REFERROLOGY SERIES: CRYSTAL ARTHROPATHY – DR AZIZAH

Diagnosis (2min 30sec)

- Clinical Diagnosis
  - Typical sites (first MTPJ, ankle, midfoot)
  - Onset middle of night/early morning with maximal pain within first 24 hours (vs septic arthritis which tends to peak in 1-2 days)
  - Resolution in < 2 week
  - Complete resolution between symptomatic episodes, tophi
- Adjuncts
  - Hyperuricemia
  - Joint radiographs: Looking for erosions
  - Ultrasound: Double contour sign
  - Dual energy CT scan: Green pixelations
- Gold Standard: Diagnostic arthrocentesis with demonstration of monosodium urate crystals
- Pitfalls
  - Polyarticular
  - Women: Usually post-menopausal
  - Atypical joint involvement
  - OA: Crystals have a predilection for damaged joints – Consider evaluating if 'flare' is inflammatory sounding
- Uric Acid Levels
  - Can be normal in flares
  - However, if raised, it adds diagnostic value

Septic Arthritis vs Crystal Arthropathy (11min 5sec)

- Procalcitonin: Limited utility; might be able to rule in but not rule out
- Can consider trial of colchicine – onset of action usually fairly fast
- Gold standard to differentiate is based on synovial fluid microscopy
- High temperatures, high inflammatory markers with monoarthritis – Suspect septic arthritis
- If suspicion for septic arthritis, to tap overnight

Uric Acid Stones and Urate Nephropathy (13min 48sec)

- Don't need to routinely screen if asymptomatic
- But consider screening if starting uricosuric agents with urine dipstick (looking for low urine pH <6 which portends risk for urate nephrolithiasis)
- While uric acid stones are radiolucent, calcium deposition might occur hence may be visible on Xray
- May be difficult to differentiate urate nephropathy from other causes of CKD - in those instances can just initiate ULT

Acute Treatment (16min 35sec)

- Principles: 1) Comorbidities 2) Drug interactions 3) Duration of attack 4) Access to injection
- Pharmacological
  - NSAIDs: Naproxen (250-500mg BD), Arcoxia (if have GI issues)
  - Colchicine
    - § If present within first 24-36 hours; limited role if late in flare
    - § Dose adjustment
      - CrCl > 45ml/min: 500mcg TDS for 3-5 days
      - CrCl 30-45ml/min: 500mcg BD for 3-5 days
      - CrCl < 30ml/min: Avoid if possible; if not 500mcg OM for 3 days and monitor closely

        - PD/HD: 500mcg single dose (not to repeat in 2 weeks)
    - Steroids
        - 20-30mg OM for 3-5 days (usually 30mg for large joints)
        - Consider in protracted course especially if not responding to colchicine
        - Can extend up to 2-week taper
    - Injections
        - Intraarticular: Monoarthritis (usually 40mg triamcinolone + 4ml 1% lignocaine to make 5mls for knee joint injection)
        - Intramuscular (e.g. kenacort): Consider for severe polyarticular gout flare
    - Others: ACTH, IL1 inhibitor

Low Purine Diet (22min 50sec)

- Difficult to manage gout by diet alone – Purine content of diet is fairly low, and most patients are under-secretors
- Avoid: 1) Red meat (internal organs) 2) Sea food 3) Alcohol 4) Fructose (sodas, fruit juice, energy drinks)
- Moderate intake of purine rich vegetables and nuts not really associated with increased risk of gout
- Food that lower uric acid levels: Coffee, vitamin C, low fat dairy products, cherries

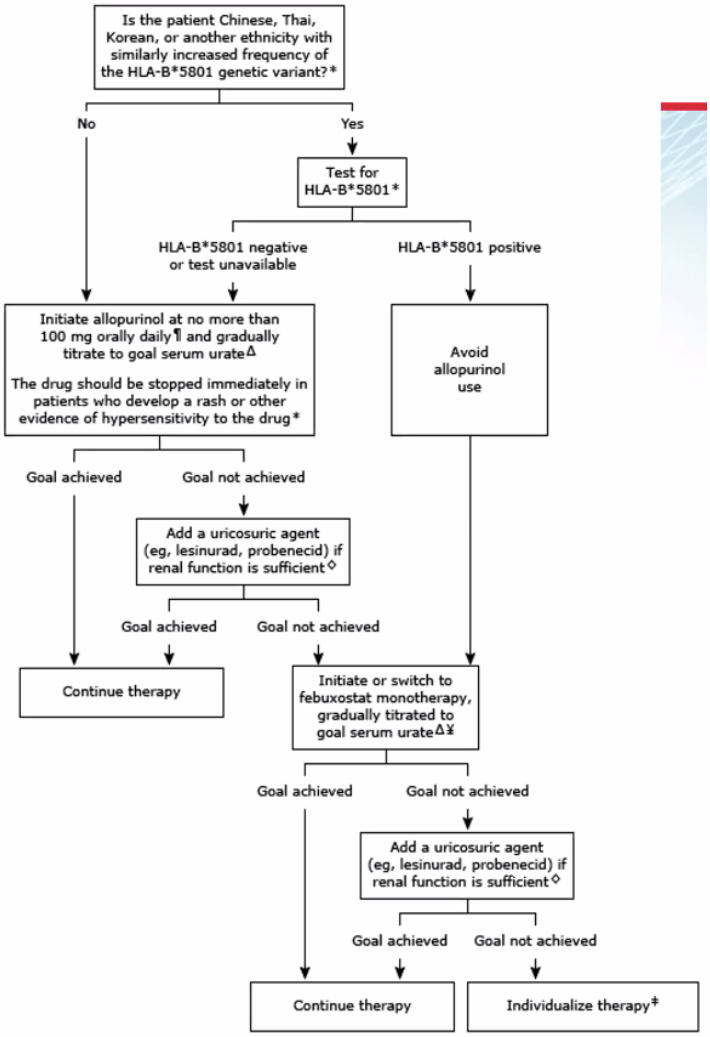
Urate Lowering Therapy (25min 39sec)

- Indications: 1) Frequent flares (>2/year) 2) Urolithiasis/Urate Nephropathy 3) Erosions on radiograph 4) Tophi
- Initiation: Can be done during hospitalization when acute flare has started subsiding (window of opportunity)
- Target: <300 (chronic tophaceous gout/frequent debilitating flares), <360 (non-tophaceous)
- Allopurinol
    - Once a day dosing (regardless of dose)
    - Starting: 100mg/day (50mg/day if stage 4-5 CKD)
    - Titrate upwards every 4-6 weeks, up to 600-900mg/day (100mg every 4 wks, if CKD, can increase in increments of 50mg)
    - SE: GI intolerance, transaminitis, hypersensitivity syndrome (fever, rash, oral ulcers; usually happens within 6-8 weeks from onset, but may sometimes happen with dose increments too)
    - HLA-B5801 Testing: Controversial
        - Hypersensitivity occurs in 2% of those who test positive; but can also happen in 10% of patients who test negative
        - Consider screening in high risk patients (Han Chinese, stage 3 CKD and beyond)
        - However, question about cost effectiveness (costs about $180)
    - Desensitisation: If it is truly SCAR, there is no role for desensitisation; but if mild rash without systemic involvement then can consider desensitisation
- Febuxostat (alternative to Allopurinol; XO inhibitor, but non purine analogue)
    - Dose: 40-120mg/day - max 40mg if CrCl < 30
    - If HLA-B5801 positive, or allopurinol hypersensitivity syndrome
    - Limited data in patients with renal impairment: Stage 3 CKD/ESRF
    - Only available in tertiary hospitals
    - Potentially higher cardiovascular risk – Caution in IHD (CARES RCT); debunked by FAST RCT - non inferior (but FDA blackbox warning still holds)
    - More expensive ~$4 per tablet
- Uricosuric Agents
    - Can be given upfront but requires adequate hydration (2-3L/day), and also usually a BD dosing hence compliance may not be as good as allopurinol
    - Often used in combination with XO inhibitors
    - Probenecid
        - Contraindicated in renal stones, CrCl at least 50ml/min
        - Dosing: Starting 500mcg/day up to 1.5g 2x/day

- Others: Benzbromarone, Lesinurad

- Prophylaxis
  - Options
    - § Colchicine: CrCl >60 (500mcg daily), CrCl 46-60 (3x/week), CrCl 30-45 (2x/week); avoid if CrCl <30
    - § Prednisolone: 5mg daily
  - Duration:
    - § Non-tophaceous gout: 3 months post achievement of target
    - § Tophaceous gout: 6 months post achievement of target/until tophi disappear
- Follow Up
  - 4-6 weekly
  - Things to check: Compliance, adverse reactions, blood tests (FBC – cytopenias, RP, LFT, Uric Acid)

Therapy Ladder



CPPD/Pseudogout (43min 21sec)

- Affects elderly patients more - >50 years
- Risk factors: Hyperparathyoridism, HypoMg, Hyperphosphatemia, Haemochromatosis

- Clinical features: Larger joints (knee, wrist, ankle, elbow), takes longer time to resolve (can be up to 2 weeks)
- Xrays to look for chondrocalcinosis
- Treatment
    - Acute: Similar to gout
    - Treat underlying cause
    - Generally limited role for chronic treatment - however in patients with chronic CPPD inflammatory arthritis (pseudo RA) - can consider add on of DMARDs like hydroxychloroquine (200mg BD); if still not improving can consider trial of MTX

Renal Dysfunction and Gout Medications

	Renal function		
	eGFR ≥ 46 mL/min	eGFR 30-45 mL/min	eGFR < 30 mL/min
Colchicine prophylaxis	0.5 mg daily	0.5 mg 3 times per week	Not recommended
Urate lowering therapy*			
Allopurinol starting dose (Absolute contraindication if patient is on Azathioprine)	100 mg OM	50 mg OM	50 mg OM
Probenecid starting dose	250 mg BD x 2 weeks then 500 mg BD	Cannot use	Cannot use
Acute Treatment			
Colchicine	0.5 mg TDS for 3 days	0.5mg BD for 3 days	0.5mg x 1 tablet ONLY Do not use in ESRF
Steroids	PO Prednisolone 20 -40 mg/day for 3-5 days OR IM Triamcinolone 40mg x 1 dose Joint injection with 40mg IA Triamcinolone (knee, shoulder) or 20mg IA Triamcinolone (wrist, elbow, ankle)		

Take Home Points (45min 15sec)

- Consider joint aspiration if suspicion of septic arthritis
- Institute therapy early – Even if septic arthritis is still a suspicion, can consider treatment with colchicine/NSAIDs (if concerned about steroids)
- Early discussions for ULT – consider inpatient initiation