A Multisystem Masquerade

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Patient introduction

Mr AB

A 52-year-old

Father of two children

A Banker

From Kandy

Presenting Complaint

presents with gradually worsening exertional shortness of breath over the past month.

Further history

- Progressive worsening of exertional shortness of breath
- NYHA Class 2-3 symptoms
- With orthopnoea and paroxysmal nocturnal dyspnoea
- On and off palpitations
- Had an on-and-off productive cough for 1 month with wheezing but responded poorly to antibiotics and inhalers given by the GP.

Two weeks into his symptoms, he experienced diarrhoeal stools.

6-8 episodes per day.

Large amounts. Watery with mucus and blood.

With associated lower abdominal pain.

1-2 episodes of nocturnal diarrhoea per day.

Complained of significant loss of appetite and weight.

Generalised malaise and fatigue.

Past medical history

- T2DM 1 year back
- On metformin and gliclazide
- Good glycemic control
- Frothy urine for the past 3 months
- Bilateral lower limbs have felt numb for the same duration.

Social history

- Nonsmoker
- Occasional ethanol consumer
- Married, father of 2 daughters
- No recreational drugs,or any high risky behaviours

HEART FAILURE

GUT INVOLVEMENT-
LARGE BOWEL TYPE
DIARRHEA

RENAL INVOLVEMENT-
PROTEINURIA

PERIPHERAL
NEUROPATHY

Plurality must never be posited without necessity

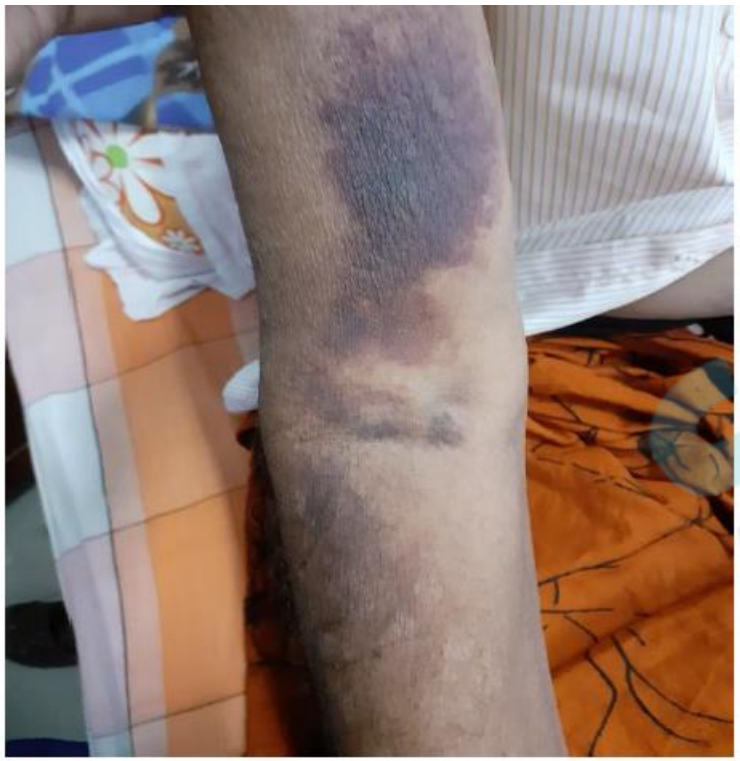
A patient can have as many diseases as they please

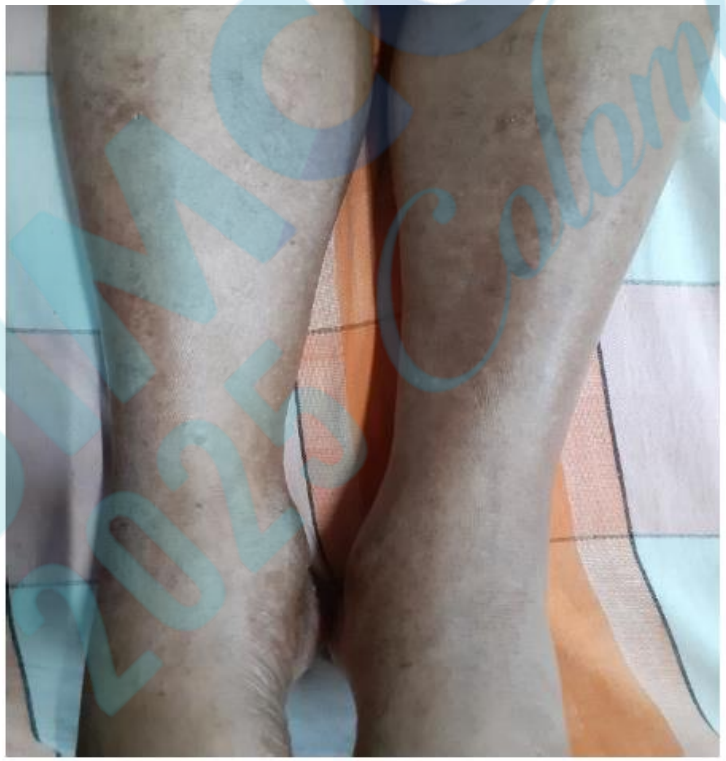
Q 1. What do you think this is mostly suggestive of with just the history at this point?

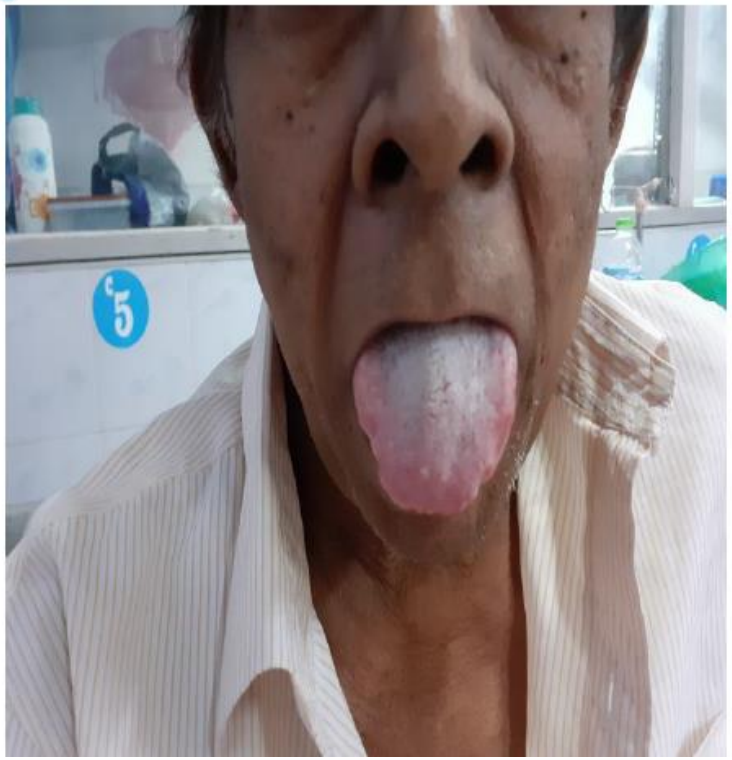
A. Carcinoid syndrome with fibrotic right-sided valvopathy and secretory diarrhoea
B. Sarcoidosis with granulomatous cardiomyopathy and colonic infiltration
C. HIV infection–related cardiomyopathy with chronic diarrhoea and peripheral neuropathy
D. Systemic AL amyloidosis with cardiac, renal, autonomic, and enteric involvement
E. Tuberculosis with constrictive pericarditis and ileocolic involvement
F. Diabetic Cardiomyopathy with congestive enteropathy

General examination

- Averagely built
- Dyspnoeic
- Not pale or plethoric
- Not icteric







Cardiovascular system

- Blood pressure: 110/70 mmHg
- Pulse: irregular, normal volume
- JVP is elevated with positive Kussmaul sign
- Apex beat is palpable in the normal position
- S3 gallop is present
- Peripheral oedema is present

Respiratory system

- On air saturation is 95%
- Central Trachea
- Lung expansion is reduced with dull percussion and absent breath sounds in both lower zones

Q2. Which of the following diagnoses BEST fits this bedside examination picture?

A. Idiopathic restrictive cardiomyopathy

B. Constrictive pericarditis

C. Acute right ventricular infarction

D. Severe tricuspid regurgitation

E. Pulmonary hypertension with RV failure

Abdomen

Mild hepatomegaly, no free fluid

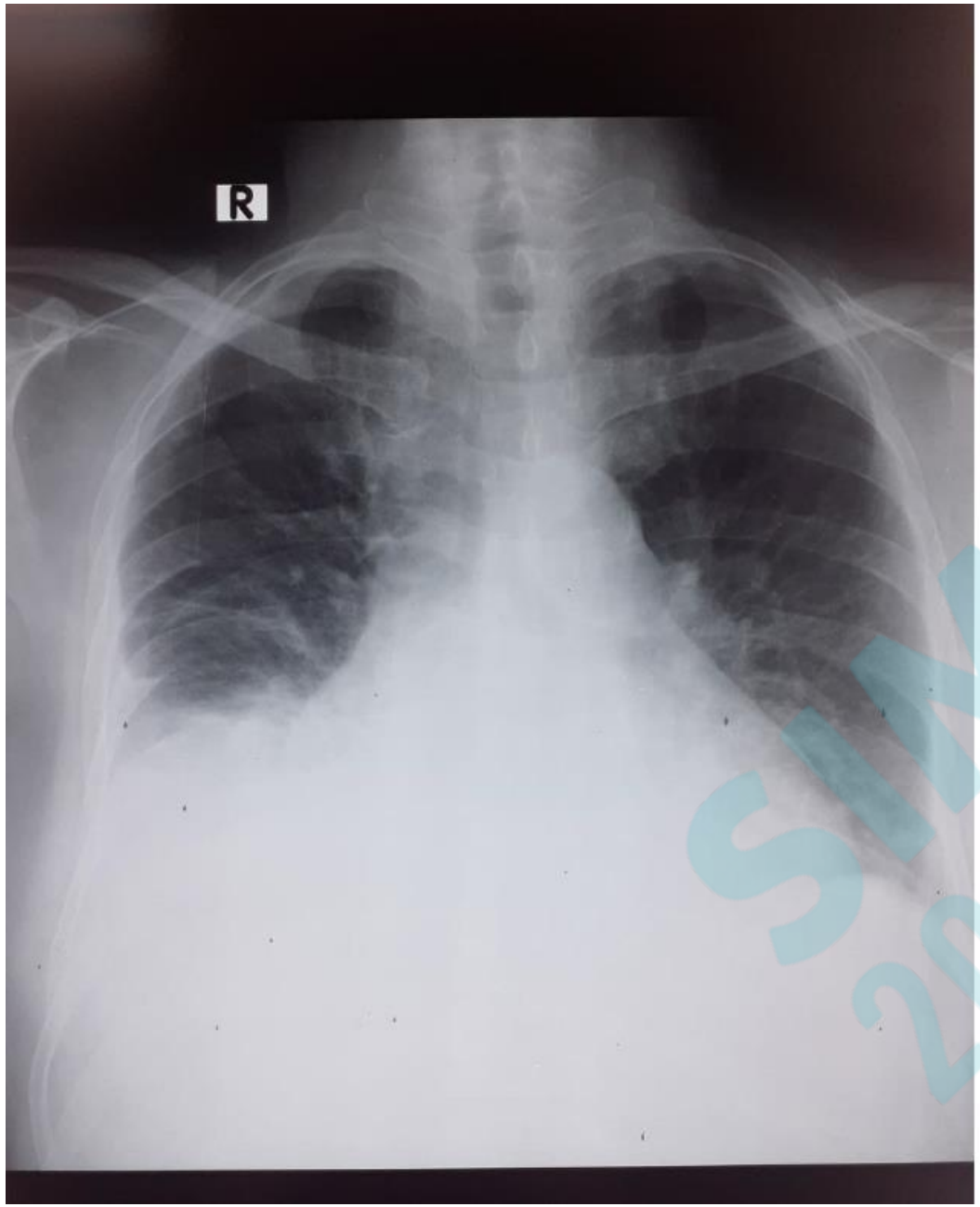
Nervous system

Stocking-type sensory loss for pain up to the level of mid shin
Absent ankle jerk and loss of JPS

Investigations

Hb 10.5 g/dL (MCV 85), Platelets 340, WBC 3.4
CRP 10
ESR 45
Serum creatinine 155 micromole/L
Na 130, K 3.1
UFR-Protein 3+, No red cells or casts

Albumin 27g/dL
Globulin 37g/dL
AST 34, ALT 54, ALP 123
Bilirubin- Normal
INR 1.43
LDH 203(150-250)
TSH-1.6 (0.4-4.0)
Ferritin- 110 (22-322)
Calcium 2.11



Pleural fluid aspirate

- WBC - 5
- POLY - 20%
- LYMPHO - 80%
- PROTEIN - 12.8
- LDH – 28
- ADA - 10.8 (15.9)
- AFB - NEGATIVE

2D Echo

EF- 31 %
dilated LA
concentric LVH
severely impaired biventricular systolic function
severe diastolic dysfunction
Possible restrictive cardiomyopathy

Q3. What is the next investigation

A. Cardiac MRI
B. Abdominal fat pad biopsy
C. Rectal Biopsy
D. Endomyocardial biopsy
E. Renal Biopsy

Abdominal Fat Aspirate- Negative

Rectal Biopsy- Negative

Renal biopsy- Negative

Q3. Which investigation is the best out of the ones given below to aid in confirming the possible diagnosis?

A. Endomyocardial biopsy to confirm myocardial infiltration when extracardiac biopsies are negative
B. Cardiac MRI to characterise restrictive physiology and assess tissue infiltration
C. Bone marrow biopsy to evaluate for a plasma cell clone
D. CT thorax/abdomen/pelvis to evaluate systemic infiltrative or malignant disease

BM biopsy-No clonal plasma cells in marrow

SPE- No monoclonal bands

Does that exclude AL amyloidosis ?

Q5. Given the likely diagnosis of amyloidosis, what should be the next best investigation that will aid in the immediate management of the patient?

A. Serum free light chain assay with serum and urine immunofixation

B. Genetic testing for transthyretin (TTR) mutations

C. Whole-body CT to search for occult malignancy

D. Repeat bone marrow biopsy with flow cytometry

E. PET-CT to assess systemic inflammatory activity

Serum light chain assay

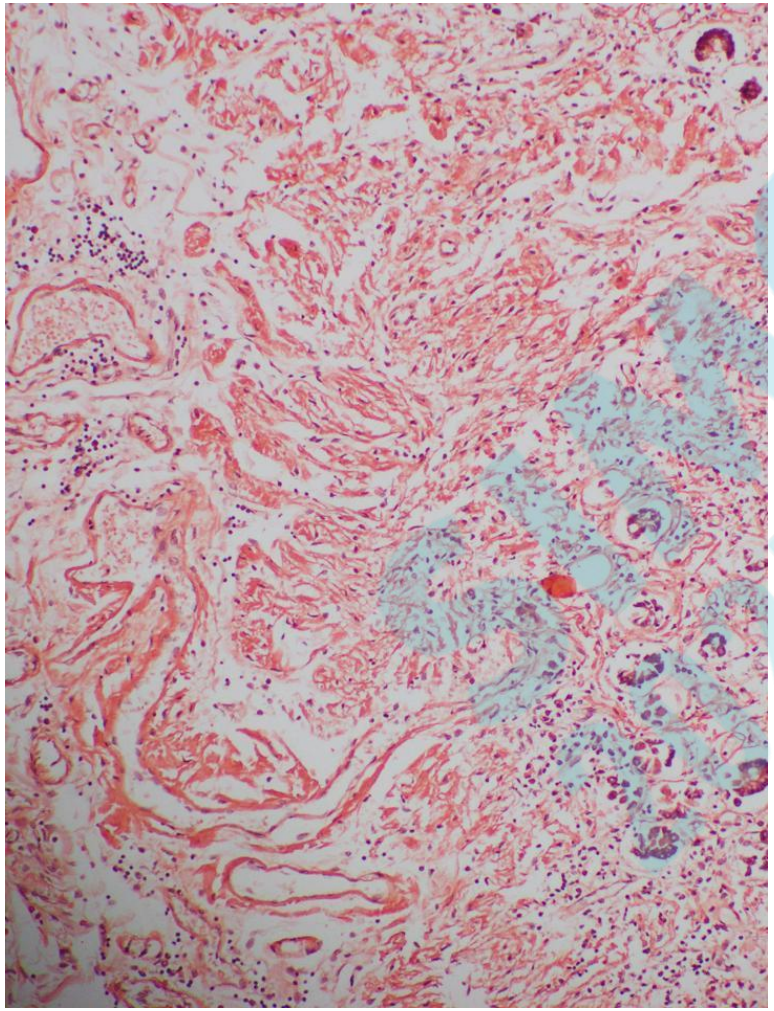
Serum free light chain ratio 110 (**Normal κ/λ ratio: 0.26–1.65)**

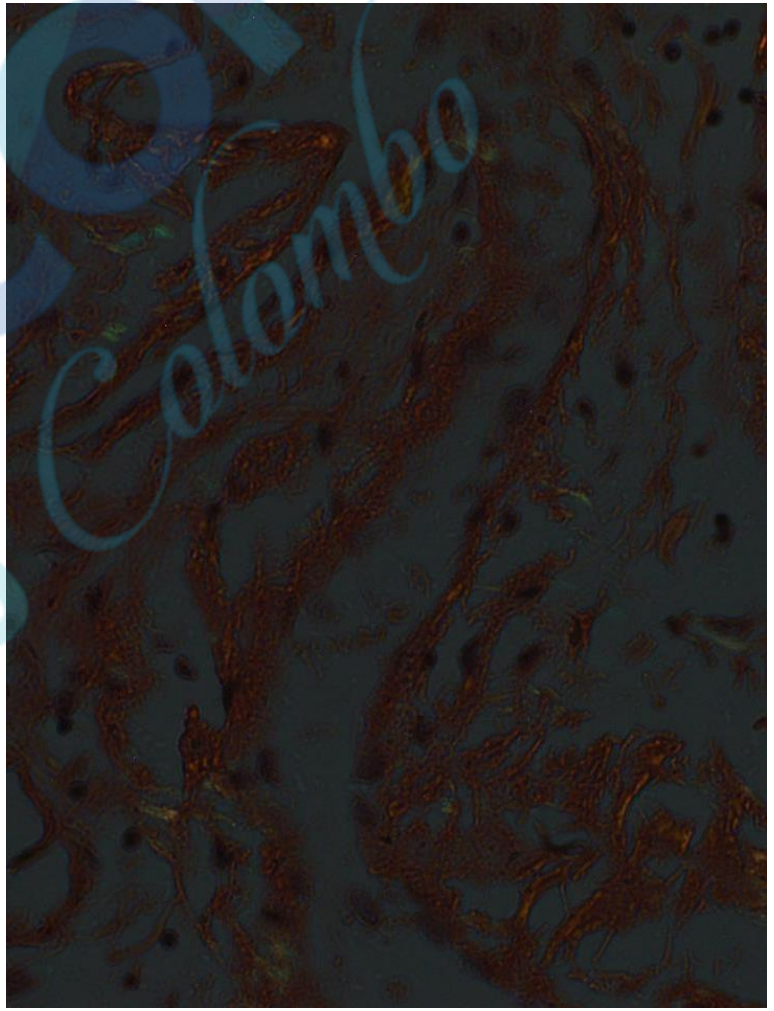
Cardiac involvement + abnormal light chain ratio = strongly suggestive of AL amyloidosis

Primary diagnosis

AL (light-chain) amyloidosis with cardiac involvement

Endomyocardial biopsy





Test	Sensitivity	Comment
Fat aspirate	70–85% (AL)	May miss AA or early disease
Kidney biopsy	>95% if kidney involved	Sampling error possible
Rectal biopsy	~70–80%	Good alternative
Bone marrow (Congo red)	50–60%	Also helps detect plasma cell clone
Endomyocardial biopsy	>98%	Gold standard for cardiac amyloidosis

1. Recognise Early, Act Fast

- Often underdiagnosed: mimics HFpEF, restrictive CM, hypertrophic heart disease
- Delay → irreversible cardiac damage
- Early detection → disease-modifying therapy possible

2. From Suspicion to Confirmation

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Suspect → Non-invasive imaging → Biomarkers → Tissue diagnosis → Typing
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Suspect in:

- HFpEF or mildly reduced EF + thickened LV walls (no hypertension)
- Low-voltage ECG vs LV mass
- History: neuropathy, proteinuria, macroglossia, orthostatic hypotension, carpal tunnel

Confirm subtype:

AL amyloidosis: Serum/urine immunofixation + free light chains

ATTR amyloidosis: 99mTc-PYP/DPD/HMDP scan + exclude monoclonal protein

3. Treat Early, Change Outcomes

AL Amyloidosis

- Urgent hematology referral
- Goal: suppress light chains

  Chemo ± stem cell trans-plant

ATTR Amyloidosis

- Tafamidis – disease-modifying therapy
- Alternative: Diflunisal if tafamidis is unavailable
- Gene-silencing therapies (hereditary ATTR
- Supportive care: maintain euvolemia, manage arrhythmias

First Do No Harm

- **Avoid/Minimize:** ACEi/ARB, beta-blockers, calcium channel blockers, digoxin

- **Diuretics** – mainstay for congestion

- **Arrhythmia management:**
  - AF → anticoagulate regardless of CHA_2DS_2-VASc
  - Conduction disease → consider pacemaker

Practical Takeaways

- ☑ Always rule out AL first – medical emergency
- ☑ A negative biopsy does not exclude amyloidosis.
- ☑ Conventional HF drugs are often harmful
- ☑ Early recognition + therapy → dramatically better outcomes
- ☑ Multidisciplinary care is essential

Thank you