

# **Crystal induced arthritis**

# Case 1:

Yasser is a 40 y/o male patient presented complaining of severe Right big toe pain which started at 3:00 am (night before presentation ) . He reported history of redness , hotness and swelling. He couldn't wear his socks in the morning . 10 months ago he had the same symptoms at his left knee and treated with an intra- articular injection.

# Questions :

- 1- What is your diagnosis ?
- 2- Mention other DDX ?
- 3- How to confirm your diagnosis ?
- 4- Mention lines of management

# Gout داء الملوك

Is the most common inflammatory arthritis (1-2% prevalence) affecting men which is caused by elevated serum urate concentration and deposition of MSU crystals within the joints and soft tissues .

Oftenly present with recurrent self limiting episodes of severe acute arthritis within 7-10 days .

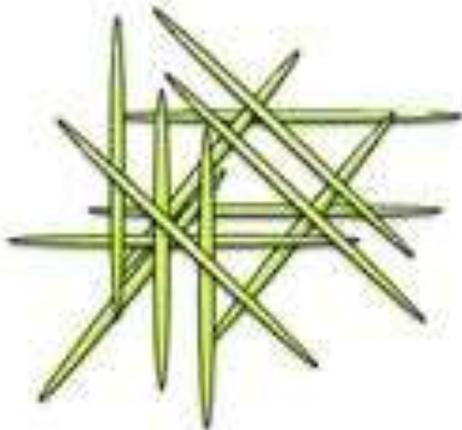
However chronic persistent hyperuricemia may lead to chronic tophaceous disease and damage .



# Pathogenesis

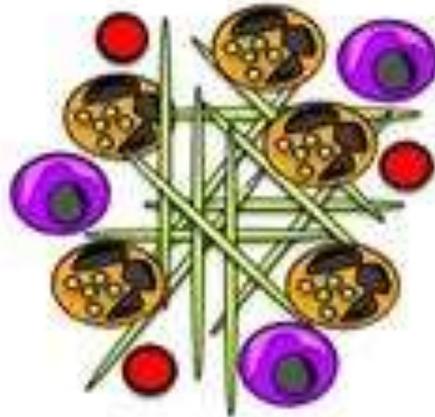
## 1. Formation of MSU Crystals

- Hyperuricaemia
- **Precipitation** of MSU crystals
- **Deposition** in articular and periarticular tissue



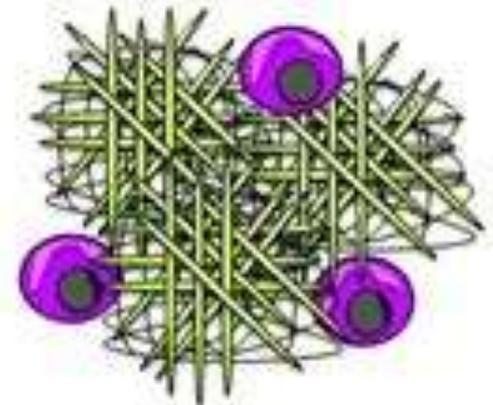
## 2. Acute Gout Attack

- **Phagocytosis** of Crystals
- Cell Swelling and **Inflammasome** Activation
- **Cytokine** production and vasodilatation
- Neutrophil and monocyte influx



## 3. Chronic Tophaceous Gout

- Neutrophil death by **NETosis**
- Packaging of MSU crystals
- Inactivation of inflammatory cytokines
- **Resolution** of Inflammation



# Risk factors

1- polynesian ethnicity (increased 3-4 folds ) then black people and Asians .

2- Sex : male prevalence (5:1)

3- Renal disease and transplantation

4-Meds : low dose aspirin , cyclosporins , pyrazinamide and diuretics

5-Diet rich in fresh fruits , red meat , alcohol , egg , milk,seafood .

6- Can be associated with other medical conditions( DM2 , IHD , HF, HTN , Hyperlipidemia , obesity )

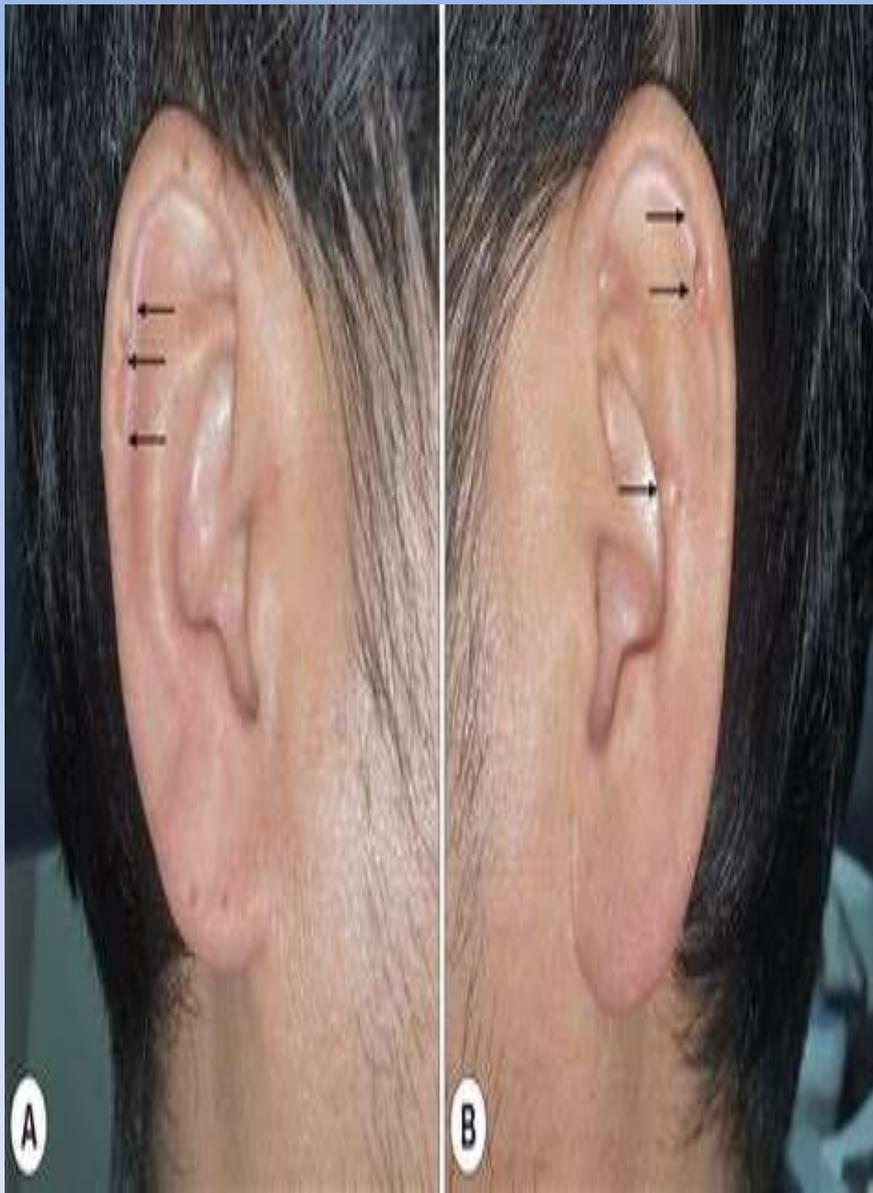
7- Hematological malignancies (Tumor lysis syndrome)

8-Inherited disorders : lesch-Nyhan syndrome and pyrophosphate synthetase 1 mutation

# Clinical presentation

- Typically patient presents with acute monoarthritis and affecting first MTP joint in more than 50%( Severe pain , swelling , hottness , redness , shiny skin , fever , loss of mobility ).
- Other common sites include midfoot , ankles knees , elbows , small joints , wrists .
- Acute attacks may manifest as bursitis , tendinitis , cellulitis or tenosynovitis .
- Chronic symptoms can be seen in elderly rather than acute attacks .
- Crystals can be precipitated in kidney causing renal stone or at the soft tissues causing tophi at the extensor surfaces .
- On examination : look , feel and move (Severe tenderness , swollen , hot , red , loss of mobility , ? Tophi)





*Tophaceous Gout - Before Treatment*  
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*Tophaceous Gout - After Treatment*  
 (copyright @ www.drbidani.com)

**Clinical presentation: Tophi over the right distal interphalangeal joint II**  
 A. Before treatment      B. After 10 months of treatment

# DDX

- 1- Septic arthritis
- 2- Pseudogout
- 3- Reactive arthritis
- 4- Infective cellulitis
- 5- RA
- 6- Sero -negative arthritis
- 7- CTD
- 8-OA

# Investigations

- 1- Synovial fluid analysis and culture
- 2- Serum urate can be normal in acute attack ? Falls during inflammation in up to 40% .
- 3- KFT , ESR , CRP , Calcium levels
- 4- Serology if other DDX suspicious
- 5- XR joints , destruction and erosions
- 6- US very helpful may show double contour sign with synovitis .
- 7- Other imaging studies can be requested if diagnosis in doubt like MRI .

# Ultrasound in the Diagnosis of Gout



Normal



Gouty  
Arthritis

"Double Contour Sign"



# Management

## 1- Managing acute attacks :

- NSAIDS (avoid in elderly with renal and cardiovascular conditions)

- Colchicine is safe and can be used as 500 mic twice or three times / day for 5-7 days . (works by inhibiting microtubules assembly in neutrophils , side effects : nausea , diarrhea and vomiting ) , dose reduction is important in patients with liver and renal diseases .

- Systemic steroids :

  - Oral 15-20 mg/day , weaning over 3-4 weeks

  - IM (80-120mg ) over 3 days

  - or intraarticular .

- IL1 inhibitors canakinomab can be effective but very expensive .

# Management of chronic gout

1- Lifestyle modifications

2- Manage other comorbidities( therapies like losartan , fenofibrate , statin , amlodipine , vitamin c , have modest urate lowering .effects)

3- Using urate lowering agents

# Urate lowering therapy

## Indications:

- 1- Recurrent attacks (more than one attack during 12 months)
- 2- Tophi
- 3- Nephrolithiasis
- 4- Renal impairment
- 5- Evidence of bone or joint damage

# Classification

1- Xanthine oxidase inhibitors like allopurinol ,  
febuxostat

2- uricosuric agents, probenecid ,  
sulphinpyrazone , benzbromarone

3- Recombinant uricase

# Urate lowering agents

## 1- Allopurinol :

-first choice , inhibite xanthine oxidase enzyme . Recommended starting dose 50-100 mg /day and can be titrated up by 50-100 mg every 4 weeks to .

reach target serum uric acid  $<360$  mmol/l.( $<300$  in tophi).

-Dose adjustment is important in patient with CKD according to creatinine clearance .

-Initiation of allopurinol can increase risk of acute flare up , therefore prophylaxis with NSADIDS or colchicine can be given during the first few months.

-Side effects : Rash , reaction AHS( Fever , rash , epidermal , necrolysis , eosinophilia , heaptitis , leukocytosis , renal failur), increase risk in Asian with HLAB5801 allele.

-Allopurinol –Azathioprine must be prescribed with great caution and azathioprine dose reduction in 50-70% (Risk : azathioprine toxicity and severe myelosupprision )

2- Febuxostat: -is a xanthine oxidase inhibitor .

-Used when allopurinol ineffective or there is contraindication to allopurinol (dose 80 -120mg / day

-It is metabolized by the liver therefore no renal dose adjustment is needed .

-Side effects: rash ,reaction. acute flare up on initiation

# Uricosuric drugs:

- They increase the excretion of uric acid through the kidneys via various urate transporters.
- Examples : probenecid , sulphapyrazole , benzbromarone .
- Adequate fluid intake is recommended and in some cases urine alkalinization.
- ? Avoid in nephrolithiasis , liver disease

# Recombinant uricase

Uricase convert uric acid allantoin which is soluble and can be eliminated easily by renal system .

Rasburicase can be used in tumor lysis syndrom as intravenous with limited use in chronic gout due to high cost , short half life and risk of hypersensitivity reactions with frequent infusions.

Pegloticase infusions seem to be effective on treating chronic refractory gout .

## Case 2 :

A 75 y/o female patient , has being treated in hospital after a • fall . She ceveloped acute severe right knee pain and swelling. She feels unwell with low grade fever.

She is known to have osteoarthritis and HTN . On examination • : her knee was hot , tender with significant effusion and movement range reduction . Palpable crepitus was detected as well . She had no hx of chronic kidney disease or diuretic use .

# Questions:

- 1- What is your diagnosis?
- 2- What is your next step to confirm the diagnosis ?
- 3- How to manage your patient ?

# Calcium pyrophosphate crystal deposition(pseudogout)

Is an age related condition where calcium pyrophosphate crystals precipitate within the articular and hyaline cartilage . Rarely presents under 55 years.

More common after age of 85 years .Most common sites are knees followed by wrists , shoulders , ankle and elbow .

In many patients are asymptomatic chondrocalcinosis which found incidentally at x ray .

Some can present with acute/ chronic inflammatory arthritis .

# Risk factors :

1- Age

2- Hyperparathroidism

3-OA

4- Familial , hemochromatosis, Wilson,  
hypomagnesemia , hypophosphatemia

# Clinical presentation

- 1- Asymptomatic CPPD
- 2- OA with CPPD
- 3- Acute CPP , Commonly monoarticular /rarely polyarticular
- 4- Chronic CPP (mono or olig in 89% of the cases )
- 5- Rarely Soft tissue , tendinitis , bursitis , tenosynovitis
- 6- Cervical spinal (crowded dens syndrome )

DDX : Gout , septic arthritis , RA

# Investigations:

- 1- synovial fluid aspiration for analysis and culture
- 2- joints x ray
- 3- US joints : less cost , no radiation . Shows hyperechoic oval calcifications and shadowing.
- 4- Inflammatory markers , cbc
- 5- Serology
- 6- Serum ferritin , calcium, ALK , Magnesium , liver function , serum copper , ceruloplasmin if metabolic disease suspected . (young age <55 , polyarticular , family history )



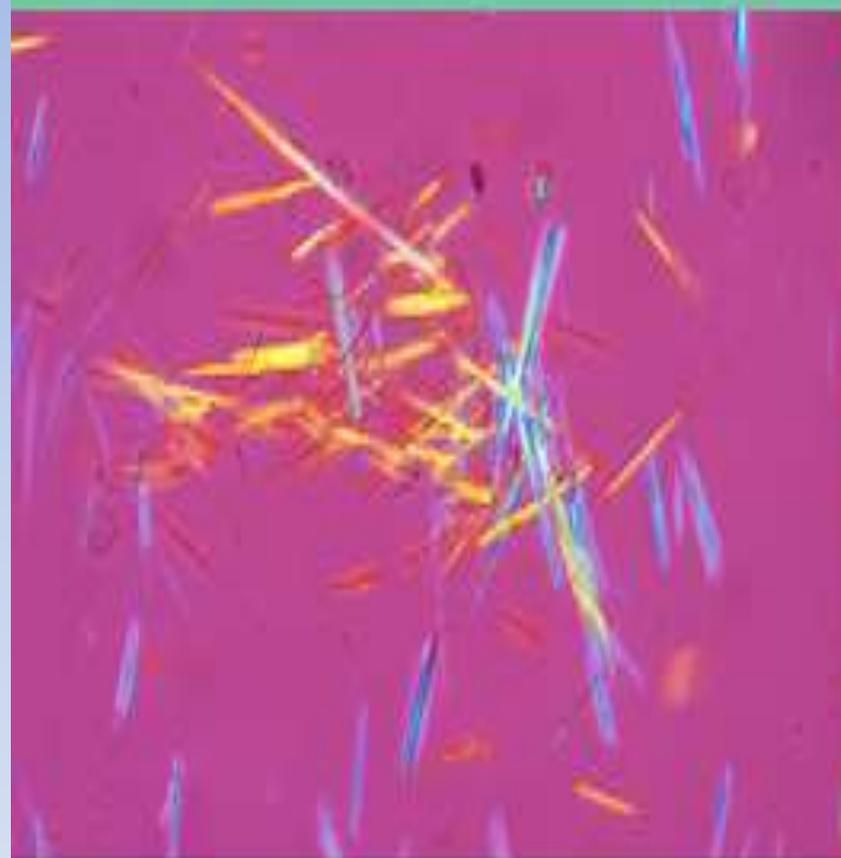
# **Knee Aspiration**

## **Practical Clinical Skills**

**FIFA** | MEDICAL  
NETWORK

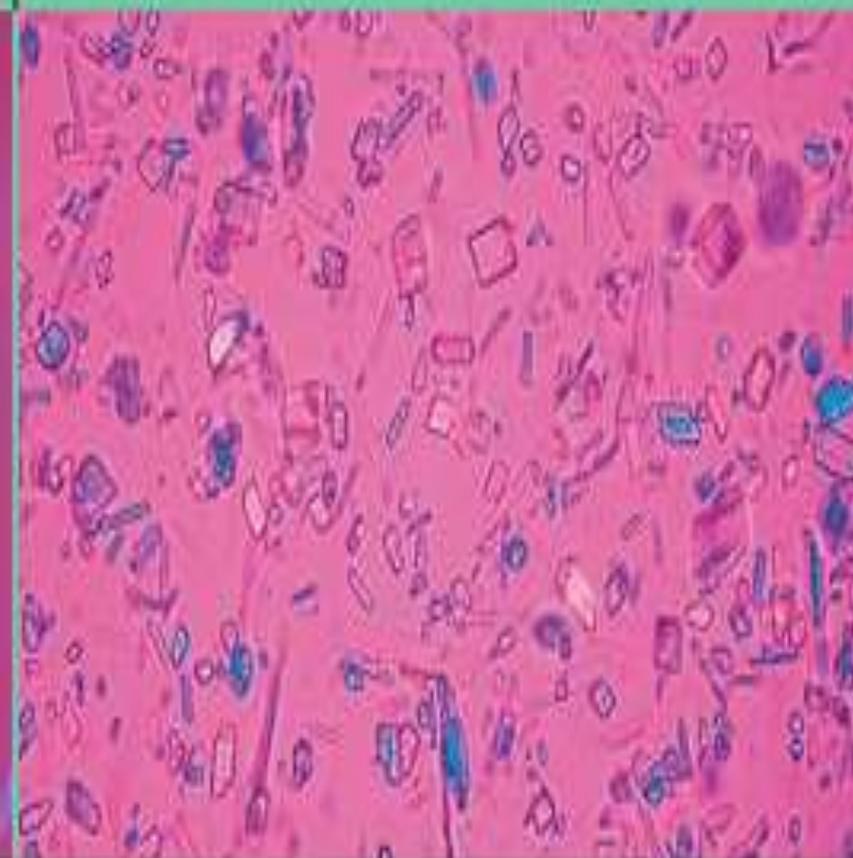


## Monosodium Urate (MSU) Crystals



Needle shaped, strong negative birefringence  
Yellow when parallel to compensator ray

## Calcium Pyrophosphate Dihydrate (CPPD) Crystals



Rod or rhomboid, weak positive birefringence  
Blue when parallel to compensator ray

# Management

- 1- OA with CPPD >> treat as OA , weight loss , •  
physiotherapy , pain control , joint  
replacement .
- 2- Acute CPPD : NSAIDS , colchicine , steroids •
- 3- Chronic CPPD: no specific treatment •  
(NSAIDS , colchicine , intraarticular steroid •  
injection for pain relief )

# Basic calcium phosphate deposition disease

- Caused by deposition of apatite crystals/hydroxyapatite and other basic calcium phosphate salts (octacalciumphosphate, tricalciumphosphate) in soft tissues including tendons , ligaments and hyaline cartilage in patients with degenerative disease , skeletal muscles and subcutaneous tissues in CTD .
- Could present with calcific periartthritis /acute inflammatory Arthritis
- Usually attack resolves within 1-3 weeks
- Treatment (NSAIDS , Analgesics, steroids injections)
- Large deposits that cause movement limitation may require surgical intervention.

# Milwaukee shoulder syndrome

- Is a rare condition where BCP deposit in large joints and caused progressive destruction.
- More in women
- Usually gradual and precipitated by injury or overuse .
- DDX Avascular necrosis/chronic sepsis or neuropathic pain .
- X ray may show : joint space narrowing with osteophytes and calcifications.
  
- Poor prognosis / analgesics , injection , physiotherapy , replacement .

Thank you

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