

## A Diagnostic Dilemma: A Patient Presenting with a Painful Swollen Leg Due to Statin-Induced Myositis

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**Abstract:** A patient with a painful swollen leg is a common clinical presentation. We present a case of a 46 year old patient, with a past medical history of deep vein thrombosis and hypercholesterolaemia, who was referred to hospital for investigation of a one day history of sudden onset of leg pain. The patient presented with unilateral calf tenderness and swelling that was initially thought to be due to a deep vein thrombosis and later cellulitis and compartment syndrome, but was found to be due to statin-induced myositis when a magnetic resonance imaging scan of the patient's leg showed areas of inflamed muscle. The patient was then taken off the cholesterol-lowering statin and prescribed non-steroidal anti-inflammatory medication which caused her symptoms to improve. This case shows how myositis may be mistakenly diagnosed as deep vein thrombosis, cellulitis or compartment syndrome, resulting in an important delay in treatment. A patient presenting with a painful swollen leg is a diagnostic dilemma with many differential diagnoses and a methodical approach must be taken to avoid the severe implications of misdiagnosis.

**Key words:** Diagnostic dilemma, statin-induced, myositis, painful swollen, patient

### INTRODUCTION

A patient with a painful swollen leg is a common clinical presentation. The cause can be potentially life or limb threatening e.g., a Deep Vein Thrombosis (DVT) or compartment syndrome. A thorough history and physical examination coupled with appropriate investigations leads to the appropriate diagnosis in the majority of cases. We present a case of a patient with unilateral calf tenderness and swelling that was initially thought to be due to a DVT and later cellulitis and compartment syndrome, but was found to be due to statin-induced myositis. Various forms of focal myositis have been reported to mimic thrombophlebitis (Garciaconseugra *et al.*, 1995) soft-tissue neoplasm or DVT (Myanie *et al.*, 1997; Gobbele *et al.*, 1999).

### CASE REPORT

A 46 year old lady was referred to hospital for investigation of a possible DVT with a one day history of sudden onset of left leg pain. The pain was mostly in the calf and the patient also complained of swelling and altered sensation in her lower leg. She had no history of trauma to her leg, although she had been wearing a new pair of sandals the previous day and had sustained a minor graze to the dorsum of the left foot. The patient also

stated that her urine had been darker than normal over the last couple of days. The patient had a past medical history of a left sided transient ischaemic attack three months previously. She also had a DVT in her left leg 16 years ago. She was taking simvastatin 20mg once a day and the combined oral contraceptive pill. She smoked 20 cigarettes per day and drank 10 units of alcohol per week.

On examination the patient had a temperature of 37.1 °C, pulse of 78 beats per minute and regular and blood pressure of 125/69 mmHg. On inspection, the left calf was moderately swollen with some erythema on the medial side. There were 2 small lacerations on the dorsum of the left foot. Peripheral pulses were present bilaterally and the capillary refill time was less than 3 sec. The left leg was extremely tender to touch but the calf was not tense. Full blood count, urea and electrolytes and C-reactive protein were all normal. A provisional diagnosis of a DVT was made and the patient was started on a therapeutic dose of low-molecular-weight heparin.

On day 2nd, an ultrasound scan of the left leg was performed and was negative for fluid, DVT and signs of inflammation. A D-dimer blood test was within the normal range at 260 mg mL<sup>-1</sup>. Creatine kinase levels were tested and were raised at 23,053 U L<sup>-1</sup> (normal 30-150 U L<sup>-1</sup>) and alanine transaminase was raised at 158 U L<sup>-1</sup> (normal 10-40 U L<sup>-1</sup>). A possible differential diagnosis was rhabdo-myolysis secondary to statin-induced myositis



Fig. 1: T1-weighted coronal MRI with increased signal intensity indicating oedema representing myositis within the left peroneal muscle group (arrow)

and the patient was started on intravenous fluids. On day 3rd the patient was complaining of feeling clammy and had vomited 6 times over the last 12 h, however, she was taking morphine 20 mg every 4 h for pain relief. All the movements of the foot and ankle joints were painful on passive movement but permissible. The patient was started on ceftriaxone, clindamycin, flucloxacillin and metronidazole for treatment of cellulitis although the white cell count and the C-reactive protein were normal. The patient's pain worsened and an orthopaedic opinion was sought to exclude a compartment syndrome. The compartment pressures in the left leg were measured but these were all found not to be indicative of compartment syndrome: anterior 24 mmHg, lateral 32 mmHg, superficial posterior 34 mmHg, deep posterior 43 mmHg.

On day 4th a Magnetic Resonance Imaging (MRI) scan of the patient's left calf (Fig. 1) showed areas of inflamed muscle confirming the diagnosis of myositis. The patient was then taken off the simvastatin and prescribed Non-Steroidal Anti-Inflammatory Medication (NSAIDs) which caused her symptoms to improve.

#### DISCUSSION

This case shows how myositis may be mistakenly diagnosed as a DVT, cellulitis or compartment syndrome, resulting in an important delay in treatment. Despite the patient having a previous history of a DVT and the

clinical presentation resembling a DVT, this was excluded by negative D-dimer and ultrasound scan. A vascular event e.g., muscle infarction, or an underlying infection were unlikely in view of the normal inflammatory markers and ultrasound scan. Compartment syndrome was excluded by measuring compartment pressures in the leg. Rhabdomyolysis secondary to statin-induced myositis was a likely diagnosis and the extensive biochemical and MRI investigations yielded the eventual diagnosis. The main abnormal features of this case were the presentation of localised calf swelling and tenderness as opposed to generalised symptoms commonly found in myositis and the distal muscles of the leg were more affected rather than the proximal muscles, also atypical of myositis.

In myositis, inflammation damages the fibers of the skeletal muscle causing weakness by interfering with its ability to contract (Gobbele *et al.*, 1999). There are many different types of myositis. Drug-induced myositis is rare and the most common medications that can cause myositis are the cholesterol-lowering statins. The overall incidence of statins exerting their toxic effects on skeletal muscle is typically less than 0.1% (Garciaconseugra *et al.*, 1995). Myositis occurring with statin use is characterised by a greater than 10-fold increase in serum CK concentration (Gobbele *et al.*, 1999). Lovastatin, fluvastatin, pravastatin and simvastatin all have been reported to cause myositis. Statin side-effects may be dose-related, associated with other drug interactions that interfere with statin metabolic pathways through cytochrome p450 pathways or glucuronidation, or related to co-morbidities (Ballantyne *et al.*, 2003). The symptoms of statin induced myositis include muscle tenderness, muscle swelling, pain and weakness, beginning after the person starts taking statins. Statin induced myositis can be treated successfully by discontinuation of the statin that may be causing the myositis, steroids or with non-steroidal anti-inflammatory drugs (Ballantyne *et al.*, 2003; Lacy *et al.*, 1999). In our patient, a combination of discontinuation of the simvastatin together with NSAIDs were effective. The overall prognosis of statin induced myositis is good provided that the statin is stopped.

Rhabdomyolysis is a severe form of myositis which may result from a variety of diseases, trauma, or toxic insults to skeletal muscle (Magarian *et al.*, 1991). It is defined as a clinical and biochemical syndrome resulting from an injury which damages the integrity of the sarcolemma of skeletal muscle, with leakage of potentially toxic muscle cell components into the systemic circulation (Knoche, 1993). This may result in potential life-threatening complications including myoglobinuric acute renal failure, hyperkalaemia and cardiac arrest, Disseminated Intravascular Coagulation (DIC) and more locally, compartment syndrome. The primary diagnostic indicator of rhabdomyolysis is an elevated serum Creatine

Phosphokinase (CK) to at least five times the normal value (Knochel, 1993). This elevation is generally to such a degree that myocardial infarction and other causes of a raised CK e.g., an acute stroke are excluded. The other important finding frequently seen in rhabdomyolysis is myoglobinuria. As myoglobin is released into the circulation from necrotic muscle cells it first becomes detectable in the urine at serum concentrations ranging from 300 ng mL<sup>-1</sup> to 2 g mL<sup>-1</sup> and produces visible pigmenturia at concentrations exceeding 250 g mL<sup>-1</sup> (Myanie *et al.*, 1997). Biochemical tests for pigmenturia are strongly suggestive of myoglobinuria in the absence of haemoglobinaemia and haematuria. Other important biochemical findings in rhabdomyolysis include hyperkalemia, hypocalcaemia, hyperphosphataemia, hyperuricaemia and raised levels of other muscle enzymes including lactate dehydrogenase, aminotransferases and carbonic anhydrase III (Lacy *et al.*, 1999). All of these were normal in our case except aminotransferases.

Acute limb compartment syndrome is a surgical emergency characterised by raised pressure in an unyielding osteofascial compartment. Sustained elevation of tissue pressure reduces capillary perfusion below a level necessary for tissue viability and irreversible muscle and nerve damage may occur within hours. Compartment syndrome is a clinical diagnosis but it is useful to use adjuvants including intra-compartmental pressure measurements to avoid unnecessary fasciotomies. The difference between the diastolic pressure and the intra-compartmental pressure has been suggested as a more sensitive indicator of tissue perfusion pressure and a value of 30 mmHg or less has been recommended as the threshold for fasciotomies. But treatment based on this measurement alone may lead to unnecessary surgery.

## CONCLUSION

A patient presenting with a painful swollen leg is a diagnostic dilemma with many differential diagnoses which a methodical approach must be taken to avoid the severe implications of misdiagnosis.

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