agents. Is this fails and neurovascular compromise continues surgical excision is occasionally indicated. It is important to exclude other potentially more dangerous diagnosis such as Cellulitis, abscess, pyogenic granuloma, anthrax, herpetic whitlow, that could look very similar but would require alternative treatments. A good history and physical is paramount in establishing the correct diagnosis. Aspirating the lesion and microscopic evaluation can be very helpful in making the correct diagnosis, however updated guidelines no longer require joint aspiration if other criteria are met, please refer to Table 1.

Gout is the most common inflammatory arthropathy and characterized by painful joint inflammation. Most common joint involved is the first metatarsophalangeal joint. Precipitation of monosodium urate crystals in the joint space followed by the bodies immune response to crystals is responsible for the painful joint inflammation. Diagnosis is made by clinical suspicion and using the 2015 Gout Classification Criteria an American College of Rheumatology Initiative (Table 1). A score of eight or greater classifies an individual as having gout. For simplicity, a web-based calculator can be accessed at http://goutclassificationcalculator.auckland.ac.nz. In the above clinical scenario, the information provided about the patient was insufficient to meet the diagnostic criteria and a joint aspiration was done. However, the new criteria no longer requires confirmation by aspiration of the synovial fluid in the affected joint showing intracellular crystals that are thin, needle-shaped, and strongly negatively birefringent. In an acute gout flare the deposition of monosodium urate crystals in the joint space are exacerbated by hyperuricemia. The hyperuricemia occurs secondary to decreased excretion of uric acid from renal failure, hypertension, thiazide diuretics, or alcohol, or less commonly, due to increased production of uric acid secondary to obesity, alcohol, hemolytic disease, or a purine rich diet. Indication for pharmacologic urate-lowering therapy in patients with a history of gout are frequent or disabling attacks of gouty arthritis, clinical or radiographic signs of chronic gouty joint disease, tophaceous deposits in soft tissues or subchondral bone, gout with renal insufficiency, recurrent uric acid nephrolithiasis despite treatment with hydration and urinary alkalinization, even without another primary indication for urate-lowering pharmacotherapy; or in the presence of either recurrent uric acid or calcium oxalate nephrolithiasis in patients with hyperuricosuria, or urinary uric acid excretion exceeding 1100 mg/day when determined in men less than 25 years of age or in premenopausal women.

Acute gout is treated with intra-articular steroids or NSAIDs such as indomethacin, whereas gout prevention is achieved with xanthine oxidase inhibitors (XOIs), including allopurinol and febuxostat, uricosuric agents, including probenecid, benzbromaron, and lesinurad, and uricase, available as pegloticase and rasburicase. It has been advocated that urate-lowering therapy should not be initiated until after an acute gout flare has resolved. Waiting up to at least two weeks after an acute flare has subsided to initiate urate-lowering medications has been generally accepted. This approach has been based upon the fact that acute urate-lowering can precipitate a gout attack and upon a concern that initiation of urate-lowering therapy during an acute attack may worsen or prolong the inflammatory arthritis. However, some experts have suggested that urate-lowering medication can occasionally be started together with antiinflammatory therapy during an acute attack. The goal range of rate-lowering therapy is serum urate < 6 mg/dL. Patients should also limit consumption of certain purine rich foods such as organ meats and shellfish and also avoid alcoholic drinks like beer and products with high fructose corn syrup.

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TABLE 1.  
The ACR/EULAR gout classification criteria\textsuperscript{a,b}

<table>
<thead>
<tr>
<th>Categories</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Entry criterion (only apply criteria below to those meeting this entry criterion)</td>
<td>At least 1 episode of swelling, pain, or tenderness in a peripheral joint or bursa</td>
</tr>
<tr>
<td>Step 2: Sufficient criterion (if met, can classify as gout without applying criteria below)</td>
<td>Presence of MSU crystals in a symptomatic joint or bursa (ie, in synovial fluid) or tophus</td>
</tr>
<tr>
<td>Step 3: Criteria (to be used if sufficient criterion not met)</td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
</tr>
<tr>
<td>Pattern of joint/bursa involvement during symptomatic episode(s) ever</td>
<td>Ankle or mid-foot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint)</td>
</tr>
<tr>
<td>Characteristics of symptomatic episode(s) ever</td>
<td>Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)</td>
</tr>
<tr>
<td>- Erythema overlying affected joint (patient-reported or physician-observed)</td>
<td>One characteristic</td>
</tr>
<tr>
<td>- Can’t bear touch or pressure to affected joint</td>
<td>Two characteristics</td>
</tr>
<tr>
<td>- Great difficulty with walking or inability to use affected joint</td>
<td>Three characteristics</td>
</tr>
<tr>
<td>Time course of episode(s) ever</td>
<td></td>
</tr>
<tr>
<td>Presence (ever) of ≥2, irrespective of anti-inflammatory treatment:</td>
<td></td>
</tr>
<tr>
<td>- Time to maximal pain &lt;24 h</td>
<td>One typical episode</td>
</tr>
<tr>
<td>- Resolution of symptoms in ≤14 days</td>
<td>Recurrent typical episodes</td>
</tr>
<tr>
<td>- Complete resolution (to baseline level) between symptomatic episodes</td>
<td></td>
</tr>
<tr>
<td>Clinical evidence of tophus</td>
<td></td>
</tr>
<tr>
<td>Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (eg, Achilles)</td>
<td>Present</td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
</tr>
<tr>
<td>Serum urate:</td>
<td></td>
</tr>
<tr>
<td>Measured by the uricase method.</td>
<td></td>
</tr>
<tr>
<td>Ideally should be scored at a time when the patient was not receiving urate-lowering treatment and it was &gt;4 weeks from the start of an episode (ie, during the intercritical period); if practicable, retest under those conditions. The highest value irrespective of timing should be scored</td>
<td></td>
</tr>
<tr>
<td>- &lt;4 mg/dL (&lt;0.24 mmol/L)</td>
<td>-4</td>
</tr>
<tr>
<td>- 6–&lt;8 mg/dL (0.36–&lt;0.48 mmol/L)</td>
<td>2</td>
</tr>
<tr>
<td>- 8–&lt;10 mg/dL (0.48–&lt;0.60 mmol/L)</td>
<td>3</td>
</tr>
<tr>
<td>- ≥10 mg/dL (≥0.60 mmol/L)</td>
<td>4</td>
</tr>
<tr>
<td>Synovial fluid analysis of a symptomatic (ever) joint or bursa (should be assessed by a trained observer)\textsuperscript{‡}</td>
<td>MSU negative</td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
</tr>
<tr>
<td>Imaging evidence of urate deposition in symptomatic (ever) joint or bursa: ultrasound evidence of double-contour sign or vDECT demonstrating urate deposition</td>
<td>Present (either modality)</td>
</tr>
<tr>
<td>Imaging evidence of gout-related joint damage: conventional radiography of the hands and/or feet demonstrates at least 1 erosion</td>
<td>Present</td>
</tr>
</tbody>
</table>
ANSWERS

Question 1: Answer B) Gouty Tophi

Question 2: Answer D) The clinical presentation is suspicious of gout. The diagnosis is confirmed by arthocentesis showing intracellular crystals that are thin, needle shaped, and strongly negatively birefringent.

Incorrect Answers:

Answer A: While serum uric acid levels are often elevated in gout, it is not specific for the disorder and cannot confirm the diagnosis. Note that serum uric acid levels may be normal during an attack of acute gout.

Answer B: While radiographs can raise suspicion for gout, there are other conditions that can have similar radiographic findings. Radiographs do not have the specificity to confirm the diagnosis.

Answer C: While MRI can raise suspicion for gout, there are other conditions that can have similar radiographic findings. MRI does not have the specificity to confirm the diagnosis.

Answer E: Arthocentesis showing intracellular crystals that are rhomboid-shaped and weakly positive birefringent would confirm the diagnosis of pseudogout, caused by deposition of calcium pyrophosphate dihydrate (CPPD) crystals within the joint space.

Question 3: Answer D) The synovial aspirate from this patient with a recurrence of gouty arthritis is most likely to yield cloudy yellow fluid with 2000-50000 WBC (70% PMNs), needle-shaped negatively birefringent crystals, and no bacteria, unless the joint is superinfected.

Incorrect Answers:

Answer A: "Color: yellow; Clarity: clear; WBC: 700 (15% PMN); Bacteria: none" best describes an osteoarthritis effusion.

Answer B: "Color: straw Clarity: cloudy; WBC: 1000 (25% PMN); Bacteria: none" best describes traumatic arthritis.

Answer C: "Color: straw; Clarity: clear; WBC: 2000 (30% PMN); Bacteria: none" best describes an inflammatory arthritis due to SLE.

Answer E: "Color: grey or bloody; Clarity: turbid; WBC: 90000 (90% PMN); Bacteria: many" best describes septic arthritis.

Question 4: Answer B) This patient is suffering from acute gouty arthritis. Intra-articular steroid injection is the preferred treatment of gout in patients with renal failure.

Incorrect Answers:

Answer A: Long-term colchicine is contraindicated in patients with renal or hepatic failure due to the risk of developing colchicine toxicity.

Answer C: Given this patient’s history of poorly controlled diabetes, intra-articular steroids would be preferred over systemic administration.

Answer D: Aspirin is not used to treat acute gout flares due to its paradoxical effect on serum urate levels.

Answer E: Indomethacin (along with other NSAIDs) is contraindicated in patients with a GFR of less than 60.

REFERENCES:

10. Neogi, et. al. 2015 Gout Classification Criteria; Arthritis and Rheumatology 67:10 (October 2015) pp. 2557-2568