High CK on the take; what should I do?

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High Creatine Kinase is common

Everyone has seen

Mostly ignored it

Hope it goes away…..

Cases from the medical take at the Royal Surrey

Case 1

- 51 year male presents with:
  - 9/7 h/o progressive muscle pain and weakness
    - Initially in legs then progress to arms
    - Associated with stiffness
  - Last few weeks "generally unwell"
    - Coryzal symptoms, sore throat, blocked nose
  - Possible facial puffiness with mild headache
  - Minimal dysuria

PMH

- Asthma
  - Difficult to control (under respiratory team)
  - On SIROCCO trial ; benralizumab for 2 years (antibody to IL-5 receptor)
- Mild bronchiectasis
- Chronic rhinosinusitis and hearing problems
- Nephrotic syndrome (diagnosed in Ireland 7 years ago)
- Hypothyroidism
- Vitamin D deficiency
- Under investigation for prostate symptoms currently; Likely benign

Hx

- Medications:
  - Symbicort, Levothyroxine, Tamsulosin, Trial drug
- Social:
  - Fit and well, Ex smoker, management consultant

Examination

- Observations – Temp 36.4, p 68, BP 150/101, RR 18, Sats 99% Air, GCS 15
- Chest – clear
- Abdo – NAD
- Neuro – mildly increased tone, brisk reflexes throughout, power felt to be normal

Blood results

- FBC – normal
- U+E – normal
- **LFT – ALT 52**, ALP/albumin/bilirubin normal
- **CK – 1023**
- **CRP – 39**
- VBG – Lactate 1.7, otherwise NAD
- CXR – NAD

What to do next?

- Monitor CK?
- Autoantibodies? Which ones?
- CT CAP?
- MRI thigh?
- EMG?
- Check HIV?
- Urine protein:creatinine?

Over the next few days…

	O/A	D1	D2	D3	D4	D5
CK	1023	479	323	438	158	91
CRP	39	71	46	20		16
ESR			15			

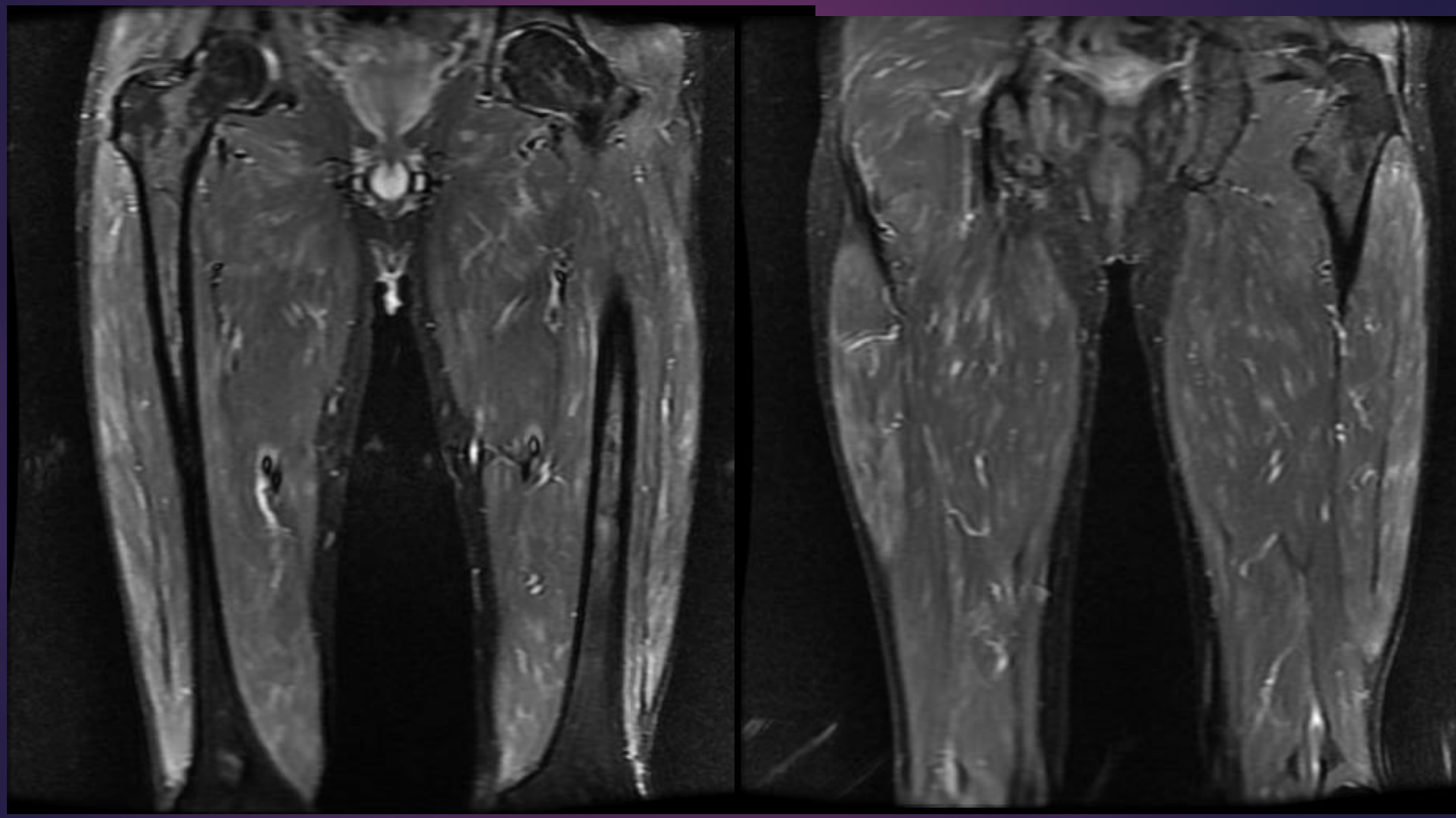
Rheumatoid Factor – 598 (NR 0-30)
ANA – Fine speckled, titre 1:160
ENA – Neg
dsDNA – 20 (NR 0-20)
C3 – 1.53
C4 – 0.28
ANCA – positive, pANCA pattern, titre 1:160
Anti MPO – 87 (NR 0-3.4)
Anti PR3 – 0.3
Urine microscopy – WBC 17, RBC 3, Epithelial cells 0
Throat swab – Enterovirus RNA, Parechovirus RNA, Influenza A+B, RSV PCR – all neg

IgG – 11.5
IgA – 1.1
IgM – 0.91
IgE – 1605
SEP – Normal
Paraprotein – No monoclonal band detected
PCR – 14
Hep B sAg – Neg
Hep C – Neg
HIV 1+2, p24 – Neg
Anti-CCP – 1.3

Over the next few days…

- MRI femurs (STIR)

MRI STIR/Fat sat thighs



Over the next few days…

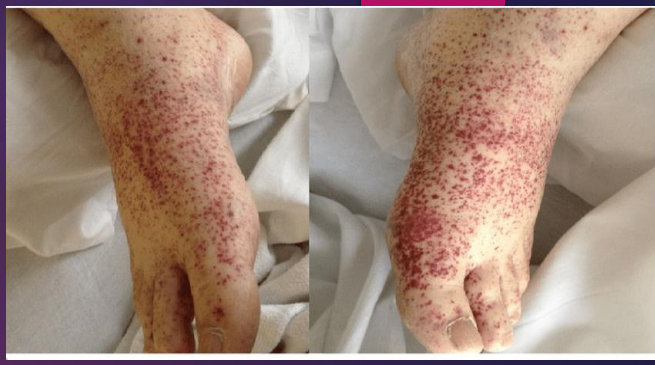
- MRI femurs (STIR) – Widespread patchy elevated signal within the muscles. No definite necrosis. No abscesses. No joint effusions. No tendon abnormalities
- EMG – normal

Summary so far:

- High CK
- Painful weak muscles
- Patchy signal change in thighs on MRI
- Normal EMG
- RF +++, pANCA+, MPO +
- Background of complex asthma on IL5 antagonist

- What next?

Then…



- Started developing **flitting** symptoms
  - Developed erythema and swelling over dorsum of both hands/wrists and right elbow
    - Urgent USS: At both wrists there is **florid tenosynovitis** involving all extensor tendons with **synovitis** in the proximal and middle carpal rows with grade 1 synovial thickening and grade 2 hyperaemia.
  - Developed petechial rash on ankle and further erythematous areas in different locations on arms
  - Episode of transient visual loss in right eye with TMJ tenderness (CT head – NAD other than sinus disease)
  - During this time:
    - Renal function remained normal, urine dip trace blood only with negative protein, CRP 18, ESR 20

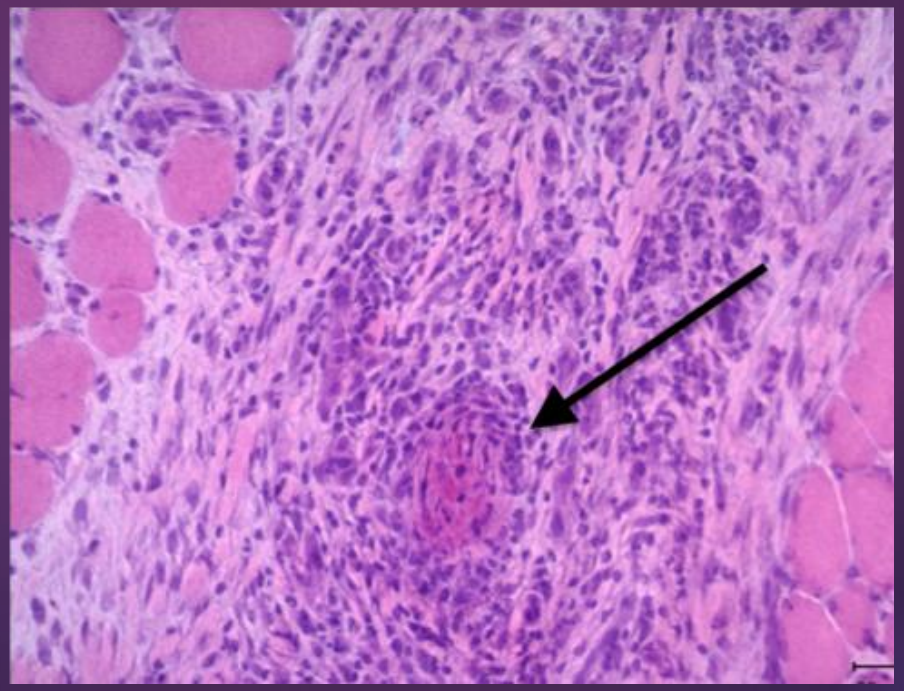
Differential Diagnosis?

- What next?

- Muscle biopsy?
- PET CT?

Further results

- Muscle biopsy: Consistent with vasculitis
- Interestingly PET CT: reported as normal



Diagnosis

pANCA/mpo associated vasculitis

- Muscle infarction secondary to vasculitis
- Abnormal MRI with normal EMG
- Rapidly resolving CK
- Evolution of multisystem involvement

Treatment:

- IV methylprednisolone
- Then oral prednisolone; weaning dose
- Cyclophosphamide for 3/12
- Consolidated on oral Methotrexate; weaned off prednisolone

- Update:
  - Asymptomatic
  - Back on biologics for asthma
  - Slowly weaning his Methotrexate

Case 2

- 24 year old male, Caucasian student

- 4/7 headache and low grade temperature
- 2/7 myalgia
- 1/7 weakness

- PMH nil
- Not on any medication
- Had taken a few paracetamol for headache
- Non smoker

O/E

- No rash
- No weakness; power 5/5, R=L
- Able to stand from sitting
- No LN
- Chest clear
- Observations were all normal

Bloods

- CK 10 473
- FBC, U&E, LFT, Bone, Gluc normal

What to do next?

- Monitor CK?
- Autoantibodies?
- MRI?
- EMG?
- Muscle biopsy?
- TSH?

Progress

	Day 1	Day 3	Day 5
CK	10 473	7339	1240

- Rapid drop in CK
- No symptoms

Progress

- Reviewed in OP 6 weeks later
- CK 213

Diagnosis

- **Viral myositis**

- Viral prodrome
- Rapid recovery of CK with only supportive Rx
- Minimal muscle signs and symptoms

- **Implicated viruses:**
- Coxsackieviruses, influenza A and B viruses, HIV, HTLV-1, hepatitis C, and hepatitis B virus
- Rarely EBV, CMV

Case 3

- 53 year old man came to A+E with ‘vasovagal’ episode

- S/E:
- Decreasing mobility over several weeks especially difficulty getting up from chair
- Transient dysphagia
- Rash
- Increasing SOB

- PMH: Recent admission to local hospital with weakness
- Asthma
- Thalassaemia trait

- DH: furosemide (for ankle swelling), salbutamol, symbicort

On examination

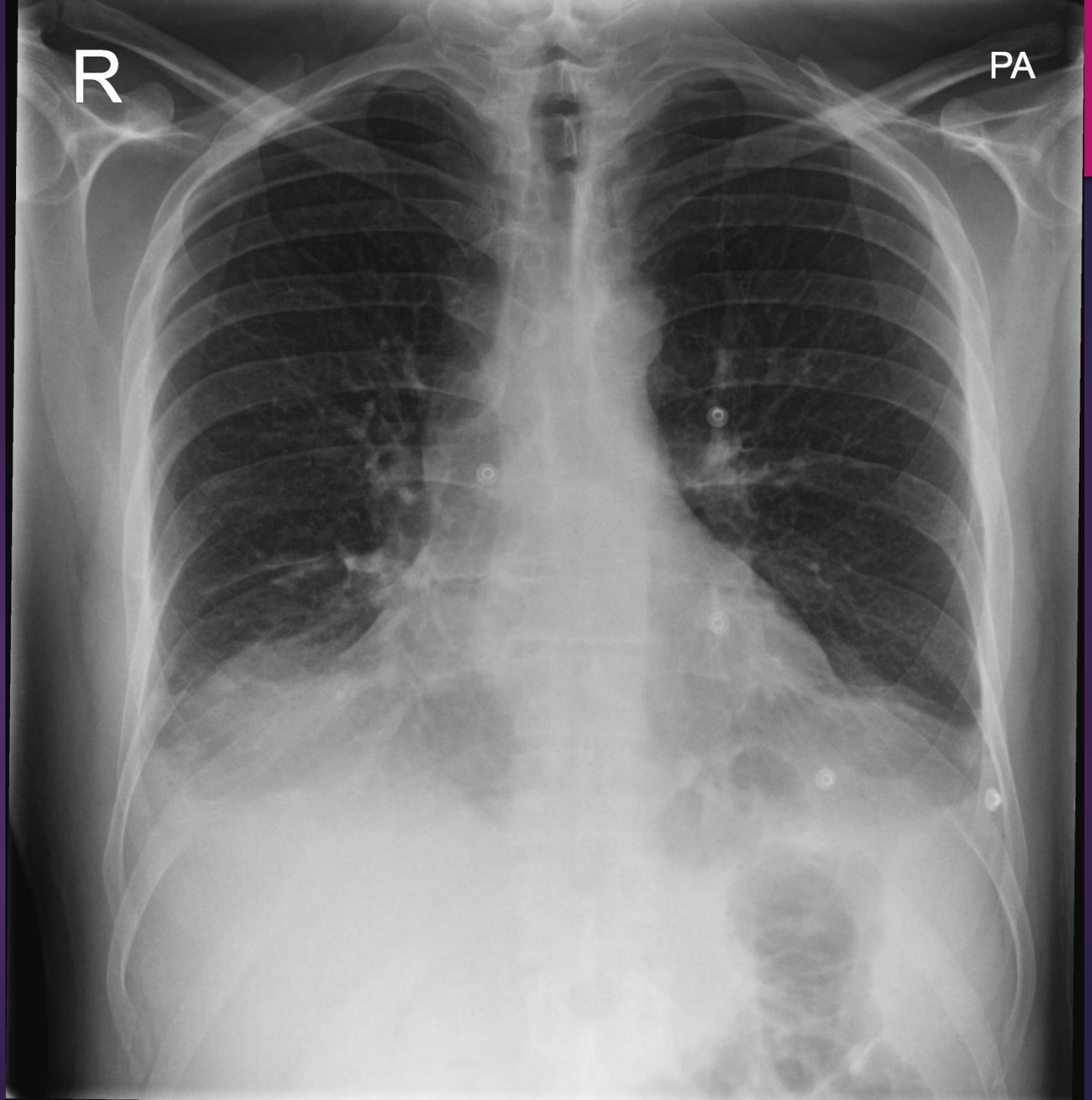
- Pale pink blanching rash on thighs with significant proximal weakness

- Unable to stand
- Unable to lift head
- Unable to roll over in bed

- Bibasal crackles

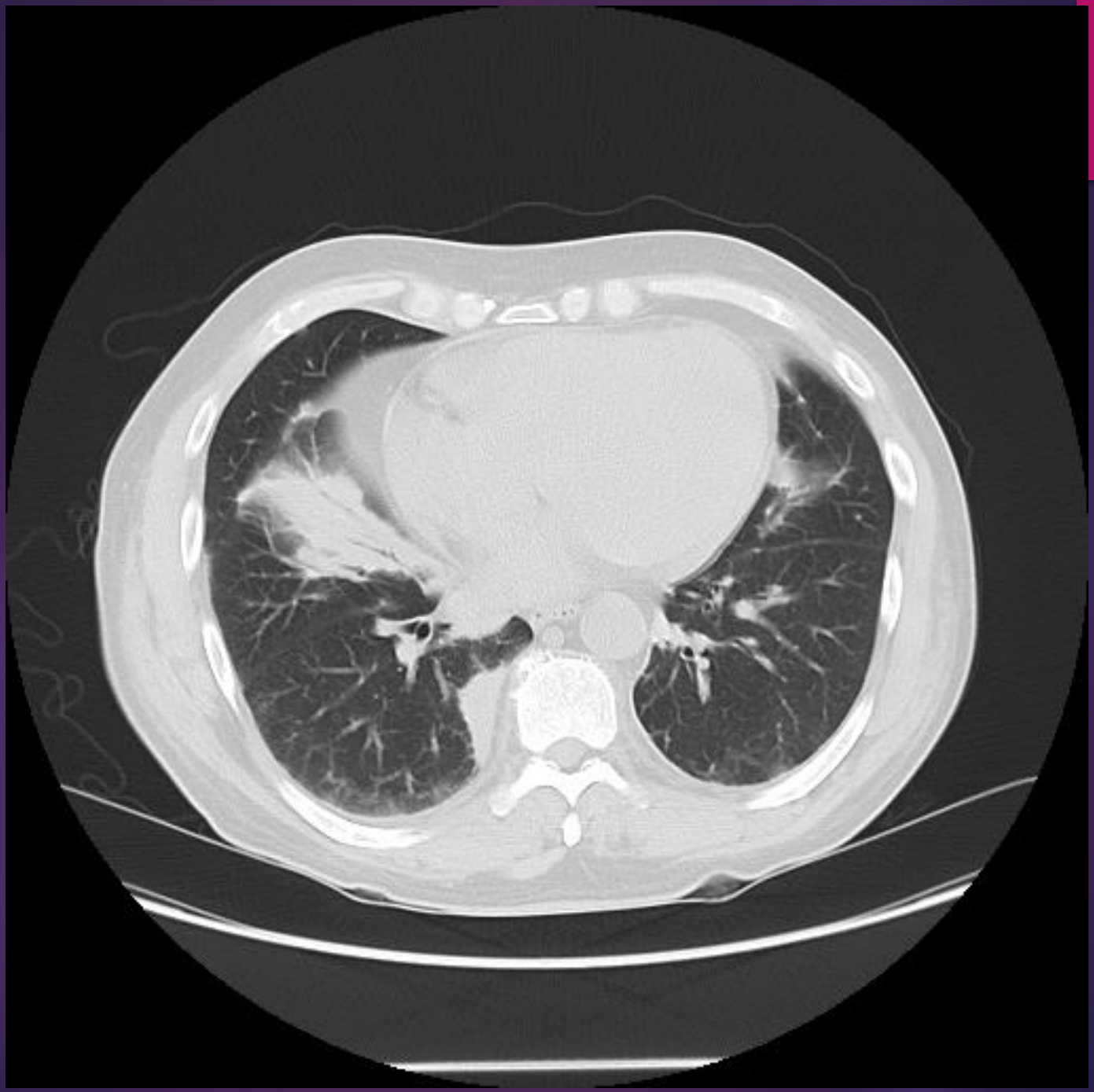
Investigations

- WCC 12.4, Hb 104, Plt 544, MCV 64 (normal for him)
- ALT 288, ALP 78, Bili 6
- CRP 57
- Trop 53, ECG – lateral T wave changes
- U+E normal
- **CK 7064**


R
PA

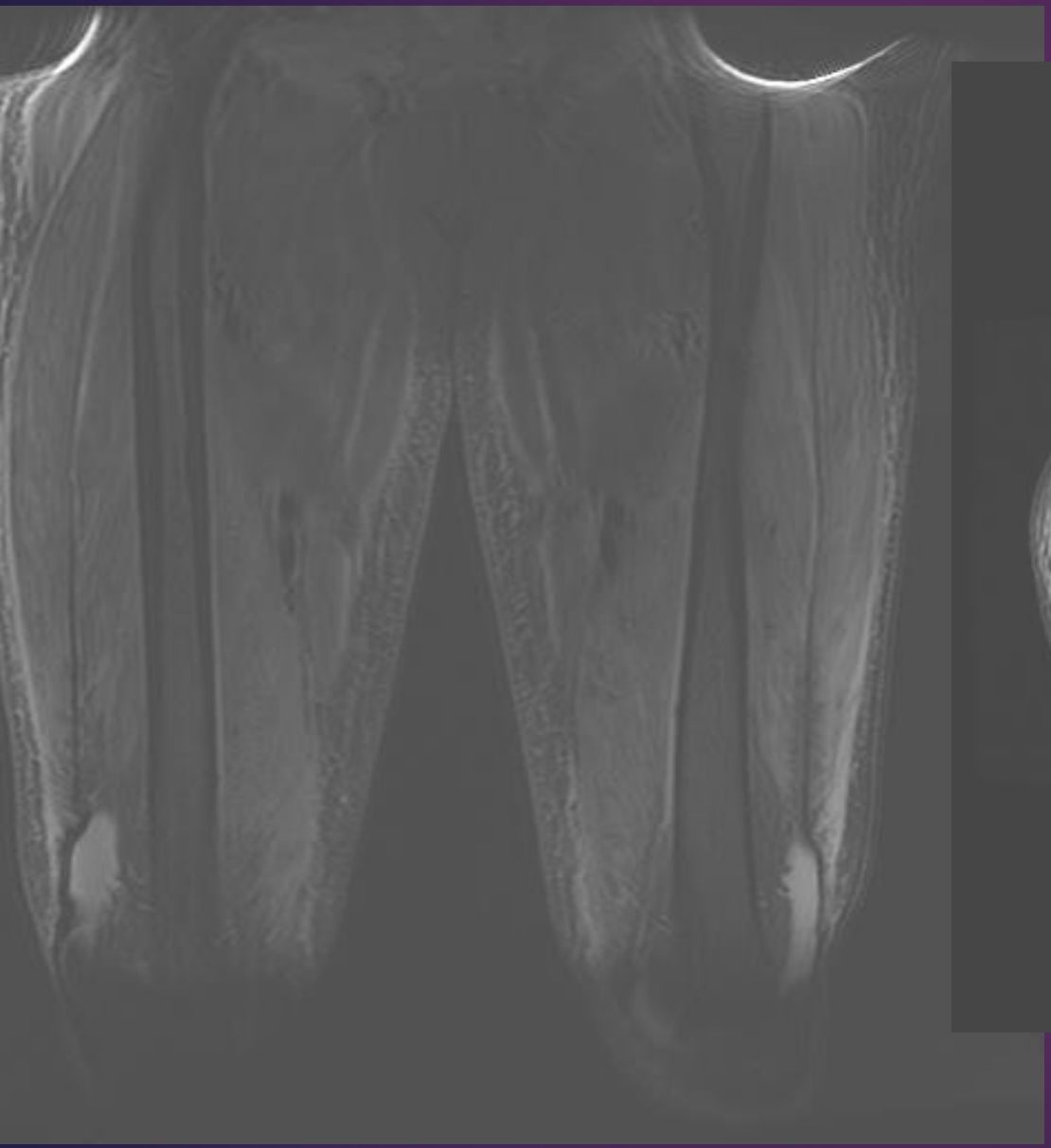
What to do next?

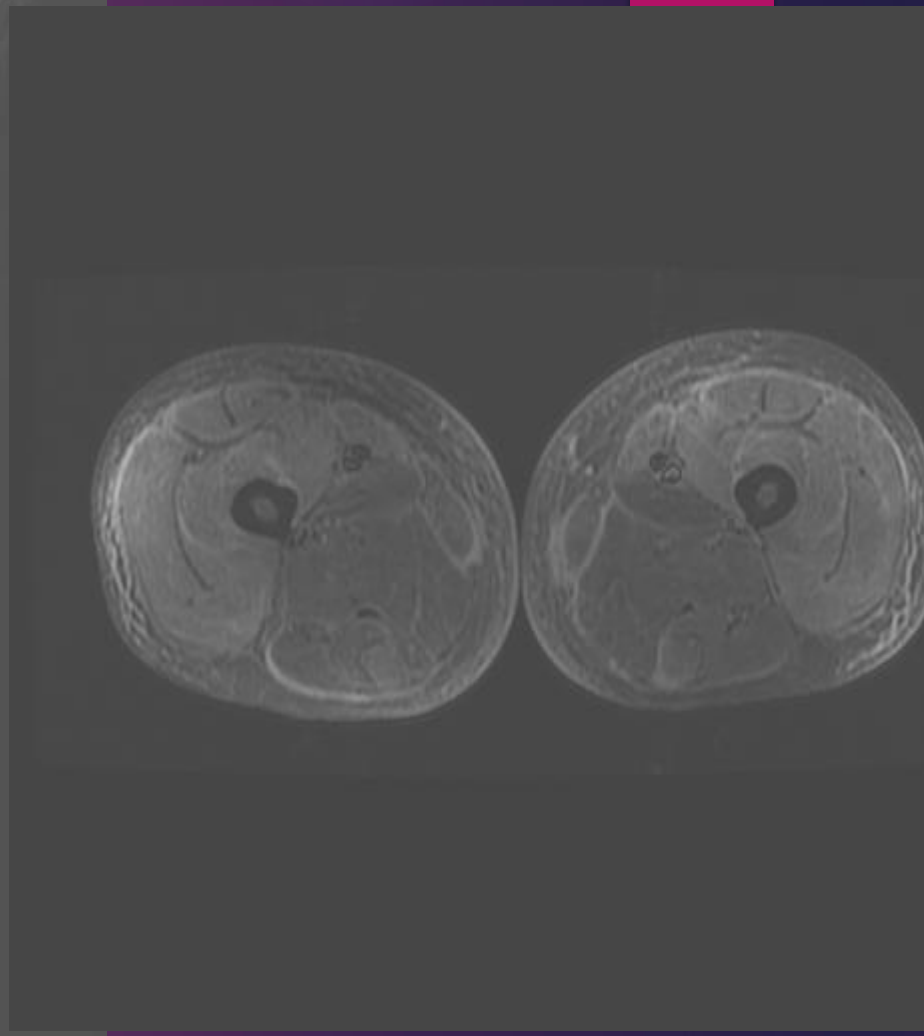
- Monitor CK?
- CT CAP?
- HRCT?
- MRI thighs?
- EMG?
- Autoantibodies? Which ones?
- Other tests?

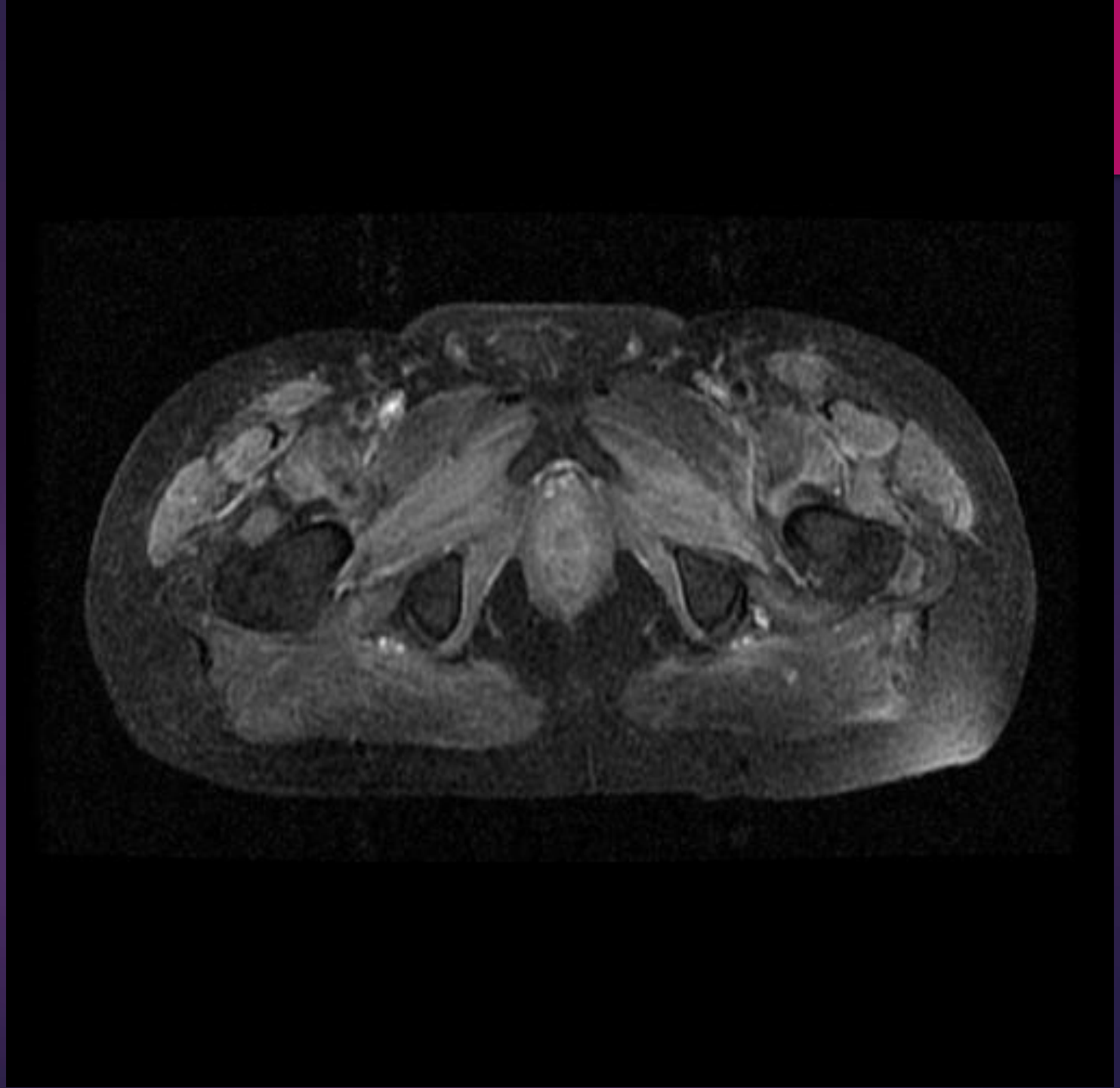


Ix

- HRCT: mid and lower zone patchy consolidation in a peri-bronchial pattern and mild airway dilatation and volume loss. Suggests **organising pneumonia**
- CT CAP: Non specific pleural plaques, small indeterminate pulmonary nodules, mild splenomegaly. L4/5 lumbar canal stenosis
- MRI head: normal
- MRI thighs







Summary of investigations so far…

- Rh factor: <11.4
- ANA: neg
- ANCA: neg
- IgG: 11.8
- IgA: 2.5
- IgM: 1.56
- SEP: normal
- Paraprotein: No monoclonal bands detected
- **ENA: Jo-1 positive, Ro52 positive**

MRI femurs: Bilateral proximal polymyositis. Also myofascial inflammation. Probable dermatomyositis

EMG: Suggests primary muscle disease

Diagnosis?

- **Jo1 positive polymyositis with interstitial lung disease**
- **Anti-synthetase syndrome**

Treatment

- 60 mg oral prednisolone
- Troponin settled quickly with appropriate Rx
- Methotrexate
  - Escalated rapidly to maximum dose
  - Steroids weaned, but CK high
  - Mycophenolate added

  - CK still high although patient now asymptomatic
  - Rituximab (monoclonal ab to CD20 B cells)
  - Partial response, now under tertiary care
  - Rapid decline
  - Jo1 +ve is meant to represent a better prognosis

Anti-synthetase syndrome

- anti-tRNA synthetase (anti-tRS) autoantibody and one or more of these clinical features in decreasing order of frequency
  - Myositis
  - ILD
  - Arthritis or arthralgia
  - Raynaud's phenomenon
  - “Mechanic's hands”
  - Fever

Myositis antibodies; current extended panal

- Anti – EJ antibody
- Jo1 tRNA synthetase
- Ku antibody
- MDA5 antibody
- Alpha Mi-2 antibody
- NXP-2 antibody
- Anti OJ antibody
- Anti PL-12 antibody
- Anti PL-7 antibody
- PM-Scl75 antibody
- PM-Scl100 antibody
- Ro-52 antibody
- SAE-1 antibody
- Anti SRP antibody
- TiF Gamma antibody
- Beta Mi-2 antibody

Case 4

- 55 year old Italian builder

- Referred with bilateral proximal leg cramps, R>L
- After industrial accident; glancing blow from large metal bar falling from crane leading to R ankle #
- Weakness in legs
- Limps on walking
- GP checked; CK 937

PMH, SHx and Drug hx

- Prn paracetamol

- 30 pack year smoking hx
- Teetotal for 15 years, previously heavy drinker

- No notable PMH

O/E

- No rash
- Right high stepping gait
- No wasting or fasciulation
- Power 5/5, R=L, upper=lower

- 3cm liver edge felt

Blood tests

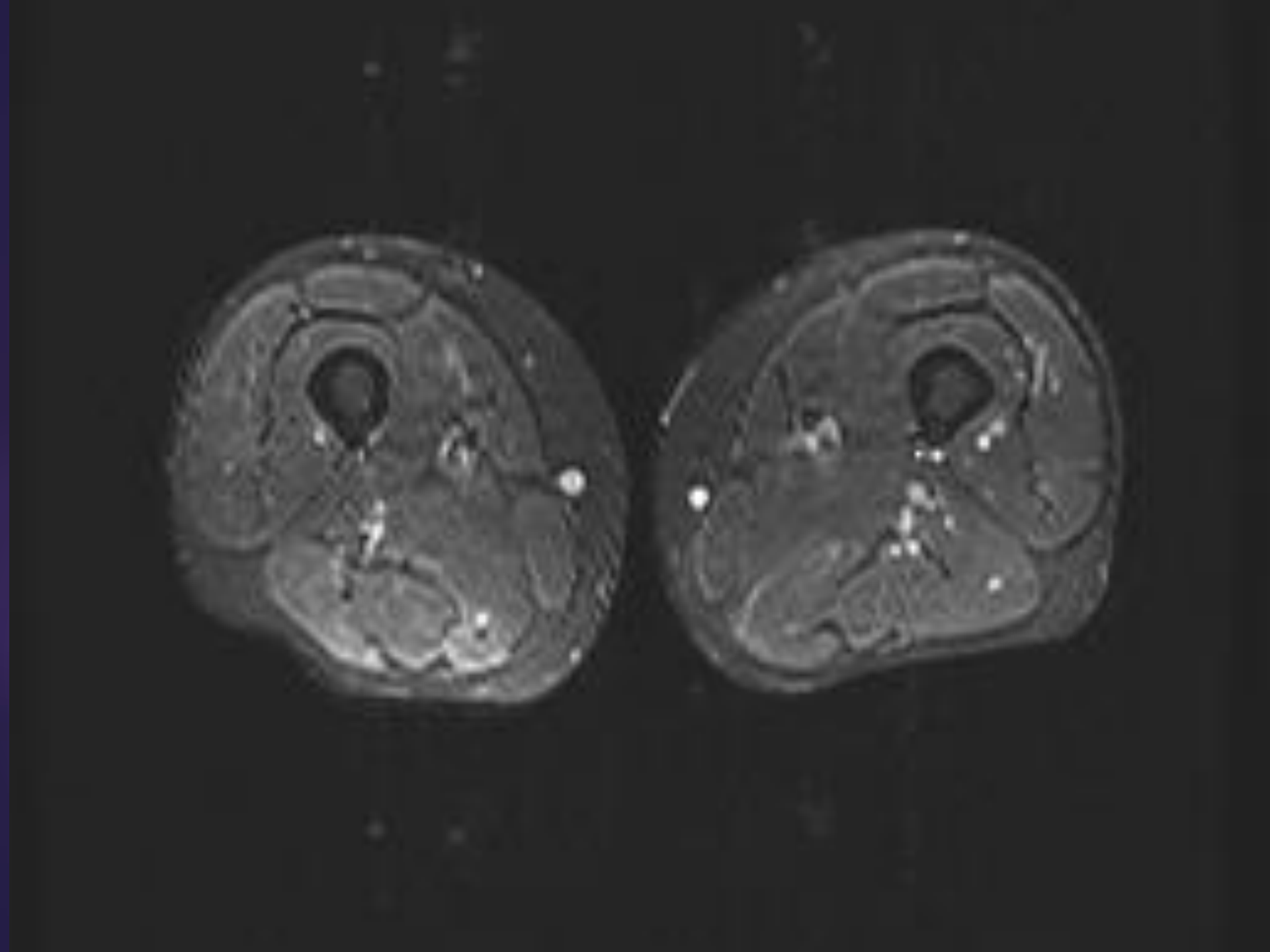
- ALT 160
- CK resting 458
- CK active 556
- ANA 1/160 homog, ENA –ve

What to do next?

- USS liver?
- MRI thighs?
- EMG?
- Other blood tests?
- Muscle biopsy?

Ix

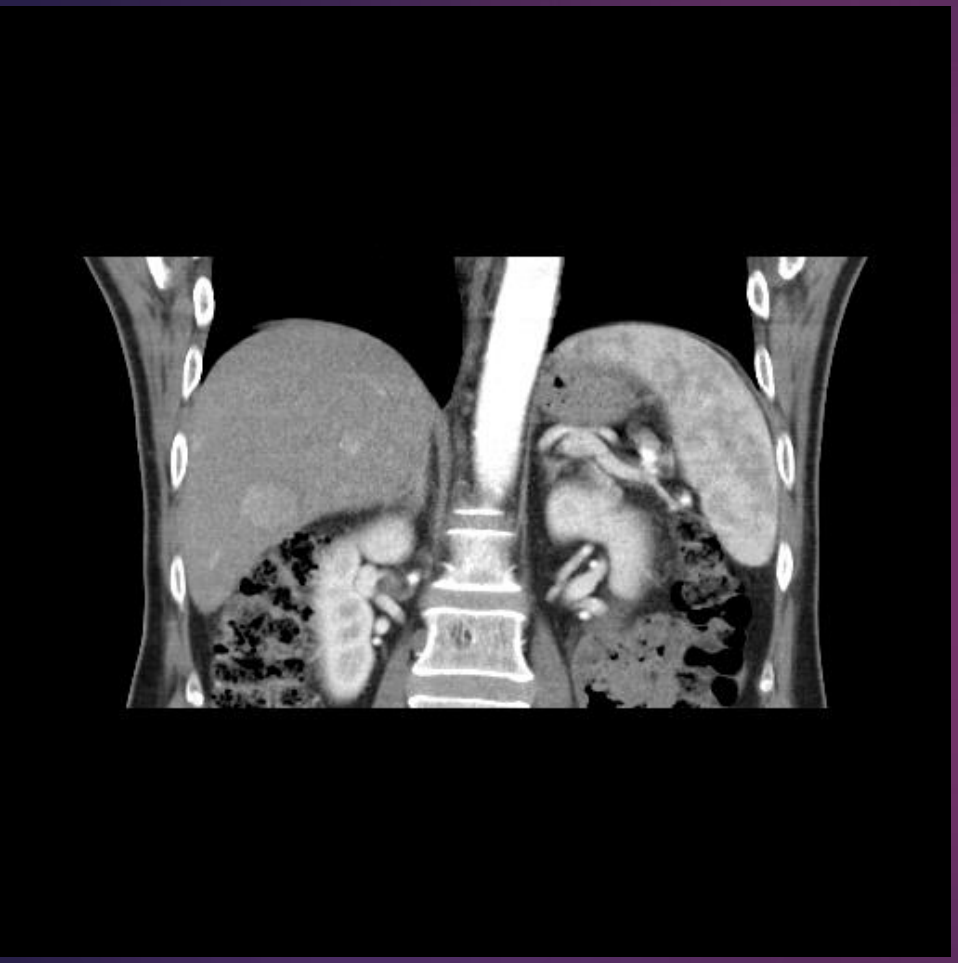
- USS liver; ?haemangioma R lobe of liver
- EMG; No EMG evidence of primary muscle disease. Neurogenic abnormalities fairly widespread in both lower limbs suggestive of ?root or anterior horn cell level as peripheral nerve conduction studies normal.
- MRI thighs; diffuse oedema in hamstrings, right >left

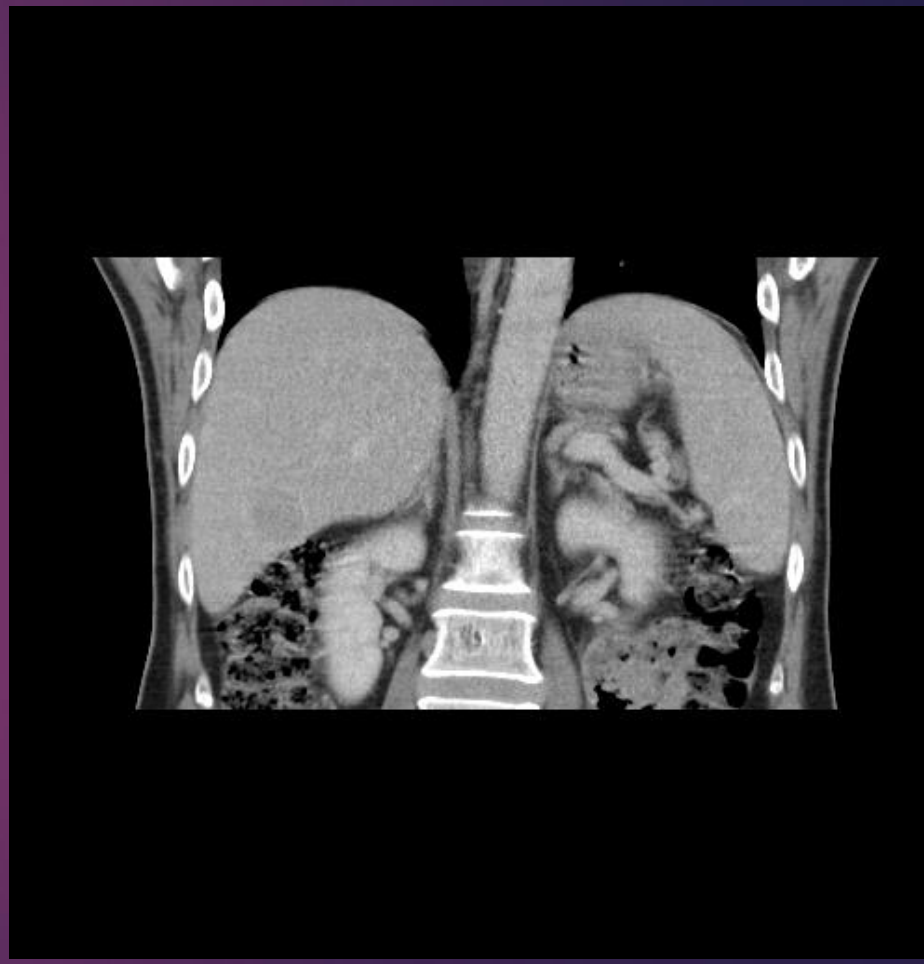


What next?

- Muscle biopsy?
- Nerve biopsy?
- Neurology review?
- CT triple phase of liver?

CT triple phase liver





Appearances are in keeping with HCC

Diagnosis

- Muscle infarction secondary to a paraneoplastic neuropathy secondary to HCC
- Differential includes polio (unlikely), hereditary spinal muscular atrophy (unlikely) and motor neurone disease

Actions

- Referred urgently to hepatobiliary MDT
- Put neurology review on hold until plan and opinion from hepatologists
- Update;
- Found to be Hep C +ve
- Had liver resection and eradication therapy

Case 5

- 21 Caucasian female student
- Several weeks of fatigue and malaise
- Myalgia
- No fevers
- No rash
- GP checked CK 1208

PMH

- Mild asthma
- Salbutamol prn
- Non smoker
- EtOH at weekends

O/E

- Normal power; 5/5, R=L, Upper=lower
- Normal reflexes
- No rash
- Chest clear

What to do next?

- Monitor CK?
- TSH?
- HbA1c?
- EMG?
- MRI thighs?
- Muscle biopsy?

What did I do?

- Repeated her CK; 196

- Fit and active
- Likes to exercise

Key question?

- May have *accidentally* taken ketamine at a party

Diagnosis

- Ketamine induced rhabdomyolysis

What is CK?

- CK is found:
  - inner mitochondrial membrane
  - on myofibrils
  - in muscle cytoplasm
- Involved in the production of ATP
  - Creatine + ATP ⇔ Creatine phosphate +ADP
- There are three main isoenzymes
  - **CK-MM** Skeletal muscles are >99%CK-MM
  - **CK-MB** Cardiac muscles are 20% CK-MB
  - **CK-BB**

Abnormal CK; No muscle disease

- Exercise
- Iatrogenic muscle injury
  - IM injection
  - EMG
  - Surgery
  - Fall
  - Fit
- MND/neurological
  - Muscle death secondary to dennervation
- Renal disease
- Cardiac

- Asymptomatic elevations
  - Ethnicity
  - Muscle mass
  - No or minimal muscle symptoms
  - No weakness
    - **Hyper CKaemia**

Abnormal CK – Neuromuscular conditions

- Inflammatory myopathies
  - Polymyositis/ dermatomyositis,
  - can be associated with other connective tissue diseases and other inflammatory processes
- Infectious myopathies (pyomyositis)
- Dystrophinopathies
  - Duchenne/Beckers

Rhabdomyolysis; muscle necrosis

- Commonest after a long lie leading to compression and secondary muscle ischaemia
- Also in compartment syndrome

- Anti psychotics
- SSRIs
- Statins
- Colchicine
- Lithium
- Anti histamines

Recreational drugs and poisons causing rhabdomyalysis

- Heroin
- Cocaine
- Amphetamines
- Methadone
- LSD

- Snake venom
- Carbon monoxide
- Mushroom poisoning

Abnormal CK; other neuromuscular conditions

- Neuroleptic malignant syndrome
  - Drug induced with, altered mental state, fever, rigidity and dysautonomia
- Metabolic myopathies
  - McArdles Disease
- Malignant hyperthermia
  - Fever and rigidity often after anaesthetic
- Endocrine myopathy
  - Thyroid, acromegaly, diabetes
- Periodic paralysis

Take home points

- Many causes of high CK
- Important to remember the pointers in the history
- Following the progress of the CK is helpful
- EMG, MRI of affected muscle
- Always consider the underlying diagnosis
- Look for other causes if investigations don't match the history

Any questions?