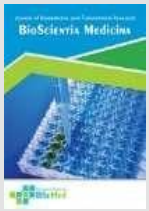
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Acute Gouty Arthritis with Knee Effusion in a Patient with Chronic Lymphocytic Leukemia: Diagnostic Confirmation and Pre-Chemotherapy Hyperuricemia Management

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ARTICLE INFO

Keywords:
Chronic lymphocytic leukemia
Gout
Hyperuricemia
Knee effusion
Monosodium urate crystals

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v10i6.1614

A B S T R A C T

Background: Gout and chronic lymphocytic leukemia (CLL) represent distinct hematologic and rheumatologic pathologies; however, their concurrent presentation presents significant diagnostic and therapeutic challenges. Tumor lysis syndrome and chemotherapy-induced hyperuricemia are recognized complications of hematologic malignancies, yet the manifestation of acute gouty arthritis with crystallographic confirmation in CLL patients remains an underreported clinical scenario requiring careful diagnostic stratification. **Case presentation:** We present a 69-year-old male farmer with newly diagnosed CLL (stage C, Binet classification) admitted for acute left knee arthritis with effusion, left ankle arthritis, and concurrent community-acquired pneumonia (CAP). Clinical examination revealed articular inflammation characterized by pain, swelling, erythema, warmth, and significant joint effusion with documented flexion limitation and positive bulging sign. Musculoskeletal ultrasound demonstrated double contour sign, synovial hypertrophy, and effusion measuring 5.8 cm in the suprapatellar recess with monosodium urate (MSU) crystal deposition confirmed by polarized light microscopy of synovial fluid (5,350 cells/mm^3, 40% polymorphonuclear neutrophils, 60% mononuclear cells, positive MSU crystals). Serum uric acid was elevated at 10.6 mg/dL. The patient was successfully managed with colchicine, methylprednisolone, arthrocentesis, and supportive care while maintaining CLL treatment preparedness. **Conclusion:** This case illustrates the importance of confirmatory synovial fluid analysis and ultrasound imaging in the diagnosis of acute gout in the context of hematologic malignancy. Optimal management requires careful coordination between rheumatology and hematology-oncology services to prevent therapeutic complications and ensure safe chemotherapy initiation in CLL patients with concurrent acute gouty arthritis and hyperuricemia.

1. Introduction

Gout represents one of the most prevalent inflammatory arthropathies affecting the adult population globally, with epidemiological data demonstrating an increasing incidence and prevalence over the past two decades.[1] Current estimates suggest that gout affects approximately 1-2% of the general population in developed nations, with age-related prevalence increasing substantially in patients over 65 years, making gout a significant public health concern in aging populations. The disease results from monosodium urate (MSU) crystal deposition within synovial joints and periarticular tissues, triggering an intense inflammatory response characterized by rapid onset of pain, erythema, swelling, and functional impairment. Although the first metatarsophalangeal

joint remains the most commonly affected site, gout can manifest in larger joints including the knees, ankles, wrists, and shoulders, particularly in the setting of longstanding hyperuricemia and advanced age.[2]

The pathophysiology of gout involves complex interactions between hyperuricemia, MSU crystal formation, and innate immune activation in the joint microenvironment. When serum uric acid concentration exceeds its saturation point (approximately 6.8 mg/dL at physiologic pH and temperature), urate crystals precipitate in tissues with cooler temperatures and lower pH, such as peripheral joints and subcutaneous tissues. The initial crystallization event triggers engagement of the resident monosodium urate-sensing system, leading to activation of the NLRP3 inflammasome, a multiprotein complex responsible for processing pro-interleukin-1β into its active form.[3] This inflammasome activation pathway initiates a cascade of pro-inflammatory signaling that recruits polymorphonuclear neutrophils to the affected joint, amplifying local tissue inflammation and producing the characteristic acute gouty arthritis presentation. Resolution of the acute attack occurs through coating of MSU crystals by apolipoprotein B and other serum proteins, rendering them immunologically inert and allowing gradual neutrophil apoptosis and inflammation resolution.[4]

Chronic lymphocytic leukemia represents a B-cell malignancy characterized by progressive accumulation of functionally incompetent lymphocytes in bone marrow, peripheral blood, lymph nodes, and spleen.[5] The disease exhibits a variable clinical course, ranging from indolent presentations requiring minimal intervention and watch-and-wait approaches to aggressive forms necessitating prompt chemotherapy initiation. Genetic and molecular markers, including TP53 mutations, FISH cytogenetics, and immunoglobulin variable region mutation status, predict clinical progression and treatment response. Modern staging systems, including the Binet and Rai classifications, utilize lymphocytosis, lymphadenopathy, splenomegaly, hepatomegaly, and cytopenias to stratify disease severity and predict prognosis. The development of CLL in elderly patients frequently coexists with age-related medical comorbidities, including osteoarthritis, hypertension, chronic kidney disease, and metabolic dysfunction, creating complex diagnostic scenarios requiring careful differential diagnosis.[6]

A critical intersection between hematologic malignancy and hyperuricemia emerges from tumor lysis syndrome (TLS), a life-threatening complication characterized by rapid cellular necrosis following chemotherapy initiation or, less commonly, spontaneous tumor cell death in high disease burden states.[7] The massive release of intracellular contents from malignant cells, including phosphate, potassium, and nucleic acids metabolized to uric acid, produces severe hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. The resulting hyperuricemia can manifest as acute urate nephropathy and, in this clinical context, may precipitate or exacerbate acute gouty arthritis. While acute gout occurring as a direct manifestation of TLS has been previously reported in lymphoid malignancies, the concurrent presentation of symptomatic acute gouty arthritis with radiographic and crystallographic confirmation in newly diagnosed CLL remains an underreported clinical entity requiring careful diagnostic consideration.[8]

The diagnostic evaluation of acute arthritis in CLL patients requires a comprehensive assessment, including clinical examination, laboratory analysis, imaging studies, and synovial fluid examination.[9] The 2015 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) gout classification criteria provide validated diagnostic discrimination with a threshold score of ≥8 yielding 92% sensitivity and 89% specificity for gout diagnosis. Conventional radiography can demonstrate osteophytes and joint space narrowing consistent with osteoarthritis but lacks sensitivity for acute MSU deposition. Modern musculoskeletal ultrasound offers

substantial diagnostic value through visualization of the double contour sign (a thin echogenic band over hyaline cartilage surface), hyperechoic aggregates within synovial fluid, and effusion characteristics. Synovial fluid analysis remains the gold standard for gout diagnosis, requiring demonstration of MSU crystals by polarized light microscopy with characteristic needle-shaped, negative-birefringent morphology appearing as black upon parallel polarizer and compensator orientation.[10]

This case report presents a comprehensive clinical vignette of acute gouty arthritis with confirmed MSU crystal deposition in the setting of newly diagnosed CLL with stage C (Binet) disease. The patient demonstrated clinical, laboratory, and crystallographic evidence of acute gout with substantial knee effusion requiring diagnostic imaging confirmation, synovial fluid analysis, and coordinated rheumatology-oncology management. The case illustrates key diagnostic considerations for acute arthritis in hematologic malignancy patients and highlights the importance of confirmatory testing prior to chemotherapy initiation in high-risk hyperuricemia scenarios.

2. Case Presentation

Patient demographics and clinical history

A 69-year-old Indonesian male farmer with 50 years occupational history in agricultural work presented to Dr. M. Djamil General Hospital on December 12th, 2023, with progressive left knee pain and swelling. The patient reported progressive knee discomfort developing over a two-month period prior to hospital admission, with acute exacerbation occurring three days before presentation. The patient characterized the pain as stabbing in nature, significantly exacerbated by movement and weight-bearing, with associated morning stiffness persisting approximately 30 minutes upon awakening. Additionally, the patient noted left ankle involvement with pain, swelling, and stiffness developing three days prior to hospitalization. The patient's prior medical history included chronic hyperuricemia without prior pharmacologic treatment, with a documented history of prior gout episodes affecting the right first metatarsophalangeal joint (MTP-1) with symptom onset approximately six months prior to the current presentation. These prior episodes were managed conservatively without diagnostic workup or antiinflammatory prophylaxis. A recent hematologic evaluation approximately one month prior to current admission had revealed an elevated serum uric acid level of 8.28 mg/dL during routine physical examination. Notably, the patient had received a diagnosis of chronic lymphocytic leukemia (CLL) on November 30th, 2023, following a routine laboratory evaluation that identified profound leukocytosis, establishing a disease duration of approximately 12 days prior to the current rheumatologic presentation. The patient also reported constitutional symptoms, including shortness of breath, fever, and productive cough with yellow sputum, persisting for five days, as well as early satiety and abdominal fullness developing over a four-month period related to hepatosplenomegaly from CLL infiltration. Table 1 presents the demographic and clinical characteristics of the patient.

Vital sign assessment at hospital admission documented blood pressure 110/60 mmHg, heart rate 110 beats per minute with regular rhythm, respiratory rate 22 breaths per minute, body temperature 37.6°C, oxygen saturation 98% on two liters per minute of supplemental oxygen via nasal cannula, and calculated body mass index (BMI) of 20.2 kg/m², indicating normal weight status. Physical examination revealed bilateral coarse crackles on pulmonary auscultation, consistent with lower respiratory tract involvement from community-acquired pneumonia. Notably, the patient demonstrated signs of pallor consistent with anemia from bone marrow involvement by CLL. Focused rheumatologic examination of the left knee demonstrated significant inflammatory changes including visible swelling with measurable joint distension, erythema overlying the joint, warmth to palpation, and marked tenderness with pain on passive and active motion.

Table 1. Clinical characteristics of the patient.

Parameter	Finding
Age	69 years
Gender	Male
Occupation	Farmer (50 years)
BMI	20.2 kg/m² (normal)
Chief complaint	Progressive left knee pain (2 months)
Duration of symptoms	Acute exacerbation 3 days prior
Prior gout history	Right MTP-1 (6 months prior)
CLL diagnosis	November 30, 2023 (Binet Stage C)
Comorbidities	OA left knee grade III, CAP
Barthel index	17 (mild dependency)
Frailty index	0.15 (pre-frail)
ACR/EULAR gout score	13/23 (≥8 = gout diagnosis)

Range of motion was substantially limited secondary to pain and mechanical restriction. Clinical examination revealed a positive patella tap sign indicating significant effusion, a ballooning sign consistent with fluid accumulation, a bulging sign demonstrating distension of the joint capsule, and fluctuance on palpation, consistent with significant intra-articular fluid accumulation. Additionally, the examiner documented crepitation within the knee joint, suggesting cartilage surface irregularities. The left ankle demonstrated similar inflammatory features, including swelling, stiffness, marked tenderness, and limited range of motion affecting both dorsiflexion and plantarflexion. Abdominal and lymphatic examination revealed hepatosplenomegaly consistent with CLL-related organomegaly, with palpable liver edge extending below the costal margin and palpable spleen edge. Neurologic examination documented appropriate orientation to person, place, and time, with normal cognition. Functional assessment using the Barthel Index score yielded 17 points, corresponding to mild functional dependency, with limitation primarily in ambulation and joint mobility secondary to acute knee arthritis.

Complete blood count analysis (detailed in Table 2) demonstrated severe leukocytosis with a white blood cell (WBC) count of 113,110 cells/mm³ (normal range 4,500-11,000 cells/mm³), with a differential revealing 1% blasts and 37% prolymphocytes, consistent with CLL involvement and stage C disease burden. Hemoglobin concentration was 9.6 g/dL (normal range 13.5-17.5 g/dL), indicating moderate anemia consistent with bone marrow infiltration. Platelet count was 99,000/mm³ (normal range 150,000-400,000/mm³), representing mild thrombocytopenia. Serum uric acid level was markedly elevated at 10.6 mg/dL (normal range 3.5-7.2 mg/dL), approximately 1.5 times the upper limit of normal and well above saturation threshold. Imaging studies including chest radiography demonstrated bilateral infiltrates consistent with pneumonic process. Left knee radiography revealed characteristic osteoarthritic changes including osteophytes, joint space narrowing, and ligament calcification, corresponding to Kellgren-Lawrence grade III osteoarthritis. Musculoskeletal ultrasound examination of the left knee provided

critical diagnostic confirmation, demonstrating simple effusion within the suprapatellar recess measuring 5.8 centimeters in maximum depth, with extension of effusion medially and laterally within the joint capsule. The examination documented synovial membrane thickening and the presence of the double contour sign, an echogenic band paralleling the hyaline cartilage surface, highly specific for MSU crystal deposition. Synovial fluid analysis obtained via arthrocentesis demonstrated a cell count of 5,350 cells per cubic millimeter with a differential revealing 40% polymorphonuclear neutrophils (PMN) and 60% mononuclear cells (MN), consistent with acute inflammatory arthritis. Critically, polarized light microscopy of fresh synovial fluid samples demonstrated the presence of monosodium urate crystals with characteristic needle-shaped morphology and negative birefringence (appearing black when aligned with the compensator), confirming the diagnosis of acute gouty arthritis and satisfying criteria for definitive gout diagnosis.

Table 2. Laboratory findings.

Parameter	Result	Reference range	Interpretation
Hemoglobin	9.6 g/dL	13.0-17.5 g/dL	Low (anemia)
Leukocytes	113,110/mm³	4,000-11,000/mm³	Critical high
Platelets	99,000/mm³	150,000-400,000/mm³	Low (thrombocytopenia)
Blast cells	1%	0%	Elevated
Prolymphocytes	37%	0-2%	Markedly elevated
Uric acid	10.6 mg/dL	3.5-7.2 mg/dL	Elevated (hyperuricemia)
Synovial fluid cells	5,350/mm³	<200/mm³	Inflammatory
PMN cells	40%	—	—
Mononuclear cells	60%	—	—
MSU crystals	Positive	Negative	Confirmatory for gout

Application of the 2015 ACR/EULAR gout classification criteria to this patient yielded a composite score of 13, substantially exceeding the diagnostic threshold of ≥8 for gout diagnosis. The criteria scoring incorporated the presence of MSU crystal deposition confirmed by polarized light microscopy (2 points for definite MSU crystal identification), acute arthritis with onset within 24 hours (2 points), characteristic inflammatory signs including erythema, swelling, and warmth (1 point), first metatarsophalangeal joint involvement in prior episodes (2 points), and elevated serum uric acid level (4 points for concentration >10.2 mg/dL). This comprehensive assessment confirmed acute gouty arthritis with high diagnostic confidence. The patient was assessed using the Fried frailty index, which evaluates five domains including unintentional weight loss, self-reported weakness, slow walking speed, low physical activity level, and exhaustion. The patient scored 0.15 on the frailty index (scale 0-1), corresponding to a pre-frail classification. This intermediate risk status indicated vulnerability to adverse outcomes and required careful medical optimization prior to intensive chemotherapy

initiation for CLL. Fall risk assessment identified instability secondary to acute left knee arthritis and pain, necessitating assistive devices and modified activity restrictions during acute phase management.

The acute gouty arthritis was managed with a comprehensive pharmacologic regimen (detailed in Table 3). Colchicine was administered at an initial dose of 1.0 mg orally, followed by 0.5 mg administered one hour later, consistent with established acute gout management protocols. Methylprednisolone 8 mg was administered twice daily via intravenous or oral route, providing potent anti-inflammatory effects. Paracetamol (acetaminophen) was provided for symptomatic pain control at appropriate dosing intervals. Therapeutic arthrocentesis was performed, providing both diagnostic synovial fluid analysis and therapeutic benefit through effusion drainage and decompression of the distended joint capsule, with approximately 58 mL of synovial fluid obtained. The concurrent community-acquired pneumonia (CAP) diagnosed as non-severe was treated with intravenous ampicillin-sulbactam (3 g every 6 hours) combined with oral azithromycin (500 mg daily), addressing both community-acquired pathogens, including Streptococcus pneumoniae, and atypical organisms. Dietary counseling emphasized a low-purine diet with restriction of red meat, organ meats, seafood high in purines (anchovies, sardines, shellfish), and alcohol consumption, particularly avoiding beer. The patient demonstrated a favorable clinical response to the instituted therapeutic regimen over the hospitalization period. Over the subsequent hospitalization period, the acute inflammatory signs and symptoms showed progressive resolution with decreased pain intensity, improved joint mobility, and reduced knee swelling and erythema within 5-7 days of admission. Functional status improved incrementally as acute inflammation subsided, with the patient regaining independence in activities of daily living and ambulation with standard walking aids by hospital discharge. The patient achieved clinical stability facilitating safe discharge planning with arrangements for outpatient rheumatology follow-up, ongoing internal medicine management, and coordination with hematology-oncology services for CLL treatment planning. Chemotherapy was deferred during the acute rheumatologic management phase to allow optimal clinical stabilization and resolution of acute gouty arthritis, minimizing risk of TLS-related hyperuricemia exacerbation during initial drug administration. As demonstrated in Table 4, our case shares similar features with previously reported cases.

Table 3. Treatment regimen and clinical response.

Medication	Dose	Route	Frequency	Purpose
Colchicine	1 mg then 0.5 mg	Oral	Day 1 loading	Acute gout attack
Methylprednisolone	8 mg	Oral	Twice daily	Anti-inflammatory
Paracetamol	500 mg	Oral	As needed	Analgesia (VAS 4-5)
Ampicillin-sulbactam	1.5 g	IV	Every 8 hours	CAP treatment
Azithromycin	500 mg	Oral	Once daily	CAP treatment
Arthrocentesis	—	Intra-articular	Once	Diagnostic/therapeutic
Low-purine diet	—	—	Continuous	Urate reduction

Table 4. Comparison of this study with previous case reports.

Feature	Present case	Dalbeth 2021	Ragab 2017	Howard 2011
Age/Gender	69/M	Review	Review	Review
Primary diagnosis	Gout + CLL	Gout overview	Gout pathophysiology	TLS in hematologic malignancy
Uric acid (mg/dL)	10.6	>6.8 (threshold)	Variable	>8.0 (TLS risk)
Crystal confirmation	MSU positive	Gold standard	Gold standard	N/A
Ultrasound finding	Double contour +	Recommended	Adjunctive	N/A
ACR/EULAR score	13 (positive)	Validated tool	Validated tool	N/A
Hematologic comorbidity	CLL Stage C	Not addressed	Not addressed	Primary focus
Key management	Colchicine + steroids	First-line	Comprehensive	TLS prophylaxis

3. Discussion

The presentation of acute gouty arthritis fundamentally relates to the physical chemistry of urate solubility and the inflammatory consequences of MSU crystal formation within synovial compartments. Under physiologic conditions, monosodium urate exists in a delicate equilibrium between dissolved and crystalline forms, with the saturation point occurring at approximately 6.8 mg/dL at body temperature and physiologic pH of 7.4. Hyperuricemia results from either purine overproduction (often secondary to myeloproliferative disorders, including CLL, characterized by massive cellular turnover) or undersecretion of urate by renal tubular mechanisms (the predominant mechanism in 90% of gout cases in non-malignancy populations). Once serum uric acid concentration exceeds saturation, crystal nucleation occurs preferentially in peripheral joints and tissues with lower temperature and a more acidic pH microenvironment, accounting for the characteristic predilection for the first metatarsophalangeal joint, midfoot, ankles, and knees in gout pathophysiology. The innate immune recognition of MSU crystals occurs through a sophisticated molecular sensing system involving multiple pattern recognition receptors and inflammasome components. Recent mechanistic investigations have demonstrated that MSU crystals, despite being endogenous molecules, function as danger-associated molecular patterns (DAMPs) recognized by the resident macrophage and neutrophil populations within synovial tissue. The NLRP3 inflammasome, a multiprotein complex assembled from NLRP3, ASC, and pro-caspase-1 components, represents the critical molecular hub mediating MSU crystal recognition and downstream inflammatory signaling. Crystal engagement with cell membranes triggers K+ efflux from the cytoplasm, leading to NLRP3 inflammasome assembly and subsequent pro-caspase-1 autoactivation. Activated caspase-1 then processes pro-interleukin-1β (pro-IL-1β) and pro-interleukin-18 (pro-IL-18) into their biologically active forms, with IL-1β serving as the primary driver of acute gouty inflammation and recruitment of neutrophils. The resulting IL-1β-mediated signaling cascade triggers prostaglandin and leukotriene generation, complement cascade

activation, chemokine production including C-X-C motif ligand 1 (CXCL1) and CXCL8, and recruitment of enormous numbers of polymorphonuclear neutrophils to the affected joint. The intense neutrophilic infiltration characteristic of acute gouty arthritis produces the visible and palpable inflammatory signs appreciated clinically: erythema from local vasodilation and increased blood flow, swelling from increased vascular permeability and edema, warmth from local hypermetabolism and mitochondrial activity, and exquisite pain from stimulation of nociceptive nerve endings by inflammatory mediators. The synovial fluid analysis typically demonstrates cell counts ranging from 2,000 to 100,000 cells/mm³ with predominance of neutrophils, consistent with this intense inflammatory infiltration. In this clinical case, the documented synovial fluid cell count of 5,350 cells/mm³ with 40% PMN composition demonstrates a level of inflammation consistent with acute gouty arthritis, though at the lower end of the typically reported spectrum, suggesting either relatively early intervention in the acute phase or partial spontaneous resolution. Resolution of acute gouty arthritis involves complex anti-inflammatory mechanisms, including apolipoprotein coating of MSU crystals, transforming growth factor-β (TGF-β) production by recruited macrophages, and programmed neutrophil death through apoptosis and clearance. These endogenous resolution mechanisms typically result in spontaneous subsidence of acute inflammation within 7-10 days if untreated, or more rapid resolution with appropriate pharmacotherapy. The role of TGF-β as an anti-inflammatory cytokine is particularly noteworthy, as this cytokine actively suppresses NLRP3 inflammasome components and IL-1β production, creating a negative feedback loop that limits inflammatory progression.[11]

Modern musculoskeletal ultrasound has emerged as a powerful diagnostic adjunct in acute arthritis evaluation, offering substantial advantages over conventional radiography in detecting MSU crystal deposition and inflammatory changes within synovial compartments.[12] The double contour sign represents one of the most specific ultrasound findings for gout, demonstrated by visualization of a thin echogenic band paralleling the hyaline cartilage surface. This echogenic band is thought to represent MSU crystal deposition along the articular cartilage surface, creating the characteristic appearance of hypoechoic cartilage (appearing dark) with a thin bright echogenic layer representing crystal deposition. The double contour sign demonstrates reported sensitivity ranging from 60-90% and specificity exceeding 95% for chronic tophaceous gout when present, with lower sensitivity in acute arthritis presentations. In this case, the presence of the double contour sign provided important supportive evidence for MSU-mediated joint disease, complementing the diagnostic certainty provided by synovial fluid crystal analysis. Additional ultrasound findings in gout include hyperechoic aggregates within synovial fluid or synovial membrane (representing crystal accumulation), effusion with varying echogenicity depending on cellularity and protein concentration, and synovial membrane thickening reflecting inflammatory hypertrophy. In this patient, the documented effusion measuring 5.8 cm in maximum depth within the suprapatellar recess with synovial thickening provided objective evidence of inflammatory arthritis and significant joint involvement. The presence of simple effusion without heterogeneous internal echoes suggests a purely inflammatory etiology without hemorrhage or purulent infection, consistent with crystal-induced arthritis rather than septic arthritis or traumatic hemarthrosis. Synovial fluid analysis remains the gold standard diagnostic modality for crystal-induced arthropathies, permitting definitive identification of MSU crystals through polarized light microscopy.[13] The characteristic appearance of MSU crystals under polarized microscopy includes needle-shaped or rod-shaped morphology with negative birefringence (appearing as black when aligned parallel to the compensator and rotating dark upon rotation of the microscopic stage). The synovial fluid analysis in this patient demonstrated several important findings: total

cell count of 5,350 cells/mm³, differential showing 40% polymorphonuclear cells and 60% mononuclear cells, and, most critically, the presence of monosodium urate crystals with characteristic morphology on polarized light microscopy, confirming acute gouty arthritis.[14]

A notable clinical feature in this case involves the concurrent presence of grade III osteoarthritis (OA) and acute gouty arthritis affecting the same left knee joint. The radiographic findings documented osteophytes, joint space narrowing, and ligament calcification consistent with Kellgren-Lawrence grade III OA, representing moderate-to-advanced degenerative joint disease. The coexistence of OA and crystal-induced arthritis is well-recognized in clinical practice and carries important diagnostic and management implications.[15] Chronic OA produces sustained low-grade inflammation within the joint microenvironment, characterized by altered synovial fluid composition with decreased proteoglycan and increased inflammatory mediator concentrations, chondrocyte dysfunction with increased matrix metalloproteinase production, and changes in joint pH and electrolyte concentration. The osteoarthritic joint microenvironment may paradoxically predispose to acute MSU crystal precipitation and gout attacks through multiple mechanisms. Degraded cartilage proteoglycans expose higher concentrations of negatively charged glycosaminoglycans that can serve as nucleation sites for MSU crystal formation. Altered synovial fluid pH in OA joints, which tends toward more acidic conditions due to increased lactate production and decreased buffering capacity, may shift the urate equilibrium toward crystal formation. Additionally, the chronic synovial inflammatory environment in OA joints enhances the responsiveness to MSU crystals, potentially amplifying the inflammatory cascade once crystal nucleation occurs. This phenomenon explains the common clinical observation that gout frequently presents in larger joints such as knees and ankles that are commonly affected by osteoarthritis, even though these larger joints are less commonly affected by gout in younger populations without significant OA. The management of concurrent OA and acute gout requires careful therapeutic planning to address both pathologies effectively. During acute gout attacks, anti-inflammatory medications including colchicine, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids are preferred over analgesics alone, as these agents address the underlying inflammatory cascade.[16]

The diagnosis of CLL stage C in this patient provided critical context for understanding the pronounced hyperuricemia and predisposition to acute gouty arthritis. CLL, characterized by progressive clonal accumulation of B lymphocytes with impaired function and shortened survival, results in dramatically increased cellular turnover rates, particularly early in the disease course or in response to disease-directed therapy.[17] The high cellular burden in CLL patients, reflected in this case by a WBC count of 113,110 cells/mm³ with significant leukemic infiltration, indicates massive ongoing cellular proliferation and death within the bone marrow and other hematopoietic tissues. Each cell contains approximately 0.8-1 gram of nucleic acid composed of purines and pyrimidines. When leukemic cells undergo apoptosis or are killed by therapeutic agents, the resulting nucleic acid catabolism through the purine degradation pathway produces abundant hypoxanthine and xanthine intermediates, which are ultimately oxidized to uric acid through the enzyme xanthine oxidase, resulting in massive uric acid production. In this patient, the serum uric acid level of 10.6 mg/dL represents substantial elevation above normal ranges and above typical gout threshold concentrations, likely reflecting both the high disease burden from CLL with its associated cellular turnover and possible underlying urate undersecretion. The prior uric acid measurement of 8.28 mg/dL documented one month before CLL diagnosis suggests that significant baseline hyperuricemia existed prior to the acute presentation, indicating either intrinsic purine overproduction tendency or renal urate underexcretion at baseline. The CLL diagnosis

occurring merely two weeks prior to the acute gouty arthritis presentation, combined with the marked elevation of uric acid to 10.6 mg/dL, indicates an additional contribution of CLL-related cellular turnover to serum urate concentration, with the 2.32 mg/dL increase over one month representing accelerated uric acid production from malignant cell turnover.[18]

The development of acute gouty arthritis in the setting of newly diagnosed CLL stage C warrants careful consideration of tumor lysis syndrome risk and chemotherapy planning. Tumor lysis syndrome represents one of the most serious complications of hematologic malignancy treatment, characterized by massive cell necrosis releasing intracellular contents including potassium, phosphate, and nucleic acids metabolized to uric acid. Laboratory evidence of TLS includes hyperkalemia (>6.0 mEq/L), hyperphosphatemia (>4.5 mg/dL), hypocalcemia (<7 mg/dL corrected), and hyperuricemia (>8 mg/dL or 25% increase from baseline). Clinical manifestations include acute kidney injury from urate crystal precipitation in renal tubules, cardiac dysrhythmias from hyperkalemia, neuromuscular manifestations including muscle cramps and tetany, and in severe cases, seizures or sudden cardiac death.[19] Risk stratification for TLS in hematologic malignancy patients incorporates both tumor burden factors and patient-related factors. High-risk tumor characteristics include high proliferative rate indicating rapid cell turnover, large disease burden as reflected by high WBC count and hepatosplenomegaly, and high sensitivity to chemotherapy predicting rapid cell death upon treatment initiation. High-risk patient factors include advanced age reducing physiologic reserve, pre-existing renal impairment reducing uric acid clearance, elevated baseline uric acid indicating pre-existing hyperuricemia, and elevated baseline lactate dehydrogenase (LDH) reflecting high cell turnover. In this patient, risk factors for TLS were present including age 69 years, CLL stage C with marked leukocytosis (WBC 113,110 cells/mm^3 representing severe disease burden), baseline hyperuricemia at 10.6 mg/dL well above saturation threshold, and clinical evidence of significant disease burden with hepatosplenomegaly on abdominal examination. These risk factors combined with the acute manifestation of gout indicated the necessity for careful chemotherapy planning with prophylactic measures including allopurinol or febuxostat to suppress xanthine oxidase and prevent uric acid overproduction, rasburicase as a rapid-acting uricolysin that directly degrades uric acid, aggressive intravenous hydration to maintain urine output and prevent crystallization, and potentially cytoreduction therapy with low-dose chemotherapy prior to full-dose therapy. The decision in this case to defer chemotherapy during acute rheumatologic management represented appropriate clinical judgment in balancing the need for CLL disease-directed therapy against the risks of precipitating or exacerbating TLS in the setting of active acute gout.

The diagnosis of acute gouty arthritis in the setting of CLL requires careful differential consideration of alternative etiologies that may present with similar clinical and laboratory findings. Septic arthritis remains an important differential diagnosis, particularly given the immunosuppressed state of CLL patients with markedly elevated WBC counts indicating immune dysfunction.[20] However, the characteristic inflammatory pattern with 40% neutrophils and 60% mononuclear cells in synovial fluid, combined with the presence of pathognomonic MSU crystals on polarized light microscopy, effectively excludes septic arthritis (which typically presents with >80% neutrophil predominance and bacterial culture positivity). Rheumatoid arthritis presents as a polyarticular symmetric polyarthritis rather than acute monoarticular arthritis, with presence of rheumatoid factor and anti-CCP antibodies as serologic markers. Systemic lupus erythematosus can present with arthritis but typically shows different serology (ANA, anti-dsDNA, anti-Smith antibodies) and does not present with MSU crystal deposition. The presence of confirmed MSU crystals by polarized light microscopy remains pathognomonic for gout and

eliminates all other diagnostic considerations. Pseudogout from calcium pyrophosphate dihydrate (CPPD) crystals presents with similar acute inflammatory arthritis but demonstrates positively birefringent rhomboid crystals rather than negatively birefringent needle-shaped MSU crystals under polarized microscopy.

Conventional radiographic findings in this case demonstrated osteoarthritis consistent with chronic joint damage from aging and mechanical stress, but conventional radiography lacks sensitivity for acute MSU deposition. Musculoskeletal ultrasound offered substantially greater diagnostic sensitivity for MSU crystal deposition, with the double contour sign serving as a specific marker for chronic crystal deposition and hyperechoic aggregates within synovial fluid indicating acute crystal accumulation. Advanced imaging modalities including magnetic resonance imaging (MRI) can provide detailed soft tissue assessment but are not typically required for gout diagnosis given the diagnostic certainty provided by synovial fluid crystal analysis.[21] Computed tomography (CT) imaging can detect tophaceous deposits in chronic tophaceous gout but has no role in acute gout diagnosis. The combination of clinical presentation, synovial fluid crystal analysis, and musculoskeletal ultrasound findings provided comprehensive diagnostic confirmation without need for advanced cross-sectional imaging, reducing healthcare costs and radiation exposure while maintaining diagnostic accuracy. In this patient, the integration of bedside arthrocentesis with immediate synovial fluid analysis provided a definitive diagnosis within hours of presentation, enabling rapid therapeutic intervention and risk stratification for subsequent cancer therapy.

The pre-frail status of this patient (Fried frailty index 0.15) indicates intermediate risk for adverse outcomes and requires careful medical optimization prior to chemotherapy initiation for CLL. Frailty assessment helps identify vulnerable elderly patients at higher risk for chemotherapy toxicity, treatment-related mortality, and functional decline. The marked anemia (hemoglobin 9.6 g/dL) and thrombocytopenia (platelets 99,000/mm^3) indicate significant bone marrow involvement by CLL and may require transfusion support prior to chemotherapy. The elevated WBC count of 113,110 cells/mm^3 indicates high disease burden and high risk for tumor lysis syndrome complications during chemotherapy initiation. Long-term management of these patients requires multidisciplinary coordination between rheumatology, hematology-oncology, nephrology, and geriatric medicine. Optimal outcomes depend on appropriate timing of chemotherapy initiation relative to resolution of acute rheumatologic complications, careful optimization of uric acid management with prophylactic therapy (allopurinol, febuxostat, or rasburicase), aggressive hydration strategies to maintain renal perfusion and urine output, careful monitoring of electrolytes and renal function during chemotherapy, and rapid recognition and treatment of tumor lysis syndrome should it occur. Patient education regarding adherence to low-purine diet, adequate hydration, and early reporting of joint symptoms facilitates long-term disease management and prevents recurrent gout episodes that could interfere with cancer therapy adherence.[22]

Gout represents a significant global health burden with increasing prevalence in developing nations including Indonesia, where this patient originated. Limited access to diagnostic facilities including polarized light microscopy and musculoskeletal ultrasound in resource-limited settings may delay gout diagnosis and increase morbidity from repeated gout attacks. This case demonstrates the importance of confirmatory diagnostic testing even in resource-limited healthcare settings, as the diagnosis of gout fundamentally changes patient management and allows appropriate therapy planning in the context of concurrent hematologic malignancy. CLL presents additional diagnostic and management challenges in developing nations due to the limited availability of targeted therapies and supportive care facilities. Access to allopurinol for uric acid lowering and rasburicase for acute uric acid reduction varies

significantly by region and income level. The occurrence of both gout and CLL in this Indonesian patient illustrates the emerging burden of age-related and metabolic chronic diseases in developing nations experiencing rapid population aging. Healthcare systems in resource-limited settings require strategic investments in diagnostic capabilities and therapeutic options to optimally manage the increasing burden of complex chronic diseases affecting aging populations.[23]

The management of acute gouty arthritis in CLL patients requires careful selection of therapeutic agents with consideration of hematologic considerations, renal function, and potential interactions with subsequent chemotherapy. Colchicine, as employed in this case, provides effective anti-inflammatory effects through suppression of neutrophil migration through microtubule disruption and inhibition of inflammasome activation, with doses of 1 mg followed by 0.5 mg one hour later representing standard dosing for acute attacks. Colchicine is renally metabolized and requires dose adjustment in renal impairment, requiring assessment of glomerular filtration rate (GFR) prior to administration in elderly patients at risk for chronic kidney disease. Corticosteroids including methylprednisolone, as utilized in this case at 8 mg twice daily, provide potent anti-inflammatory effects through multiple mechanisms including suppression of neutrophil recruitment and migration, reduction of prostaglandin and leukotriene synthesis, and inhibition of IL-1β production and inflammasome activation. Corticosteroid use in CLL patients requires careful consideration of immunosuppression effects and potential acceleration of disease progression; however, short-term corticosteroid use for acute gout management typically produces minimal immunologic impact and was appropriate in this clinical context. Urate-lowering therapy requires particular attention in CLL patients, as excessive urate lowering immediately prior to or during chemotherapy can paradoxically worsen TLS by causing rapid cell death and massive urate release from lyzed cells. Standard recommendations suggest initiating allopurinol or febuxostat several weeks prior to chemotherapy in high-risk patients to achieve steady-state urate lowering before chemotherapy initiation, or alternatively using rasburicase which acts immediately without requiring xanthine oxidase inhibition and offers faster uric acid reduction in urgent situations.

4. Conclusion

This case report presents a comprehensive clinical vignette of acute gouty arthritis manifesting in the setting of newly diagnosed chronic lymphocytic leukemia stage C (Binet classification) with important implications for diagnostic evaluation, therapeutic management, and multidisciplinary coordination. The patient presented with acute left knee and ankle inflammatory arthritis with large-volume effusion occurring in the context of newly diagnosed CLL, elevated serum uric acid (10.6 mg/dL well above saturation threshold), and constellation of systemic symptoms including fever, respiratory symptoms, and constitutional manifestations related to CLL disease burden.

Diagnostic evaluation including comprehensive clinical examination, laboratory analysis, imaging studies, and definitive synovial fluid analysis with polarized light microscopy confirmed acute monosodium urate crystal-induced arthritis. Musculoskeletal ultrasound documented characteristic double contour sign and significant intra-articular effusion, providing objective imaging confirmation of crystal-induced pathology. ACR/EULAR gout classification criteria scoring of 13 (threshold ≥8) established high diagnostic confidence for acute gouty arthritis. The simultaneous diagnosis of CLL stage C with marked leukocytosis (WBC 113,110 cells/mm^3), hepatosplenomegaly, and significant disease burden created complex management considerations regarding tumor lysis syndrome risk, urate management, and chemotherapy planning.

Management employed colchicine for inflammasome inhibition, methylprednisolone for potent anti-inflammatory effects, arthrocentesis for therapeutic decompression and diagnostic confirmation, low-purine dietary counseling for uric acid reduction, and supportive care including pain control and mobility assistance. Chemotherapy was appropriately deferred during acute rheumatologic management to prevent potential tumor lysis syndrome exacerbation during initial drug administration. The patient achieved clinical resolution of acute inflammatory symptoms with restoration of functional independence and improved joint mobility within days, demonstrating the effectiveness of conservative rheumatologic management when properly coordinated with hematology-oncology services.

Key clinical pearls from this case include the paramount importance of synovial fluid analysis and crystal identification in acute arthritis evaluation, even in patients with suspected hematologic malignancy, to avoid diagnostic errors; the value of musculoskeletal ultrasound in documenting crystal-related findings including the pathognomonic double contour sign; the necessity for careful risk stratification for tumor lysis syndrome in hematology patients with concurrent hyperuricemia and high disease burden; the importance of multidisciplinary coordination between rheumatology and hematology-oncology services in managing patients with overlapping acute systemic diseases; and the effectiveness of conservative management with appropriate anti-inflammatory therapy in CLL patients with acute gout who require safe chemotherapy planning.

This case contributes to the medical literature by documenting a relatively uncommon but clinically important scenario of acute gouty arthritis with crystallographic confirmation occurring in the setting of newly diagnosed CLL. The thorough diagnostic evaluation and successful clinical outcome provide a model for approaching acute arthritis in patients with concurrent hematologic malignancy. The integration of clinical, laboratory, imaging, and crystallographic findings demonstrates best-practice diagnostic approaches in complex patients. Future case reports and clinical studies examining acute rheumatologic manifestations of hematologic malignancies will enhance understanding of these complex presentations and refine management strategies in the increasingly elderly and medically complex cancer populations.

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