

# Gout: Clinical Presentation

# Inflammatory monoarthritis

- Peter is a 41 year-old African-American male who presented to clinic two days ago complaining of awakening with severe, 8/10 left knee pain, erythema and swelling x3 days.
- States the pain was “in and all around the joint area.” Denied being able to ambulate without his wife’s assistance and stayed home from work as a teacher. He thought he “overdid it” playing with his kids.
- The pain persisted throughout the day despite taking two OTC NSAID tablets. Pain partially improved by the next morning. States had a similar episode of sudden onset pain upon waking in the morning in his right great toe, but thought he stubbed his toe.
- He denies left knee injury, fever, rash, chills.

# Inflammatory monoarthritis

## Peter at a Glance

- Height: 5'11"
- Weight: 239 lbs
- History of hypertension
- Takes 25 mg HCTZ a day
- Reports drinking beer on most weekends

## Vitals upon exam:

- » Temp: 98.8°F
- » HR: 79 bpm
- » BP: 136/78
- » Resp: 17

# Is it Gout?

- Based on Peter's presentation, you suspect he may be experiencing an acute gout flare. Sometimes referred to as the "disease of kings," gout is a rheumatic disease resulting from uric acid crystal (monosodium urate) deposits in tissues and fluids within the body. Though gout is caused by hyperuricemia, they are not the same condition and asymptomatic hyperuricemia does not require treatment.
- **The most common form of inflammatory arthritis among men**, gout may remit for extended periods of time and then flare for days to weeks or may become chronic.
- Certain health conditions and medications may put patients at risk for hyperuricemia or gout

## HEALTH CONDITIONS

- Renal insufficiency
- Hypertension
- Hyperthyroidism
- Psoriasis
- Hemolytic anemia
- Kelley-Seegmiller syndrome
- Lesch-Nyhan syndrome

## MEDICATIONS

- Diuretics
- Salicylate containing drugs
- Niacin
- Cyclosporine
- Levodopa (L-dopa)

## LIFESTYLE AND OTHER FACTORS

- Diet
- Alcohol consumption
- Age
- Gender
- Family history

**Kelley-Seegmiller syndrome (KSS)** is a disorder that occurs when there is a partial deficiency of the enzyme hypoxanthine guanine phosphoribosyl transferase. It is involved in the metabolism of purines, clinically manifesting as hyperuricemia, hyperuricosuria, gout arthritis, and urolithiasis

**Lesch-Nyhan syndrome (LNS)** is a rare, inherited disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT). LNS is an X-linked recessive disease carried by the female parent and passed on to a male child. LNS is present at birth in males.

Gout can be viewed in four stages:

**1. ASYMPTOMATIC TISSUE DEPOSITION**

- Patient has no symptoms of gout but has hyperuricemia
- Crystal deposition is occurring and causing damage

**2. ACUTE FLARES**

- Acute inflammation of joints caused by urate crystal deposition
- Characterized by pain, redness, swelling and warmth which may last days to weeks

**3. INTERCRITICAL SEGMENTS**

- Occur after an acute flare and are characterized by continued crystal deposition
- Segments will shorten as disease progresses

**4. CHRONIC GOUT**

- Characterized by chronic arthritis with soreness and aching of joints
- Patients may develop firm clumps of uric acid crystals called tophi, usually in toes, distal finger joints, elbows or ears



# Gout complications

- Gout related joint pain, discomfort or inflammation can impede normal self-care, recreational or social activities. Complications related to gout, including kidney stones, irreversible joint damage or loss of motion may further restrict daily activities.
- Long-term gout may lead to cataracts or respiratory complications (as uric acid crystals build in lung tissue), as well as tophi, which may grow to the size of golf balls and can destroy joint bones and cartilage.
- **While Peter has no history of disability, his hypertension, use of a diuretic, alcohol use and inability to go to work corroborates your suspicion of gout.**

# Making a gout diagnosis

- Peter may be tentatively diagnosed with acute gout clinically, but such a diagnosis can **only be confirmed with arthrocentesis**. Initial onset of gout pain is usually confined to one joint, and gout is more likely if the pain begins in the big toe. **60% of all first-time monoarticular gout pain initially presents in the big toe, an occurrence known as podagra**. Peter indicated he had a similar episode of pain three months prior in his right great toe. This may have been his first acute attack. Polyarticular gout typically involves other joints in the lower legs or feet, but may involve elbows, wrists or hands.
- Associated symptoms include:
  - swelling near and beyond the affected joint
  - redness or shiny skin
  - mild fever or chills
  - loss of appetite
- Patients experiencing polyarticular gout are more likely to exhibit fever, chills or loss of appetite.<sup>5</sup> Polyarticular gout does not refer to multiple joints at different times, but multiple joints at the **SAME** time. Though pain in the knee may indicate Peter has polyarticular gout, he denied having any fever or chills.

# Gout case

- If acute or chronic gout is suspected, a serum uric acid test can be performed. A low serum uric acid level makes a gout diagnosis much less probable, but hyperuricemia and joint pain does not confirm gout. During an acute gout flare, a patient may paradoxically have normal or even low SUA levels. Suspicion of gout could warrant a referral to a rheumatologist for arthrocentesis.
- **The definitive test to confirm or rule out gout is to aspirate and examine the synovial fluid of the affected joint for uric acid crystals.**
- Even in the setting of hyperuricemia or classic podagra, when there is no available synovial fluid, other conditions should be ruled out. Osteoarthritis, septic arthritis, pseudogout (caused by calcium pyrophosphate crystals), and other rheumatic autoimmune diseases may all present similarly to gout.

## Remember the 3 C's:

1. **CELL COUNT:** order a cell count
2. **CULTURE**
3. **CRYSTAL ANALYSIS** under a polarizing light microscope



The American College of Rheumatology outlines preliminary criteria for gout. Gout may be diagnosed if one of the following is present:

- Monosodium urate crystals in synovial fluid
- Tophi confirmed with crystal examination

If at least six of the following criteria are identified, gout may also be diagnosed:<sup>7</sup>

- Asymmetric swelling within a joint on a radiograph
- First metatarsophalangeal joint is tender or swollen (i.e., podagra)
- Hyperuricemia
- Maximal inflammation developed in one day
- Monoarthritis attack
- More than one acute arthritis attack
- Redness observed over joints
- Subcortical cysts without erosions on a radiograph
- Suspected tophi
- Synovial fluid culture negative for organisms during an acute attack
- Unilateral first metatarsophalangeal joint attack
- Unilateral tarsal joint attack

## Gout By The Numbers



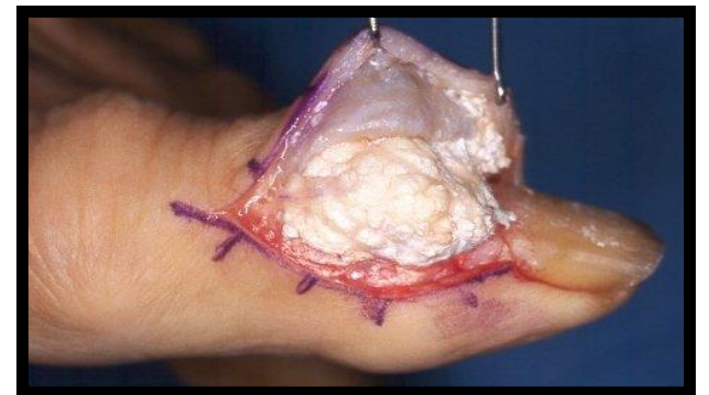
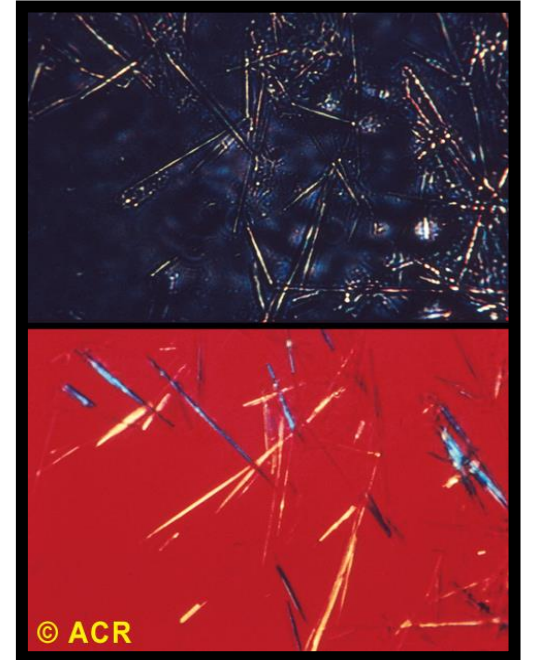
*Note the soft tissue swelling and bony erosion with “overhanging edge”*

- **8.3 million** Americans are affected by gout<sup>2</sup>
  - **>20%** of the U.S. population is affected by hyperuricemia<sup>2</sup>
  - The incidence of gout among Black men is almost **twice** that of White men<sup>2</sup>
  - **20-80%** of patients with gout have a family history of the disease<sup>3</sup>
- 

*While gout mortality is low, gout-related disability remains underestimated and understudied.<sup>4</sup>*

# Hallmarks of Gout

- Group of conditions which may be characterized by
  - An elevation of serum uric acid (usually)
  - Recurrent attacks (flares) of an acute inflammatory arthritis with monosodium urate crystals demonstrated in synovial fluid leukocytes
  - Bone and joint destruction in some cases
  - Aggregates of uric acid crystals (tophi in and around joints, soft tissues, and various organs)
  - Tophus in bone leading to erosions in some cases
  - Kidney disease and stones



# Flare: Classic Description

*The victim goes to bed and sleeps in good health. About two o'clock in the morning he is awakened by a severe pain in the great toe; more rarely in the heel, ankle, or instep. The pain is like that of a dislocation, and yet the parts feel as if cold water were poured over them . . . Now it is a violent stretching and tearing of the ligaments – now it is a gnawing pain, and now a pressure of tightening. So exquisite and lively meanwhile is the feeling of the part affected, that it cannot bear the weight of the bedclothes nor the jar of a person walking in the room. The night is spent in torture.*

Sydenham, 1683

Sydenham, T: The Works of Thomas Sydenham, London, New Sydenham Soc. 1850  
(translation)

# Podagra

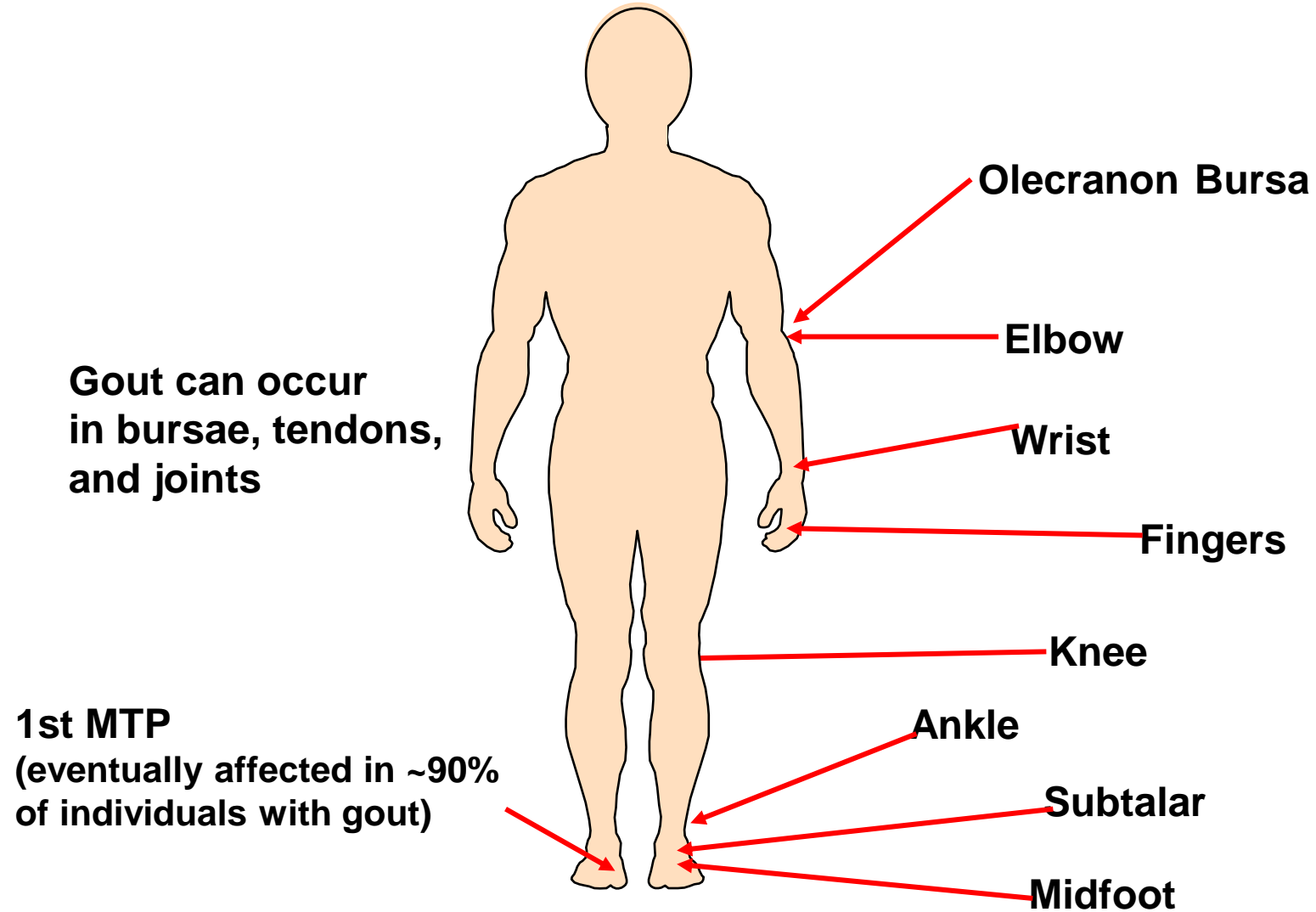


# Flare: A Vet's Description

“I've been shot, beat up, stabbed and thrown out of a helicopter, but none of that compared to the gout.”

Birmingham, Alabama  
VA Hospital  
March, 2001

# Common Sites of Acute Flares



# Intervals Between 1<sup>st</sup> & 2<sup>nd</sup> Acute Flares

Majority experience second acute flare within  
1 year of first gout flare



# Advanced Chronic Tophaceous Gout



- Tophi can be seen clinically, with obvious deformity demonstrated in hands and foot
- Tophi may be associated with bony destruction as seen on the x-ray on right

# Case Presentation #2

- + 47 year old male - Severe pain in right great toe – wore open toe sandals to clinic. Began previous evening and kept him up through the night (acute onset). Taking extra-strength acetaminophen to keep the pain under control. Unable to bear weight on his right foot. No history of injury to right foot.
- + Hypertension (HTN) X 9 years. Transient Ischemic Attack (TIA/Mini Stroke) 3 months ago, appears to have no residual neurological deficits. Chronic sinus drainage/rhinitis (S/P laryngoscopy). Allergies: NKDA.
- + Why should the use of pseudoephedrine by this patient be carefully monitored by the primary care provider? Patient already on Flunisolide (corticosteroid) for Nasal Rhinitis. High use of a nasal decongestant could be detrimental. Hydrochlorothiazide (HCTZ) 25 mg po QD with supper. Aspirin (ASA) 325 mg po Q AM, Atorvastatin 10 mg po QD. Flunisolide 2 sprays each nostril QD, Pseudoephedrine 60 mg po Q6h PRN

- + Mother with type 2 DM
- + Father died at age 68 from osteosarcoma
- + Four adult children are all healthy
- + No siblings
- + Diet is heavy on red meat and other high- purine foods
- + Non-smoker
- + Uses alcohol weekly (averages 5-6 drinks/week)
- + Married x2 with 4 adult children (1 from 1st marriage)
- + Employed 17 years as a truck driver and is frequently away on the road
- + Denies headache (HA) , dizziness, chest pain, SOB, and generalized swelling or tenderness
- + Weight has increased approximately 15 lbs in the last year
- + No previous episodes of joint pain

# Physical Exam

- + Neck/Lymph Nodes: Normal with no swelling, thyromegaly, masses or jugular vein distention
- + Eyes: Pupils equal at 3mm, round and reactive to light and accommodation (PERRLA). Normal fundoscopic exam
- + Lungs: Clear to Auscultation
- + Cardiac: Regular Rate and Rhythm. S1 and S2 with no extra cardiac sounds. No g, r, m
- + Abdomen: Non-tender and non-distended. No Hepatosplenomegaly. Normal bowel sounds.
- + Musculoskeletal/Extremities: Pulses full throughout. Muscle strength 5/5 throughout. Right first metatarsophalangeal joint hot, tender, erythematous, swollen, and painful
- + Neuro: A&O x 3 . CNs II-XII intact. Deep Tendon Reflex Normal. Babinski (-)

- + X-ray: acute attacks can't be seen, but chronic gout appears as thickened regions
- + Serum levels of uric acid may not be elevated, but in >95% of patients it is elevated (>7.5mg/dL) during an acute attack
- + Erythrocyte sedimentation rate (ESR) can also be elevated during episode of gout.
- + 24 hr urinary uric acid: 985 mg/day
- Would probenecid, sulfinpyrazone, or allopurinol be more appropriate medication for this patient? Why?

Probenecid is not used to treat acute attacks, and instead is used to prevent chronic attacks.

Sulfinpyrazone is also used to prevent attacks but is also contraindicated for this patient because of the high rate of excretion of uric acid.

Since the patient is excreting >800 mg urate/day, allopurinol is required.

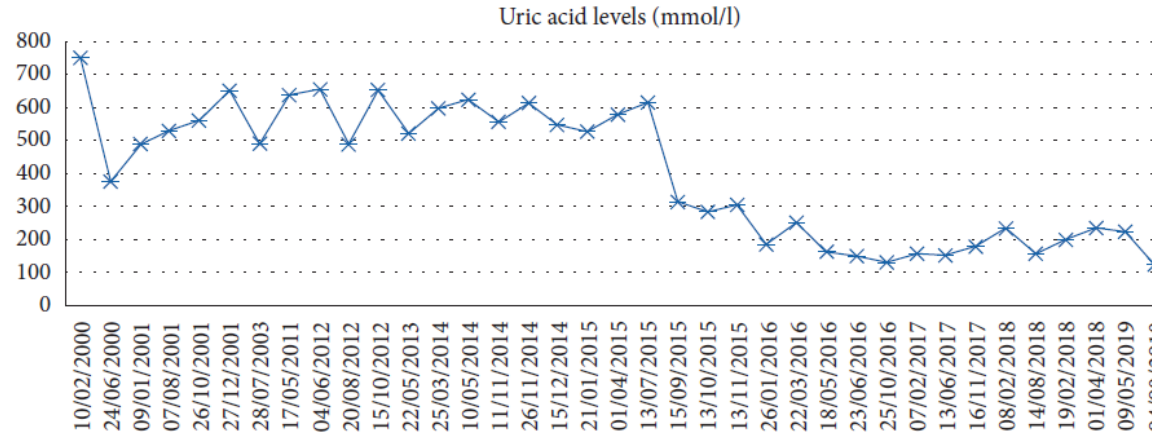
Allopurinol decreases the synthesis of uric acid, rapidly lowers plasma urate, and facilitates mobilization of MSU while shrinking tophi.

Allopurinol acts by inhibiting xanthine oxidase, the enzyme that catalyzes the conversion of hypoxanthine to xanthine and xanthine to uric acid.

# Case Presentation #3

- 50-year-old patient who has, since a month, a state of general malaise characterized by widespread pain and intermittent episodes of fever and night sweats. He refers fever with spikes up to 39°C in two days prior to hospitalization at the Department of Rheumatology.
- The pains are especially at night to the chest level. Despite a home drug therapy with NSAID (nonsteroidal anti-inflammatory drug), symptoms do not regress.
- The patient's anamnesis is for a chronic gouty arthritis characterized by the presence of tophi and frequent arthritis; the first gouty attack was in 2011 on the ankles treated with steroids. In 2014, he has undergone surgical operation with the removal of tophaceous masses [1] at the sixth compartment of the right hand because of severe pain and losing ROM in affected joint.

- He also had high uric acid levels as he used febuxostat (allergic to allopurinol).



- He is also known for type 2 diabetes (diagnosis in 2011) in pharmacological treatment with metformin, sitagliptin, and gliclazide poorly controlled due to eating habits without regular physical activity.
- Patient states he drinks 2–3 liters of carbonated soft drinks a day.
- He has a class 1 obesity (BMI 31.5 Kg/m<sup>2</sup>) - underwent gastric banding surgery in 2004 with partial success.
- Another cardiovascular risk factor is a chronic renal failure G3a (KDIGO, 2012) due to diabetic nephropathy (albuminuria grade A2).
- Also with lumbosacral radicular syndrome, irritative L3 on the left side

# Physical exam

- Good general condition, 102 kg weight, 180 cm height, with eupnea, normal heart rate, normal heart rhythm, and normal cardiac rhythm.
- 1<sup>st</sup> left MTP and left ankle swollen without pain on pressure or mobilization. Bilateral knees are swollen, warm to touch, aching with joint effusion mostly on the left.
- Inflammation in left MCPs (II, III, and IV) where, in the past, tophi had been removed surgically.
- Extension of left elbow is limited. Lumbar spine mobility is reduced by 1/3 in lateral-bilateral flexion and in forward flexion with soreness at lumbosacral level.
- Swelling with localized pain in left sternoclavicular joint. Normal heart sounds, no murmurs. Lungs clear.
- Abdomen is painless, no organomegaly.
- Neurological unremarkable.



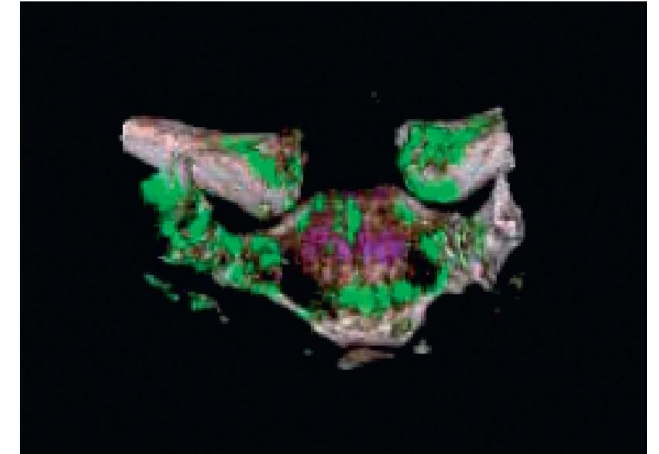
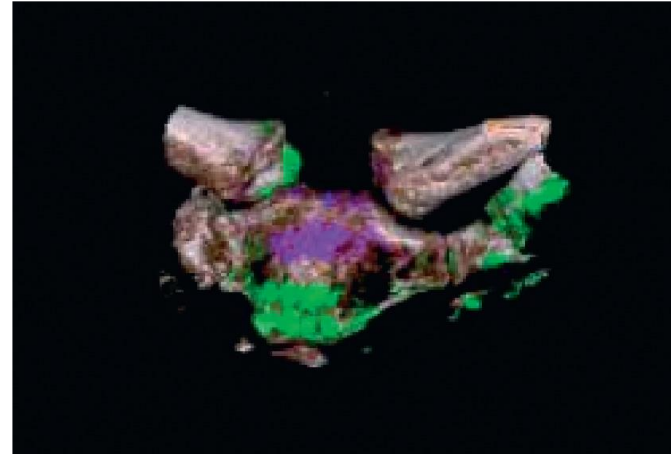
- ECG with no significant alterations.
- Lab: CRP of 134 mg/l and ESR of 70 mm/h. Uric acid is within the normal limit (263 mmol/l [4.4 mg/dL]).
- Differential diagnosis of sternoclavicular swelling:
  - (i) Infectious arthropathy
  - (ii) Crystals arthropathy (uric acid or calcium pyrophosphate crystals)
  - (iii) Tumor pathology
  - (iv) Psoriatic arthropathy
  - (v) SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis)
  - (vi) Osteoarthritis

- PsA was eliminated due to no skin changes, and no Family Hx.
- CT scan, performed to r/o neoplasia, showed no masses but reported nonspecific alterations of sternoclavicular joint.
- Negative procalcitonin reducing the chance of bacterial infection.
- Trauma was not reported in recent period.
- OA excluded due to absence of classical x-rays signs (JSN, osteophytes, subchondral bony sclerosis and cysts)
- Knee ultrasound showed synovitis with joint effusion and characteristic double contour- synovial fluid confirmed presence of uric acid crystals.

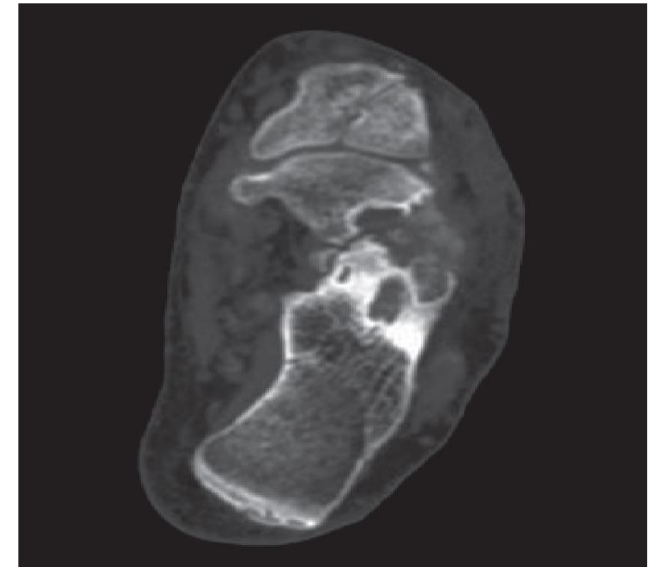


## Sternoclavicular details with Dual Energy CT 3D reconstruction

- Chest ultrasound showed effusion in sternoclavicular joint and thickening of synovial capsule.
- Lack of joint fluid: arthrocentesis not performed.
- DECT performed: confirmed suspicion of gout-originated arthropathy at sternoclavicular joints, explaining patient's chest symptoms.
- Patient has a systemic disease with destructive deforming arthritis



Left foot with Dual energy CT 3D-reconstruction.



Erosion and intra-articular swelling with tophaceous masses (CT left foot).

# Case Presentation #4

- 55 year-old male: W: 65 kg, H: 5'2"
- Complains of chronic pain and swelling in the foot with an inability to walk on concrete and waking at night, resistant to medication [allopurinol and NSAIDs].
- Medical Hx: HTN and hyperlipidemia
- GFR: 40 ; Uric acid: 7.5 mg/dL
- Right foot x-ray: Extensive juxta-articular erosions with dense soft tissue swelling in bilateral 1<sup>st</sup> MTPs, right 1<sup>st</sup> IP, left 2nd toe PIP, and right PIP 2<sup>nd</sup> and 3<sup>rd</sup> toes.
  - Bone density is of normal range.
- MTX 15 mg PO weekly initiated
- Pegloticase 8 mg IV started 4 weeks after MTX



# Case #5



Arrows indicate the classic “punched-out” defects in bones and swelling of soft tissues (the grey bulge beside the 1<sup>st</sup> joint of the big toe).



Huge erosions and joint surface of proximal phalanx (1<sup>st</sup> toe) is partially destroyed. Soft tissue protrusion is also striking and represents uric acid crystals which have accumulated *within* the soft tissues.



Hand x-ray with similar findings

# Case #5

- Subject with chronic refractory gout and sUA of 7 mg/dL
- GFR of 25
- MMF 1000 mg BID initiated
- Pegloticase 8 mg IV every 2 weeks added