Pennine GP Learning Group Meeting – Rheumatology Update with Dr Cheryl Fernandes (CHFT Consultant)

Thursday 8th October 2020: 7.30-9pm

Notes/key learning points/Q&A from saved "zoom chat" and discussion.

Case presentation: Patient with non-specific myalgia symptoms

- ***How long would Lyme disease antibodies remain positive for after initial infection?***

  IgM remain elevated for a short time and then normalise but IgG remains positive for longer

  Laboratory testing of the disease follows a two-step approach:

  First stage - enzyme-linked immunosorbent assays (ELISA) (1, 2). IgM peaks at 3-6 weeks; IgG appears more slowly and may take months or years to normalise.

  Diagnose and treat Lyme disease without laboratory testing in people with Erythema Migrans (1)

  Use a combination of clinical presentation and laboratory testing to guide diagnosis and treatment in people without Erythema Migrans. If IgG +ve and never had treatment, worth giving a course of antibiotics.

  Do not rule out diagnosis if tests are negative but there is high clinical suspicion of Lyme disease

  FJ: *thanks, I suppose if it was negative in the early stages you would just treat anyway but not so sure if it was many months ago*

- **Comment (CS):** I assume he was trialled off/stopped the PPI? I've had two achey patients on PPIs, though started not long after initiation. Patients had normal bloods but symptoms still resolved after stopping. Omeprazole can cause Mg deficiency, but lansoprazole does not.

- ***What is McArdle disease?***

  One of the differential diagnoses for the patient was McArdle disease. McArdle disease is a metabolic muscle disorder first described in 1951 by Dr Brian McArdle. The disorder is also called Glycogen Storage Disease Type V (GSD V). People born with McArdle disease are unable to produce an enzyme called muscle

phosphorylase. This enzyme is important in producing the fuel source required by the skeletal muscles for exercise.

Incidence thought to be 1:100,000. Most patients are diagnosed in adulthood traditionally using the ischaemic forearm test when there is a rise in ammonia but not lactate http://www.rheumaknowledgy.com/ischemic-forearm-exercise-test/

https://www.musculardystrophyuk.org/about-muscle-wasting-conditions/metabolic-myopathies/mcardle-disease-factsheet/

- **Comment (AM):** Twitching is a sign of LMN issues and so can be related with any myopathy

- **Comment (SH):** Myoadenylate deaminase deficiency (MADD) was mentioned as another possible differential diagnosis. One of the commonest inherited muscle disorders affects 1-2% of populations on European descent (much lower in Asian or African populations)

  The diagnosis of MADD needs to be considered in patients suffering exercise induced myalgia, cramps and sometimes weakness. A mildly elevated creatine kinase may also occur. Exclusion of other muscular diseases such as McArdle's Disease and carnitine cycle abnormalities should occur. MADD may be identified if there is a lack of ammonia rise but a rise in lactate after forearm exercise testing. The diagnosis may then be confirmed with genetic testing.

  https://en.wikipedia.org/wiki/Adenosine_monophosphate_deaminase_deficiency_type_1

  MW: *madd commonest… wow! I had never heard before either until researched!*

- ***In primary care, what first line investigations would you advise for myositis?***

  Assessment to help differentiate from other causes of myalgia –
  - "B" symptoms - new onset of fever, night sweats, weight loss - should make you think of paraneoplastic syndrome
  - inflammatory
  - Renal
  - Thyroid
  - Infections
  - trauma

  How long have the myalgia symptoms been present?
  Exclude infections/trauma
  Proximal /distal symptoms – If distal myalgia – unlikely to be immune myositis.

PMR vs immune Myositis – PMR tends to affect older patients and Myositis affects younger patients, CK is normal in PMR
Diurnal association – inflammatory diseases are worse in mornings

Investigations in primary care – Fbc/electrolytes/LFT/CRP/ESR/CK/TFT/ Vitamin D
Bone profile, Mg, urine dipstick for proteinuria
Consider Lyme Disease, PMR, immunoglobulins

CK rises quickly but comes down much slower (over days)
IM injections can increase CK to 500-600
CK is very sensitive – will rise with exercise, drugs, endocrine disorders etc.

In myositis – CK 1500-2000 at least, usually around 7000.

Causes of raised CK https://www.yorkhospitals.nhs.uk/seecmsfile/?id=3319

If elevated CK – then EMG, myositis-specific antibodies, MRI scan, muscle biopsy are second line investigations.

- ***How long should a patient abstain from exercise prior to checking CK?***

  1 week

- ***Any benefit of doing HLA B27 and its significance?***

  The patient was positive for HLA B27 antigen without obvious symptoms of Ankylosing Spondylitis. Usually it would only be tested for in the setting of inflammatory back pain, uveitis, bowel symptoms and Psoriasis. Can indicate a higher risk of developing autoimmune diseases such as Ankylosing Spondylitis and reactive arthritis. Relative of someone with Ankylosing Spondylitis is at higher risk of developing it but no treatment to prevent it so no benefit in screening relatives.

Top Tips – Gout

Easy to treat with time and a motivated patient!

Main reason for referral is non-compliance (with lifestyle and/or treatment)

Don't forget to think of Pseudogout especially in elderly (another crystal deposition disorder – CPPD) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3383522/

Acute gout can affect any joint. X-rays can show chondrocalcinosis.

Target uric acid – 0.3 or below – to prevent further acute attacks which is lower than the upper limit of lab reference ranges

Can still get flares of gout even if uric acid is low and stable. Usually takes about 6 months to lower uric acid to target level.

Allopurinol is nephrotoxic so monitor renal function whilst patient is taking it.

Can use allopurinol or febuxostat even if patient continues to drink excess alcohol/not adjust lifestyle/diet – won't be as effective though and these have narrow therapeutic window so easy to get into toxic levels.

Colchicine alone is not recommended in gout treatment as it is basically an anti-inflammatory, not a urate lowering agent even though patients may feel symptom free whilst taking it. Colchicine does work well in pseudogout.

Rheumatologists not seeing complications of gout or even gouty tophi anymore as generally managed well in General Practice.

Asymptomatic hyperuricaemia (no gout symptoms) is associated with increased cardiovascular risk but no evidence that urate lowering therapy has any significant on outcomes, therefore no guidelines for treatment.

- ***I was taught not to check urate during acute attack as level can fall, but how long after a flare should it be checked?***

  With a new episode check after 4 weeks. In acute attack, uric acid is artificially low as all the uric acid has gone into the affected joint

- ***How effective do you find Febuxostat vs Allopurinol for those that don't tolerate 1st line?***

  Febuxostat is more effective at lowering urate levels and can be used in renal impairment, (unlike allopurinol which is nephrotoxic) but not in heart failure. It can cause an acute rise in uric acid and flares of gout like allopurinol so may need to give with colchicine for first 6 months.

- ***What is the longest period you would use Colchicine alongside Allopurinol (if this was required). I think NICE recommends up to 6 months?***

  Yes can use Colchicine for 6 months at 500mcg bd dose. Caution in elderly or hepatic/renal impairment as narrow therapeutic window and extremely toxic in overdose.

- ***Can you use both Febuxostat and Allopurinol together?***

  Yes if one drug alone is not working/ lowering uric acid but is important to address lifestyle factors which may be contributing to high uric acid levels.

- ***When trying to lower uric acid with allopurinol, how often do you do monitoring bloods post change in Allopurinol dose?***

  Usually start Allopurinol dose at 200mg od and repeat EGFR/uric acid after 3 weeks then repeat after every 4 weeks when titrating. Don't need to monitor uric acid routinely /annually once stable as generally they will become symptomatic of gout again if uric acid rises. So be guided by clinical symptoms.

- ***Can we prescribe Febuxostat in primary care?***

  From MW:

  yes - well I have…

- ***Should you wean patients off Allopurinol if you feel it's no longer necessary - sometimes there are elderly patients that seem to have been on it forever and can't remember why. Is there any risk to just stopping it abruptly?***

  Fine to stop Allopurinol abruptly.

- ***Our prescribing guidelines recommend max course of 6mg colchicine (12 tablets) in one period for acute attacks - and to not repeat course within 4 days - what is the basis for this?***

  Doesn't seem to be any basis for this except most patients develop GI side effects /diarrhoea if taking qds/tds – but if bd can give for up to 6 months so some flexibility

  Comment (IA): *I think bd dose usually works in my experience*

- ***Am I right in advising patients to avoid dehydration?***

  Yes.

- ***Is there any point in checking uric acid if confident diagnosis is gout in acute presentation?***

  Don't have to check it in acute presentation as uric acid could be artificially low in an acute flare up. Usually check a few weeks later to monitor levels and titrate treatment as necessary.

- ***Are some kinds of alcohol worse than others for gout?***

  Yes – beer is worse than others.

  Gout lifestyle advice here (NB: its more than a diet sheet!) :

  https://patient.info/news-and-features/gout-diet-sheet

Top Tips - Osteoporosis

Estimate Fracture Risk using FRAX tool - https://www.sheffield.ac.uk/FRAX/tool.aspx?country=1

If patient has a fragility fracture – Rx – DEXA is done mainly to have a baseline and for monitoring purposes.

- ***What is your first line supplement, we tend to use calci-d as once daily dosing. Any other recommendations?***

  Any is fine – as long as 1000mg calcium – can get from diet and at least 1000IU vitamin D daily. Oral bisphosphonate. Strontium not indicated any more – too many issues – cardiovascular risks but also difficult to monitor as affects BMD so don't get an accurate reading. Vit D level needs to be 50 or above

  Comment (SH) *I think there is a good dietary calcium table on patient.co.uk or whatever it's called these days*

  https://patient.info/bones-joints-muscles/osteoporosis-leaflet/calcium-rich-diet

- ***If you had osteoporosis what would you take?***

  Alendronic acid. Lower risk adverse effects and is effective.

- ***We tend to get the occasional patient discharged after #NOF with "GP to request DEXA then consider bisphosphonate" - Surely they should just start those patients on it at discharge?***

  Yes they should be and Rheumatology are working on a pathway with Orthopaedics.

- ***Does everyone get dental review prior to starting bisphosphonate?***

  Advise all patients to inform their dentist that they are starting this treatment due to risk of avascular necrosis of jaw.

- ***Secondary care options for Osteoporosis treatment if first line not working/unable to tolerate:***

  IV Zolendronic acid once yearly (unable to tolerate oral bisphosphonate)
  Denosumab 6 monthly
  Teriperatide
  Biosimilar of Denusomab

These are more expensive than Alendronate and Risedronate and higher risk of atypical fractures, renal impairment and avascular necrosis of the jaw.

- ***If Alendronate is not tolerated is it worth trying Risedronate before referring and moving to Denosumab?***

  Yes it is worth switching to Risedronate but Dr Fernandes recommends referring to Rheumatology at the same time as likely they may not tolerate that as well.

  Comment (IA): *patients tolerate Risedronate better than Alendronic in my experience especially from GI symptoms*

- ***Any role for HRT type meds?***

  They do help but not mainstay treatment.

  Raloxifene (Selective oestrogen receptor modulator) is good for less severe osteoporosis

- ***Is the max duration of bisphosphonate still 5 years, any further research on benefits longer periods and when would you reconsider DEXA after a treatment holiday?***

  Continue oral bisphosphonate for 5 years unless they have a fragility fracture whilst taking the treatment.

  For IV bisphosphonate continue for 3 years

  Warn patients they need to inform dentist if on bisphosphates

  If no further fractures in this time then ok to have a drug holiday for 2 years and have repeat DEXA at this time (i.e. 2 years after stopping).

  Theoretical problem with continuing bisphosphonate is that they stop the osteoblasts and osteoclasts from functioning and so get an adynamic bone – which can't repair itself if inhibit osteoclasts too much so you can get atypical fractures. Need to assess risks vs benefits for each patient.

Top Tips – Giant Cell Arteritis/Temporal Arteritis

Review of clinical features and pathway – Updated pathway to be shared by Dr Fernandes as pathway included in PowerPoint not up to date.

Headlines:

***Refer all to rheumatology**

***Do CXR in all as they are at risk of aortic aneurysm.**

***Refer all with eye signs to ophthalmology**

Comment (MQ): *In terms of referrals, pts with eye symptoms need referring to 3 specialities - rheumatology, vascular and ophthalmology*

- ***How likely is Temporal Arteritis if normal ESR?***

  Not very likely. But if symptoms suggestive give trial of steroids and stop if no response

- ***Baseline tests for GCA on protocol indicate need for CXR… why?***

  Due to risk of aortic aneurysm with the disease need a baseline. Do not have the same risk with PMR.

  Suspected cases need referral for temporal artery biopsy whilst starting treatment.

- ***So would you always try and get one (a biopsy) even if other 3 or 4 criteria met?***

  Yes it's good to try given the nature of the treatment – want as much information as possible to support the diagnosis. However do not delay starting steroid treatment if there is a delay in getting biopsy.

- ***How reliable will the ultrasound diagnosis be? And what's the delay? (dare I ask?)***

  Pathway being developed to look at using Ultrasound with special probe instead of biopsy – very reliable for diagnosis of GCA – high specificity – equal to biopsy.

- ***Who reviews the biopsy result after it's done, do the vascular surgeons refer any positive results to rheumatology?***

  Positive results go to Rheumatology.

- ***All GCA need referring, but are we referring all PMR?***

  No. All PMR patients don't need referring as they can be managed in primary care.

- ***Given that we are using DMARDS instead of steroids in other inflammatory conditions like Rheumatoid Arthritis – why is this not the approach in the treatment of PMR?***

  DMARDs do not work well in bringing PMR symptoms under control /bringing down inflammation markers but are used as second line steroid sparing agents. So when trying to wean off/stop steroids then can use DMARDs to try to get to lowest possible steroid dose to maintain symptoms/try to wean off. Usually stop DMARDS after steroids stopped as no evidence of benefit in continuing to prevent the disease from flaring.

  So do the DMARDs keep it under control once settled on steroids? Yes.

Final question for the session – What's the most annoying thing GPs do? :)

Requesting ANA in patients without clinical symptoms/evidence of inflammatory arthropathy – Rheumatologists don't do anything with them except repeat and monitor if they are positive… So don't do them routinely, only if inflammatory marker is high.

Feedback

From AM: 09:00 PM

Thanks

From FJ: 09:03 PM

Thank you very much Cheryl, it was very helpful

From TR: 09:07 PM

Thanks for organising. Much appreciated! Good night.

From CS: 09:07 PM

Thank you v useful!

From NP: 09:07 PM

Thank you

From MQ: 09:07 PM

Great session.

From SM: 09:07 PM

Thank you!

From IH: 09:07 PM

Thank you Cheryl

From DM: 09:07 PM

Thank you

From AY: 09:08 PM

Very useful, many thanks

From SM: 09:08 PM

Really useful session, thank you!

From AM: 09:08 PM

Thanks for the update

From SI: 09:08 PM

Thank you for the useful talk

From SH: 09:08 PM

And thank you too!

From MW: 09:08 PM

Thank you Cheryl, Rukhs and Farrukh. Great session

From OO: 09:08 PM

Thank you for the session

From SH: 09:09 PM

Thanks for organising too Rukhsana

From SI: 09:09 PM

Thanks for organising

From IA: 09:09 PM

Thanks for organising

From AM: 09:09 PM

Thanks Mark and Rukhsana

From SM: 09:09 PM

Thank you Rukhsana

From IH: 09:09 PM

Thanks for hosting Rukhsana!

From CI: 09:09 PM

Thanks for organising

From CS: 09:09 PM

Thanks guys!