Question 1 – Cardiology

A 57-year-old man with hypercholesterolaemia and hypertension treated with simvastatin 80 mg/day and hydrochlorothiazide 25 mg/day develops myalgia and atypical chest pain. A stress test and coronary angiogram are normal. Diltiazem (controlled delivery) 180 mg/day is added for persisting hypertension. Four weeks later he presents with shoulder and pelvic girdle pain and stiffness of seven to ten days duration and more recent ‘bloody discoloration of the urine’. Examination reveals mild proximal weakness, normal neck flexor and extensor power, no difficulty with swallowing and no rash.

Laboratory tests reveal:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Range</th>
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</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>2.7 mmol/L</td>
<td>[3.4-5.0]</td>
</tr>
<tr>
<td>Creatinine</td>
<td>80 μmol/L</td>
<td>[60-110]</td>
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<tr>
<td>Bilirubin</td>
<td>24 μmol/L</td>
<td>[0-25]</td>
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<tr>
<td>Alkaline phosphatase (ALP)</td>
<td>48 U/L</td>
<td>[38-126]</td>
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<tr>
<td>Alanine transaminase (ALT)</td>
<td>112 U/L</td>
<td>[14-51]</td>
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<tr>
<td>Aspartate transaminase (AST)</td>
<td>259 U/L</td>
<td>[15-45]</td>
</tr>
<tr>
<td>Gamma glutamyltranspeptidase (GGT)</td>
<td>38 U/L</td>
<td>[0-30]</td>
</tr>
<tr>
<td>Albumin</td>
<td>32 g/L</td>
<td>[33-48]</td>
</tr>
<tr>
<td>Total protein</td>
<td>65 g/L</td>
<td>[61-79]</td>
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<tr>
<td>Creatine kinase (CK)</td>
<td>30,568 U/L</td>
<td>&lt;170</td>
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</tbody>
</table>

The most likely diagnosis is:

A. hypokalaemic myopathy.
B. hypothyroid myopathy.
C. polymyositis.
D. simvastatin myopathy.
E. diltiazem myopathy.

Answer D (This question is probably more about myalgia than cardiology…..just realized it )

Approach to myopathy

Differentials:
1) Inflammatory disorders
2) Endocrinopathy: hypothyroidism or Cushing’s syndrome
3) Electrolyte disorders
4) Metabolic myopathies (disorders of carbohydrate, lipid and purine metabolism)
5) Drugs and toxins
6) Infections
7) Various causes of rhabdomyolysis (trauma, seizures, alcohol, exertion)

Hypokalaemic myopathy
- severe hypokalaemia can also cause muscle weakness, rhabdomyolysis, and myoglobinuria
- usually does not occur at K concentrations above 2.5 if hypokalemia develops slowly.

Hypothyroid myopathy
- hypothyroidism should always be excluded in patients with an unexplained increase in serum CK.
- can range from asymptomatic elevation in serum CK, myalgia (with no enzyme rise) and proximal muscle weakness with CK rise that clinically resembles polymyositis.

Polymyositis (onset of Sx is the difference)
- T cell mediated muscle injury, idiopathic
- clinical suspicion of PM is raised by Sx of weakness, myalgia and elevation of serum levels of muscle enzymes(CK, LDH, AST, ALT)
- also have to eliminate use of drugs causing myalgia eg. Colchicine, statin, alcohol, cocaine, hydroxychloroquine
- onset is insidious with gradual worsening over a period of several months

Statin myopathy (uncommon)
- affects 0.1% of patients
- range from myalgias to myositis to rhabdomyolysis

**time course**
- mean duration of onset of Sx from start of therapy: 6.3 months
- mean time to resolution of Sx after discontinuation: 2.3 months

**a) myalgias:**
- people complaining of muscle aches "benign myalgia" → **2-11%** (no diff from placebo)
- elevation in CK above normal → **30%** (statin treated & placebo)
- pts with new onset myalgias and easy fatiguability resolved with discontinuation of drug

**b) myositis**
- CK X 10 times normal + myalgia → **0.5%** of pts in large clinical trials
- consider other causes of CK elevations: hypothyroidm, trauma

**c) rhabdomyolysis (0.1%)**
- large trials, massive rhabdomyolysis with ARF not seen in pts who did not have other risk factors
- RF: given concurrently with cyclosporine or gemfibrozil,
  - case reports of concurrent use with niacin, macrolide, digoxin, warfarin, antifungal meds (drugs that interfere with CYP3A4)
- muscle biopsy: myonecrosis without vasculitis or significant inflammation

Pravastatin (statin of choice with cyclosporine) & fluvastatin have less intrinsic muscle toxicity. After CK has returned to baseline, pts may be tried on a statin less likely to cause muscle toxicity with careful monitoring.

**Diltiazem myopathy**
Not in the literature.