Feedback on pharmacotherapy-related short structured questions

Question #: 42

This question requires students to identify critical investigations and blood tests (besides serum uric acid level) that can differentiate between gout, pseudogout, rheumatoid arthritis and septic arthritis.

Many students accurately suggested drawing joint aspirate for further evaluation:

- **Observing the joint aspirate for crystals**
  - **Presence of monosodium urate** crystals (spindle negatively birefringent crystals) confirms the diagnosis of gout
  - **Presence of calcium pyrophosphate** crystals (rhomboid positively birefringent crystals) confirms the diagnosis of pseudogout
- **Performing gram stain** and **culture of joint aspirate** can differentiate presence of septic arthritis For septic arthritis (partial credit is given for observing for green colour of joint aspirate)

Lastly, **testing for anti-CCP/RF** in serum is helpful for confirming RA

Do note that although observing for an increase in WBC in joint aspirate, testing for inflammatory markers and imaging (such as X-ray) of the joint to detect joint erosion/destruction can contribute to the clinical picture suggestive of inflammatory-related joint diseases, these are non-specific in differentiating between gout, pseudogout, RA and septic arthritis. Similarly, measuring temperature to assess for presence of fever is suggestive of an infection but may not be specific enough to confirm septic arthritis.

Question #: 43

This question requires students explain their recommended pharmacological treatment regimen (along with dosing) and non-pharmacological strategies for managing symptoms of acute gout attack in the given patient.

Generally, Colchicine and NSAID/COX-2 inhibitor are commonly used for management of acute symptoms (i.e. pain), while use of corticosteroids is often reserved as the alternative for those who cannot use either colchicine or NSAID/COX-2 inhibitors.

Students should compare these available pharmacotherapy options from the perspective of effectiveness and safety.

Before making deliberating which should be used for patient, students should review the patient-specific information. Specifically, students should note the patient's current medications and renal function. While many attempted to calculate CrCl, only some made use of eGFR and uACR to assess for possible proteinuria and CKD.

- eGFR 50 ml/min/1.73m^2 and uACR 35 mg/g suggests **possible Stage 3a CKD**
- **ClCr** about 73 ml/min
- Concurrent Rx include **thiazide diuretic and ACE inhibitor**

Based on the above info:

- The **use of NSAID / COX-2 inhibitors is not recommended** for this patient as it can increase the risk for **AKI due to the "triple whammy" effect** (i.e. concurrent use of

thiazide diuretic, ACE inhibitor and NSAID/COX-2 inhibitor). Colchicine is therefore preferred (in addition to its favorable MOA unique for arresting the gout flare).

- Acceptable **colchicine dosing** for management of acute gouty attack is 0.5 mg BD or TDS until symptom resolution (also accepted: 1 mg STAT followed by 0.5 mg an hour later). Renal adjustment is not required for ClCr > 60 ml/min. NB: dosing of 1 mg STAT followed by 0.5 mg an hour later should be used for ClCr < 30 ml/min. Advice to take colchicine with or after food can be given, to reduce GI side effect of nausea & vomiting.

Acceptable non-pharmacological recommendation to resolve / prevent aggravation of current symptoms include:

- **rest/ice/elevate**
- **increase hydration**
- **diet modification** (e.g. reduce consumption of alcohol, sugary drinks and foods with high purine content).

Recommendations such as weight reduction (ivo patient's high BMI of about 27) can also be provided to patients, however, do note that the benefit would take time to effect and is thus more helpful for preventing future gout attacks, but not directly pertinent for the resolution of current attack/symptoms (which is what the question is asking for).

ULT is for prophylaxis of gout attack (not for acute management) and should NOT be initiated now (NB: ULT can be considered if there are at least 2 gouty attacks in a year, and should be initiated at least 2-4 weeks after resolution of gouty attack). Some students also pointed out the need for better control of BP (135/89), however, the slight elevation of BP readings could be related to pain. **While switching hydrochlorothiazide to an alternative anti-hypertensive treatment (e.g. amlodipine) is a reasonable suggestion** (as hydrochlorothiazide can decrease urate excretion), patient can continue to be on ACE inhibitors for now ivo DM diagnosis & the treatment's renal protective and potential uricosuric effects. As such, initiation of ULT, review of BP & pulse along with the necessary medication optimisation may be pursued at the subsequent follow-up consult.

Question #: 46

This question requires students to explain their recommendation of Allopurinol or Febuxostat as the appropriate ULT (along with dosing) for the given patient.

In this case, either Allopurinol or Febuxostat can be used.
Thus, student can recommend **shared decision-making** with patient and proceed to explain (or compare) the 2 pharmacological options.

The following points should be discussed:

- Contraindication / precautions for use (i.e. renal function and possible CKD)
- Tolerability: ADR risk (e.g. SCAR) and other side effects
- Drug interactions
- Monitoring needed
- Cost of treatment
- Approach for dosing

For dosing instructions, students should mention the following:

- Initiation dose and approach for dose increment

i.e. Allopurinol can be used, but…:

- As patient has possible CKD stage 3a, patient should be **tested for HLA-B*58:01 with negative result,** before initiating Allopurinol
- Need to **resolve DDI of allopurinol with hydrochlorothiazide & lisinopril**, e.g. by switching hydrochlorothiazide to amlodipine (and switching lisinopril to ARB) to prevent severe cutaneous adverse reaction (SCAR) from combination of allopurinol with hydrochlorothiazide and ACEi (also acceptable: close **monitoring for SCAR** especially in the first 3 months, if antihypertensives are not switched since patient's BP control with current meds is not too bad)
- Allopurinol has **GI side effects** >> need to monitor for tolerability in patient
- **In view of patient's CKD, the initiation dose of allopurinol should be lower than 100mg OD** (i.e. 50mg OD or lower) and **dose increment of 50mg every 2-4 weeks until goal** of serum urate level < 360 umol/L
- **Allopurinol is inexpensive (subsidised drug)**
- **Prophylaxis against gout flare for first 3 months of ULT needed**

Febuxostat can be used…:

- Since **Febuxostat has lower risk for SCAR** compared to Allopurinol
- Since **Febuxostat has lesser side effects** compared to Allopurinol
- Although Febuxostat is more **expensive** than allopurinol, this would not be an issue if patient prefers it and can afford it
- As Febuxostat may **cause hepatitis / increase liver aminotranferases** >> regular monitoring of liver function (e.g. LFT and bilirubin) would be needed
- Febuxostat may increase risk for MACE >> monitor and ensure adequate control of BP & DM is needed
- **Initiation dose of febuxostat should be 40mg OD** (no dose adjustments needed as ClCr is > 30 ml/min) and **dose increase to 80mg OD after 2-4 weeks** if goal of serum urate level < 360umol/L not achieved
- **Prophylaxis against gout flare for first 3 months of ULT needed**