American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2021; 22: e932683
DOI: 10.12659/AJCR.932683

Received: 2021.04.12
Accepted: 2021.07.23
Available online: 2021.08.10
Published: 2021.09.20

Gout Storm

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Financial support: Financial support was provided by CNPq (Proc. n. 310876/2018-4) and PROPe, UNESP
Conflict of interest: None declared

Patient: Male, 55-year-old
Final Diagnosis: Gout • spinal gout
Symptoms: Back pain • fever • incontinence • pain • paresthesia of extremities • tachycardia
Medication: —
Clinical Procedure: Antibiotics • arthrocentesis • biopsy • CT scan • surgery • ultrasonography
Specialty: General and Internal Medicine

Objective: Unusual clinical course

Background: Gout is a chronic disease characterized by deposition of monosodium urate crystals, typically manifesting as arthritis. Clinical presentation of gout usually results from activation of local inflammatory response. Despite being one of the oldest diseases in the world, gout pathophysiology is incompletely understood and clinical features are still surprising. Recent reports describe unusual manifestations including atypical joints involvement, tenosynovitis, panniculitis, and multinodular inguinal swelling. Another atypical feature is the acute polyarticular gout with severe systemic inflammatory response.

Case Report: We report the case of a 55-year-old man presenting with fever, tachycardia, cauda equina syndrome, left-knee arthritis, and systemic inflammatory manifestations. Lumbar spine magnetic resonance imaging showed a 4.0×1.3×2.2 cm calcified mass inside the vertebral canal at the L4-L5 level, causing stenosis of the dural space and intervertebral foramen. Clinical diagnoses were septic knee arthritis and lumbar spine meningioma. Despite antibiotic therapy and left-knee surgical drainage, fever and increased C-reactive protein persisted, and arthritis developed in the elbows and right knee. As cultures were negatives, we then diagnosed gout flare in the affected joints accompanied by a severe systemic inflammatory reaction. A few days after starting colchicine and anti-inflammatory drugs, symptoms and inflammatory markers subsided. It was such a severe attack that we called it a "gout storm".

Conclusions: The report highlights the difficulty in diagnosing acute polyarticular gout affecting atypical joints, particularly when faced with a severe systemic inflammatory reaction.

Keywords: Cauda Equina Syndrome • Diagnosis • Gout

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Background

Gout is characterized by acute and chronic joint inflammation in response to monosodium urate crystal deposition, most commonly affecting the first metatarsophalangeal joint, knees, ankles, wrists, and hand joints [1,2]. Gout is one of oldest diseases in the world, first recognized by the Egyptians in 2640 BC [3]. Despite this long knowledge, gout pathophysiology is incompletely understood and clinical features are still surprising [4-8]. Acute manifestations are caused by immune reaction to the monosodium urate crystals that damage tissues surrounding the joints. Innate immune cells such as monocytes, macrophages, mast cells, and neutrophils are involved in the pathogenesis of acute gout inflammation [9]. Recent case reports in the literature have described unusual gout manifestations including tenosynovitis, panniculitis, multinodular inguinal swelling, and involvement of atypical joints [4-6,8,10-12]. We report the case of a patient presenting with a polyarticular gout attack affecting the knees, elbows, and lumbar spine, with intense systemic inflammatory manifestations simulating infection with systemic inflammatory response syndrome. In this case, as in several reports from literature [8,12,13], the patient was primarily managed for infection. Therefore, we would like to highlight to internist physicians the possibility of this clinical presentation of acute gout, which reminded us of a "gout storm".

Case Report

A 55-year-old man presented to our hospital with a 5-day history of low back pain with lower-limbs paresthesia, gait impairment, and fecal and urinary incontinence. In the last 2 days, he also had fever and left-knee arthritis. His medical history included hypertension, diabetes, dyslipidemia, obesity, and gout, characterized by inflammation crises involving his first right metatarsophalangeal joint and both knees since 2013. The patient had been taking enalapril, metformin, simvastatin, and insulin. Allopurinol was interrupted by the patient some months ago. There was no history of recent trauma, infection, or neoplastic disease.

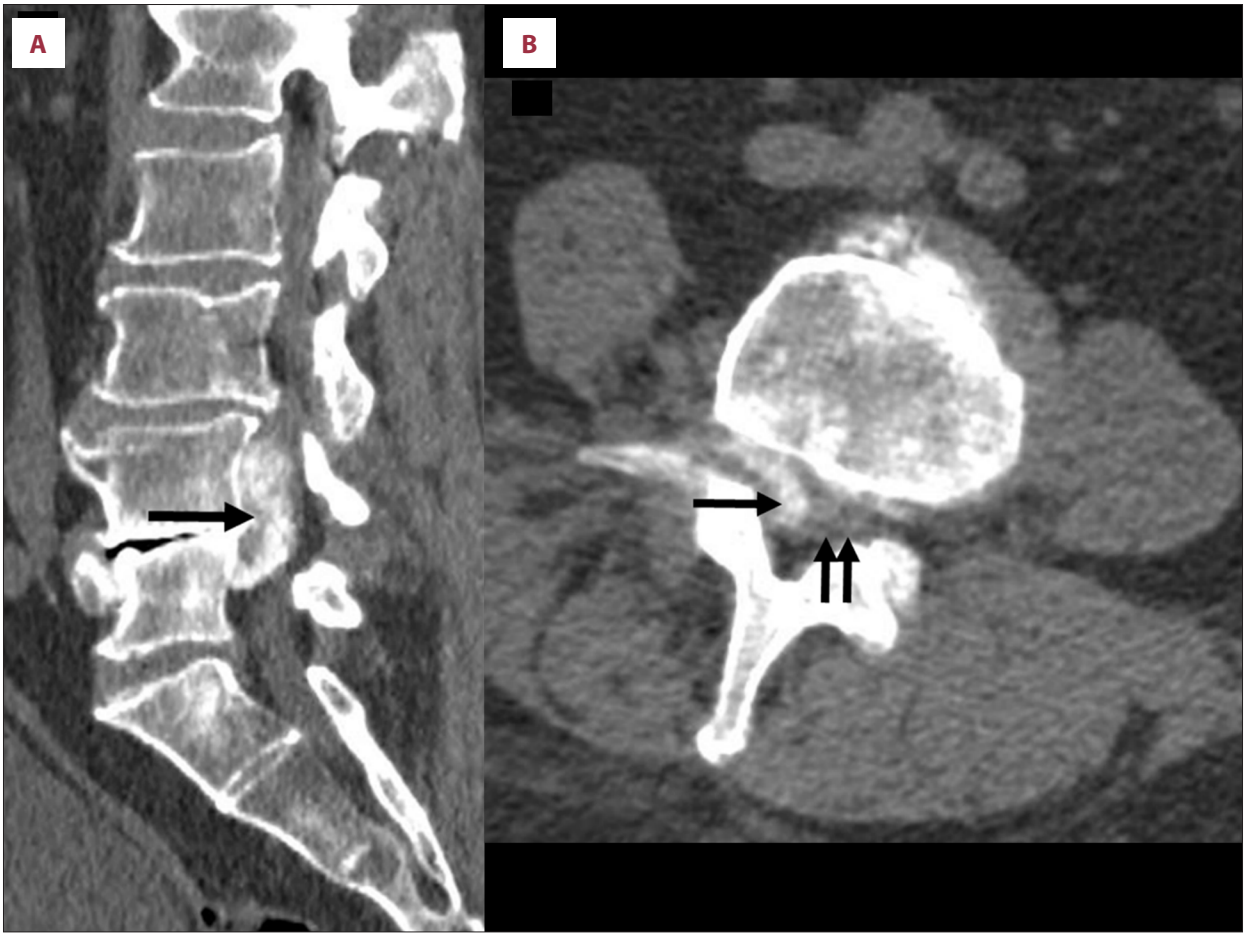

Figure 1. Non-contrast computed tomography scan sagittal (**A**) and axial (**B**) views showing a heterogeneous calcified epidural mass (arrow in **A**) compressing and displacing posterolateraly the dural sac (arrows in **B**).

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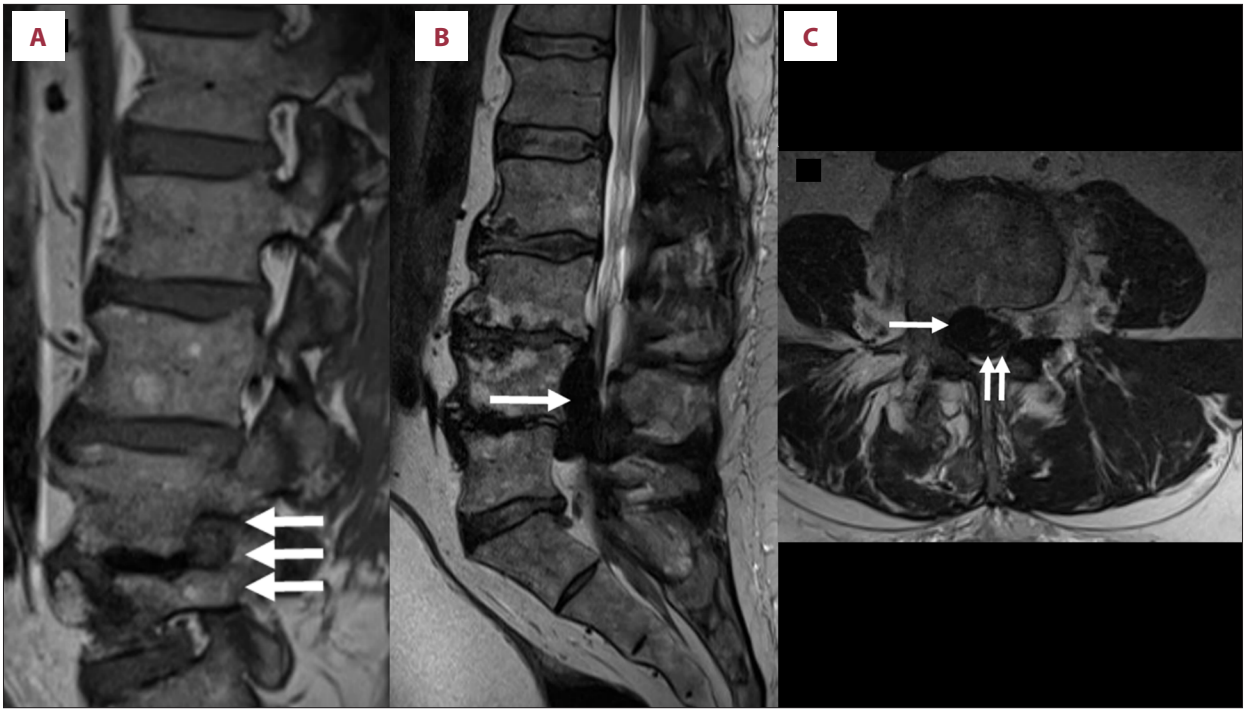

Figure 2. Magnetic resonance imaging in T1-weighted sagittal (**A**) and T2-weighted sagittal (**B**) and axial (**C**) images showing a heterogeneous hypointense epidural mass (arrow) compressing and displacing posterolateraly the dural sac (double arrow), and causing right foraminal stenosis at the L4-L5 level (triple arrow). As a consequence, the descending and emerging roots were compromised.

Physical examination showed a temperature of 38°C, heart rate 118 bpm, left-knee arthritis, grade IV reduction in left leg muscle strength, anesthesia in the left foot, and hypoesthesia in both lower limbs. No gout tophus was observed in physical examination. The remainder of physical examination was unremarkable. Laboratory evaluation revealed hemoglobin 13.5 g/dL (reference range for men 13.5-17.5 g/dL), white cell count 14 100/mm^3 (10 039/mm^3 neutrophils, 1424/mm^3 monocytes, and 2200/mm^3 lymphocytes), and creatinine 1.1 mg/dL (reference range 0.8-1.5 mg/dL), with an estimated glomerular filtration rate of 75 mL/min/1.73 m^2 according to the CKD-EPI formula, erythrocyte sedimentation rate (ESR) 65 mm/h (reference < 15 mm/h), C-reactive protein (CRP) 19.8 mg/L (reference <1 mg/dL), and uric acid 5.0 mg/dL (reference 3.5-8.5 mg/dL). His medical record showed a serum uric acid concentration dated 2016 of 11.5 mg/dL.

A non-contrasted computed tomography (CT) scan showed a heterogeneous calcified epidural mass compressing and displacing posterolateraly the dural sac (**Figure 1**). Lumbar spinal magnetic resonance imaging (MRI) showed an extensively calcified lesion measuring 4.0×1.3×2.2 cm located inside the vertebral canal at the L4-L5 level, causing stenosis of the dural space and intervertebral foramen and compressing the receptive descending and emerging roots (**Figure 2**). Ultrasonography of the left knee revealed thick fluid and echogenic debris with an estimated volume of 16 cm^3 located at the left suprapatellar bursa extending to the lateral and medial surfaces of the knee. Initially, the main clinical diagnoses were septic knee arthritis and lumbar spine meningioma. The patient received intravenous ciprofloxacin and clindamycin and was subjected to left-knee surgical drainage, producing a thick brown liquid. Cultures from blood and knee fluid collected before antibiotic therapy and knee tissue fragment were negative.

In spite of receiving antibiotics, the patient persisted with fever, fatigue, malaise, and elevated inflammatory markers. A few days later, arthritis developed in both elbows and the right knee. Left elbow arthrocentesis revealed a thick yellow synovial fluid with 1700 leukocytes/mm^3 and 96% segmented cells. Crystals were observed at microscopic evaluation; unfortunately, it was not possible to examine arthrocentesis fluid under polarized light. Right elbow arthrocentesis showed citrine yellow synovial fluid with no leukocytes. Both synovial fluid cultures were negative. Ultrasonography of the right knee revealed a heterogeneous image next to the patellar tendon measuring 2.6×1.2 cm, which might correspond to a gouty tophus.

After observing synovial crystals and excluding infection, antibiotics were discontinued and gout treatment was initiated with colchicine, 0.5 mg twice a day, anti-inflammatory drugs, and finally the xanthine oxidase inhibitor allopurinol. Fever,

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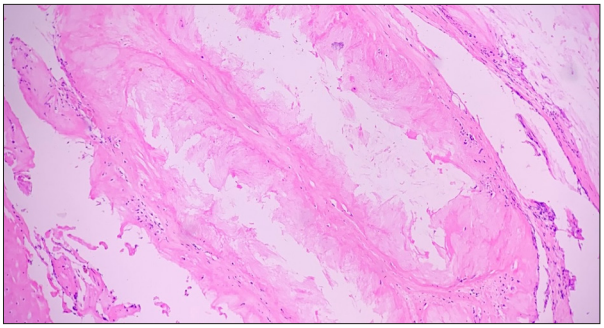

Figure 3. Histopathology section of spine mass showing a thin layer of mononuclear inflammatory infiltrate with giant cells surrounding the amorphous crystalline material, typical of gout tophi. Hematoxylin-eosin staining, ×100.

general health status, and CRP levels improved significantly a few days later, and the polyarthritis quickly resolved; neurological changes persisted. One month after hospitalization, laboratory tests revealed leukocytes of 9300/mm^3, CRP 3.7 mg/dL, and creatinine 0.7 mg/dL.

The patient was then subjected to incisional removal of the spinal mass and lumbar spine arthrodesis. The spine mass had a hard consistency, which at this point reinforced our diagnosis of gout tophus. Histopathological examination showed tissue fragments with mononuclear inflammatory infiltrate and partially calcified acellular material with giant cells surrounding the amorphous crystalline material, compatible with a gout tophus (**Figure 3**). Unfortunately, pathology analysis could not show uric acid crystals as the surgical specimen was fixed in formalin, which causes dissolution of uric acid crystals [14,15]. The patient was discharged after improvements in lower-limb paresthesia and left-limb muscle force and remission of fecal and urinary incontinence. Twelve days after surgery, he returned to our hospital presenting mental confusion, surgical site infection, and suture dehiscence. He underwent surgical debridement and wound washing. Surgical site and blood cultures revealed *Klebsiella pneumoniae;* surgical tissue fragment and wound secretion growth cultures revealed *Staphylococcus aureus*. Despite clinical treatment, the patient developed refractory septic shock and died 1 week later.

Discussion

This patient had 2 important clinical features: the polyarticular involvement of joints, including an atypical joint, the spine, and a severe systemic inflammatory reaction, similar to that seen in sepsis. Despite his previous gout, the current history and physical examination pointed to left-knee infectious arthritis in a patient with a spinal tumor. Only after the involvement of both elbows and the right knee was gout flare diagnosed. The fact that a very severe attack of gout involving an atypical joint occurred in a patient with no gout tophus makes this a rare case. Although not previously used in the literature, the term "gout storm" appeared appropriate to define these serious clinical and laboratorial manifestations. Some reports from the literature reinforce the dilemma in diagnosing acute polyarticular gout or spinal gout to explain the whole clinical picture at the time of presentation [6-8,12].

Although gout physiopathology is not completely understood, it is recognized that monosodium urate crystals deposition in the synovium induce direct cytotoxicity, inflammation, and cell necrosis. Furthermore, synovium release of reactive oxygen species and reactive nitrogen species enhances the inflammatory process [16]. Activated immune cells produce pro-inflammatory cytokines, tumor necrosis factor, and cyclo-oxygenase [9]. Monosodium urate crystals also activate the NLRP3 inflammasome, which leads to caspase-1-dependent cleavage of pro-interleukin (IL)-1β, thereby triggering mature IL-1β release and enhancing the inflammatory response [16]. We assume that, in this case, the inflammatory response hyperactivation was triggered by the polyarticular involvement.

Several triggers for gout attacks have been described [1]. The only precipitating factor we could find in this case was a slight renal function impairment. However, it was not possible to establish whether worsening renal function was a precipitating factor or followed an acute attack, which could have impaired oral ingestion and led to dehydration.

This case emphasizes the importance of cytological examination of synovial fluid, which is often mistaken for a purulent exudate of septic arthritis. Even though fever, neutrophilia, and raised inflammatory markers are common in acute gout [8,11,17-19], their presence guides physicians toward a diagnosis of bacterial infection. CRP, ESR, and procalcitonin at high levels as observed in infectious disease have been described during acute gout attacks and chronic gout [17,18,20,21]. A severe systemic inflammatory response syndrome simulating sepsis has also been observed in acute polyarticular gout [22] and immediately after spinal surgery for axial gout [14]. On left-knee ultrasound, our findings of thick fluid and echogenic debris have low specificity and accuracy for diagnosing gout, but a double contour sign and articular tophus have a high specificity for gout diagnosis [23].

Spinal tophaceous gout is not a common finding. In most cases in the literature, a diagnosis of spinal tophi was not initially suspected [7,17,18,24,25]. The most common clinical presentation was back and neck pain, followed by neurological impairment. The main anatomical site was the lumbar spine [17]. The imaging tests most often performed are MRI and CT. In a review on spine gout, 96.6% of CT scans were abnormal, with 18.6% of scans interpreted as a high probability of tophaceous

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gout [18]. MRI is the most commonly used method to analyze spinal lesions; in a review on spine gout, 98.9% of the cases had abnormal MRI. However, scans were read as a gouty or tophaceous lesion only in 21% of the patients [18]. As in our case, gouty tophi usually appear as a hypointense mass on T1- and/or T2-weight MRI [24].

The treatment of gout involves drugs to reduce inflammation in the acute phase, such as nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and colchicine, and drugs to lower uric acid levels and prevent acute flare. NSAIDs inhibit production of cyclo-oxygenase; glucocorticoids inhibit transcription of inflammatory genes, and colchicine blocks activity of the NLRP3 inflammasome [26]. Recent studies have shown that IL-1 antagonists can be used in gout flare. The xanthine oxidase inhibitor allopurinol is the first line treatment and uricosuric agents are the second-line treatment for chronic gout [27]. The urate oxidase pegloticase can be used in refractory cases [27]. Treatment for spinal tophi depends on the clinical picture [19]. Although medical treatment may be sufficient, neurological impairment warrants surgical intervention [7,17,18]. In many cases, surgery was performed to assess suspected epidural abscess or spinal mass [13]. As drugs failed to decrease spinal symptoms, our patient was subjected to spinal decompression, which was initially successful. Unfortunately, postoperative surgical site infection led to patient death.

Conclusions

This report highlights the difficulty in diagnosing acute polyarticular gout affecting an atypical joint, particularly when faced with a severe systemic inflammatory reaction. Furthermore, it emphasizes the importance of properly controlling serum uric acid concentration to prevent acute gout flare. Treatment should also include avoidance of risk factors for gout development, flare management, and healthy lifestyle.

Patient Consent

The patient's wife provided written consent for reporting this case.

Acknowledgements

The authors are grateful to Colin Edward Knaggs for English editing.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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