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Case Study

Statin-Induced Toxic Myopathy Masquerading as Recurrent Falls and De-Conditioning in an Older Adult

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Abstract

Statins, widely prescribed for their efficacy in reducing low-density lipoprotein cholesterol (LDL-C) and preventing atherosclerotic cardiovascular disease, are generally well tolerated. However, muscle-related adverse effects, particularly statin-associated myopathy, can significantly impact patient function and adherence. This case report describes an 83-year-old man who developed progressive proximal muscle weakness, fatigue, and recurrent falls following initiation of high-dose atorvastatin after a ST-elevation myocardial infarction. Clinical and laboratory evaluation, along with the temporal association and improvement after drug withdrawal, supported a diagnosis of self-limited toxic statin myopathy. Extensive differential diagnosis excluded other neuromuscular, endocrine, and vascular causes. Prompt discontinuation of atorvastatin, supportive care, and physiotherapy led to marked functional recovery. This case highlights the spectrum of statin-induced muscle toxicity, emphasises diagnostic vigilance in older adults, and underscores the importance of personalised therapy and early intervention to mitigate adverse outcomes.

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Quick Response Code:

Introduction

Statins, which are competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase within the mevalonate pathway, have revolutionised the prevention and treatment of atherosclerotic cardiovascular disease. By effectively lowering low-density lipoprotein cholesterol (LDL-C) levels—often by more than 60% statins substantially reduce the incidence of major adverse cardiovascular events (MACE), thereby establishing their role as first-line lipid-lowering agents across global clinical guidelines [1].

Although statins are widely prescribed and their efficacy in reducing cardiovascular morbidity and mortality is well established, concerns regarding muscle-related side effects particularly statin-associated myopathy remain a significant barrier to patient adherence and long-term treatment continuation. Muscle-related symptoms account for approximately two-thirds of all adverse events associated with statin therapy, and their occurrence often leads to premature treatment discontinuation despite the significant cardiovascular benefits provided by statins [2].

However, recent clinical guidance provides important context regarding the true prevalence and clinical significance of statin-induced myopathy. According to the 2019 European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Guidelines for the management of dyslipidemias, true statin-induced myopathy is rare, and the overall frequency of reported muscle symptoms is often overestimated. This overestimation is attributed, in part, to the nocebo effect in which negative expectations contribute to perceived side effects and to the misattribution of non-specific or unrelated musculoskeletal symptoms to statin use [3]. This distinction is vital in clinical practice, as the disproportionate concern over muscle-related adverse effects can lead to unwarranted statin discontinuation and, consequently, suboptimal cardiovascular risk management.

Statin-associated myopathy encompasses a heterogeneous spectrum of muscle-related adverse effects, ranging from mild, self-limited myalgias to severe, immune-mediated or life-threatening forms of muscle injury [4,5]. The following phenotypes are clinically recognised:

Myalgia with or without Mild HyperCKaemia

This is the most common manifestation, characterised by muscle pain, cramps, or weakness—often affecting the calves and thighs—with or without mild elevations in serum creatine kinase (CK), typically less than five times the upper limit of normal (ULN). This form is generally self-limiting and may resolve with dose adjustment, temporary interruption, or discontinuation of statin therapy.

Self-Limited Toxic Statin Myopathy

Patients present with proximal muscle weakness that may impair daily activities. CK levels are usually elevated between 10 and 100 times the ULN. Symptoms commonly resolve following cessation of the statin, and immunosuppressive therapy is typically not required [4].

Immune-Mediated Necrotising Myopathy (IMNM)

IMNM is a rare but serious autoimmune complication of statin therapy. It presents with progressive, symmetrical proximal muscle weakness and markedly elevated CK levels (often 10–100 times the ULN). The condition is frequently associated with the presence of anti-HMG-CoA reductase (anti-HMGCR) antibodies. Electromyography typically shows a myopathic pattern, while muscle biopsy reveals necrosis and regeneration of muscle fibres with minimal inflammatory infiltration. Unlike other statin-induced myopathies, IMNM persists despite statin withdrawal and generally requires immunosuppressive treatment [6,7].

Rhabdomyolysis

This represents the most severe form of statin-induced muscle injury. It is characterised by widespread muscle breakdown, CK levels exceeding 100 times the ULN, and myoglobinuria. Rhabdomyolysis can lead to acute kidney injury due to myoglobin-induced renal tubular toxicity. Management includes immediate cessation of the statin, aggressive intravenous hydration, and renal support as needed [4,5].

The pathogenesis of statin-induced myopathy is multifactorial and not yet fully understood. Several molecular mechanisms have been proposed, including mitochondrial dysfunction due to the depletion of ubiquinone (coenzyme Q10), impaired biosynthesis of isoprenoids, inhibition of mitochondrial respiratory chain complexes, induction of apoptosis, calcium dysregulation, and altered expression of enzymes such as carnitine palmitoyltransferase-2[8]. These mitochondrial disturbances may not only contribute to myopathy but also play a role in other systemic effects associated with statin therapy, such as new-onset diabetes mellitus and potential cognitive impairment—possibly through mechanisms involving oxidative stress, impaired oxidative phosphorylation, and disruptions in amyloid-β metabolism.

Genetic factors significantly influence susceptibility to statin-induced muscle toxicity. Polymorphisms in the *SLCO1B1* gene, which encodes the hepatic transporter OATP1B1 responsible for statin uptake, are strongly associated with an increased risk of simvastatin-induced myopathy. Additional genetic variants in *COQ2* and *GATM* genes have been implicated, although the evidence remains inconclusive for the latter [9,10]. Furthermore, the presence of the HLA-DRB1*11:01 allele has been associated with a higher risk of autoimmune statin myopathy mediated by anti-HMGCR antibodies, as seen in IMNM.

Certain populations exhibit increased vulnerability to statin-associated muscle toxicity. These include older adults, females, individuals with underlying hypothyroidism or neuromuscular disorders, and patients with diabetes mellitus [11,12]. While diabetes itself is a major indication for statin therapy due to its strong association with cardiovascular risk, diabetic patients may also be at greater risk of statin-induced myopathy, likely due to a combination of demographic factors, disease-related metabolic changes, reduced physical activity, vitamin D deficiency, and polypharmacy.

Beyond classical myopathy, recent evidence has expanded the scope of statin-associated neuromuscular complications to include impaired balance and an increased risk of falls, particularly among elderly patients [13,14]. These atypical manifestations further complicate clinical recognition and management and underscore the importance of personalised therapeutic strategies and close monitoring in high-risk populations.

Case report:

An 83-year-old man with no known past medical history presented with generalised fatigue and recurrent unexplained falls, described as sudden buckling of the legs without preceding loss of consciousness. One year prior to this presentation, he had suffered a ST-elevation myocardial infarction (STEMI) and was subsequently initiated on secondary prevention therapy with atorvastatin 80 mg daily, ramipril 5 mg daily, bisoprolol 1.25 mg daily, and aspirin 75 mg daily. Approximately six months after commencing this regimen, he began to experience progressive exertional dyspnoea, progressively worsening fatigue, imbalance, and falls. At the time of presentation, these symptoms had deteriorated to the extent that he was immobile and bedbound.

Notably, one month before hospital admission, his Rockwood Clinical Frailty Score was recorded as 4, indicating a degree of vulnerability but preserved independence in instrumental activities of daily living. There was no history of recent trauma, and his previous health had been unremarkable before the myocardial infarction. On examination, he appeared lethargic but was haemodynamically stable. Orthostatic blood pressure measurements revealed a postural drop, though he remained asymptomatic. Mild bilateral pedal oedema was noted without signs suggestive of deep vein thrombosis. Cardiovascular,

respiratory, thyroid, and abdominal examinations were unremarkable. Neurological examination demonstrated symmetrical proximal muscle weakness, graded 3+/5 in both upper and lower limbs using the Medical Research Council scale. Muscle bulk was preserved with no evidence of fasciculations or wasting. Reflexes, coordination, sensation, and cranial nerve function were intact.

The clinical picture raised suspicion of statin-induced myopathy, given the temporal relationship between the initiation of high-dose atorvastatin and the onset of neuromuscular symptoms. A range of differential diagnoses were considered but deemed less likely. Although a postural blood pressure drop was observed, it occurred between lying and sitting positions and was asymptomatic, making medication-induced orthostatic hypotension an unlikely primary cause. The symmetrical proximal weakness and gradual symptom progression also argued against this. Stroke was considered; however, the absence of focal neurological deficits, lack of asymmetry, and the subacute course made this diagnosis improbable. Inflammatory myositis was unlikely due to normal inflammatory markers and absence of systemic features such as rash or arthritis. Similarly, hypokalaemic periodic paralysis was excluded by normal serum potassium levels, the absence of typical precipitants, and lack of episodic weakness. Normal thyroid function, preserved reflexes, and absence of clinical hypothyroidism excluded hypothyroid myopathy. Motor neurone disease was also considered but lacked characteristic upper or lower motor neuron signs. Myasthenia gravis was regarded as unlikely in the absence of ocular involvement, bulbar symptoms, or fluctuating fatigable weakness.

Investigations were undertaken to further evaluate the presentation. Electrocardiography revealed normal sinus rhythm without arrhythmia. Chest radiography and computed tomography of the brain showed no acute abnormalities. Transthoracic echocardiography demonstrated preserved left ventricular systolic function with an ejection fraction of 55–60% and no significant valvular pathology. Urinalysis, microscopy, and culture were unremarkable, excluding findings suggestive of rhabdomyolysis. Baseline laboratory results prior to this admission were unavailable, as the patient was newly presenting to this facility and prior data were inaccessible. However, serial monitoring of serum creatine kinase and renal function was performed during admission and continued post-discharge.

In view of the working diagnosis, atorvastatin was discontinued, and intravenous hydration was administered to support renal function. Enoxaparin was initiated for venous thromboembolism prophylaxis due to his immobility, and physiotherapy was commenced. Notable clinical improvement was observed within 48 hours of statin withdrawal, and by 72 hours, the patient regained ambulatory capacity with the aid of a walking frame. He was discharged with structured community-based rehabilitation and showed progressive functional recovery.

At outpatient review 20 days post-discharge, the patient’s mobility had further improved, now using a walking stick. Laboratory results showed continued normalisation of creatine kinase levels and stable renal function, in alignment with his clinical recovery. Future evaluation—including autoimmune myositis serology (e.g., anti-HMGCR antibodies), electromyography, muscle MRI, or biopsy—was considered, but a clinical decision was made to reserve these investigations for consideration only if clinical progress failed to continue or if symptoms worsened.

Variable	Reference Range	Day 1	Day 2	Day 3	Clinic Visit
HB g/l	120-160	123	-	-	113
WBC10*9/l	3.6-11.0	9.8	-	-	5.9
Platelet 10*9/l	150-400	249	-	-	189
MCV fl	82-100	97.7	-	-	96.8
MCHC g/l	300-360	323	-	-	330
NEUT 10*9/l	1.80-7.50	5.93	-	-	3.51
Basophils 10*9/l	0.01-0.25	0.02	-	-	0.05
Esinophils 10*9/l	0.04-0.40	0.27	-	-	0.40
Lymphocytes 10*9/l	1.10-3.50	1.39	-	-	1.59
ESR mm/h	2-10	-	-	-	30
Cortisol nmol/l	140-620	-	-	-	473
TSHmiu/L	0.4-4.0	-	-	-	2.41
Vitamin D nmol/l	50-125	-	-	-	59
Sodium mmol/l	133-146	141	142	140	141
Potassium mmol/l	3.5-5.3	5.0	4.5	4.5	4.3
Creatinine umol/l	45-84	118	112	107	101
eGFR	≥90 mL/min/1.73 m²	51	54	57	62
Urea mmol/l	2.5-7.8	9.7	9.9	11.5	-
ALT iu/l	0-33	81	88		30
Total Bilirubin umol/l	0-21	11	25	-	10
ALP iu/l	30-130	112	94	-	63
Albumin g/l	35-50	34	31	-	33
CRP mg/l	<=5	7	11	-	01
Explanatory notes: "–" indicates test not performed					

Table I: The patient's laboratory data

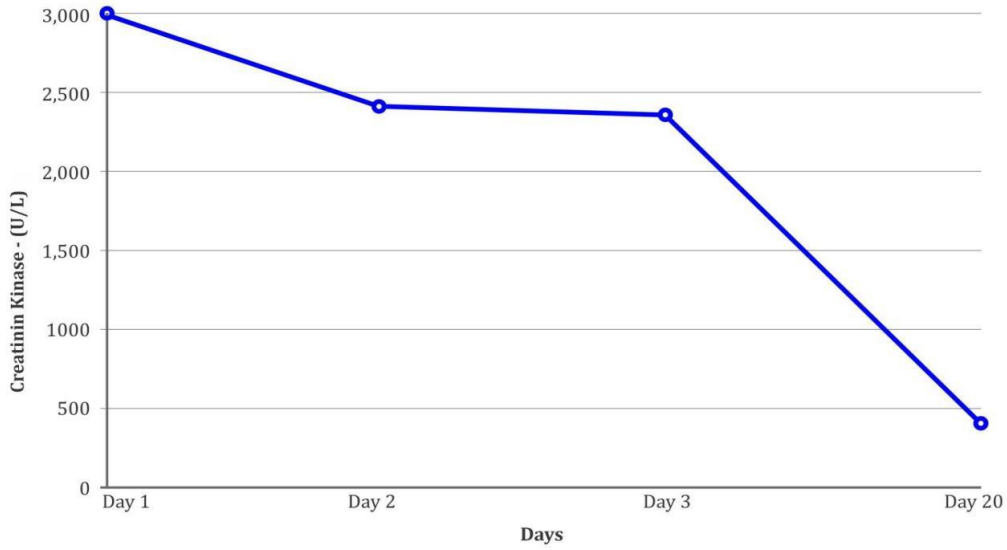

Figure 1: Trend of creatinine kinase levels

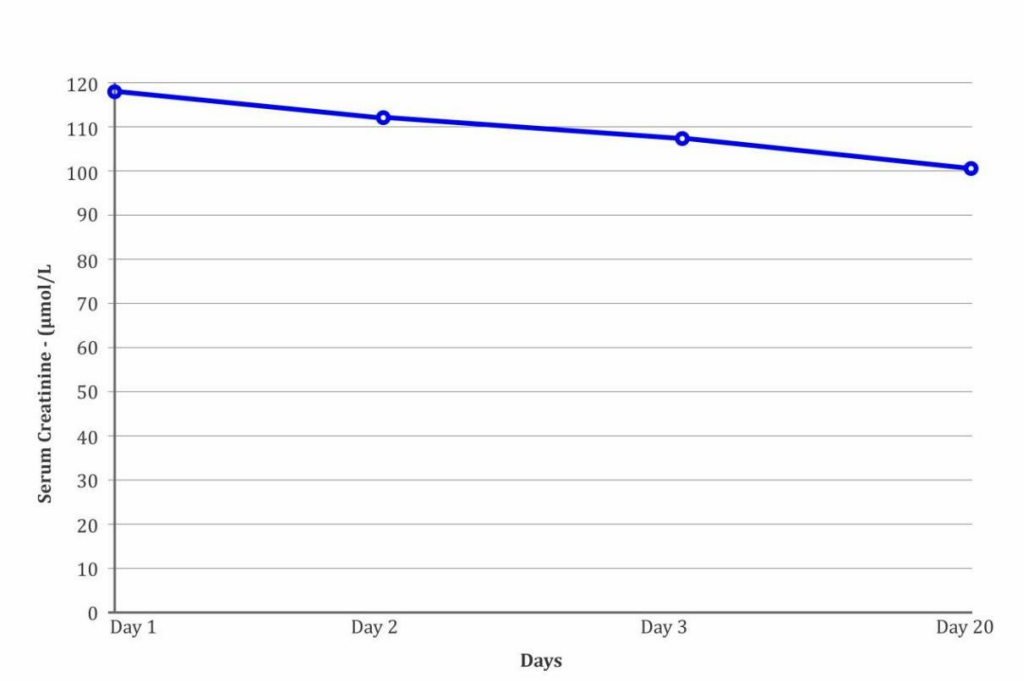

Figure 2: Trend of serum creatinine levels

Discussion

Statin-induced myopathy encompasses a clinical spectrum ranging from mild myalgia with minimal creatine kinase (CK) elevation to severe immune-mediated necrotising myopathy (IMNM) and rhabdomyolysis. IMNM is typically marked by progressive proximal muscle weakness, elevated CK levels, and persistence of symptoms despite statin discontinuation, often associated with anti-HMGCR antibodies.

Our patient presented with generalised proximal muscle weakness impairing daily activities, CK elevation exceeding five times the upper limit of normal (ULN), and marked symptomatic improvement following atorvastatin withdrawal and physiotherapy.

This case is most consistent with self-limited toxic statin myopathy, given the subacute onset of symmetrical proximal weakness, CK elevation in the moderate range (10–100× ULN), and prompt clinical improvement after stopping the statin [3,4,6]. Unlike IMNM, which requires immunosuppressive therapy due to ongoing progression of weakness, the rapidly resolving symptoms and muscle weakness made this diagnosis unlikely [5]. Nonetheless, if symptoms were to persist or worsen, further evaluation with anti-HMGCR antibody testing, electromyography (EMG), or muscle biopsy would be warranted to differentiate IMNM from toxic myopathy. Electrolyte abnormalities, including potassium and magnesium disturbances, were excluded with normal serum levels.

Importantly, while the patient reported recurrent falls, cerebellar pathology such as stroke or small-vessel disease was considered unlikely. Neurological examination revealed no cerebellar signs (e.g., ataxia, dysmetria, dysdiadochokinesia, nystagmus, or dysarthria), and the timing of falls correlated with progressive muscle weakness rather than impaired coordination. In the absence of focal neurological deficits, brain imaging was not clinically indicated.

This case contrasts with mild statin-related myalgia, which generally involves minimal CK elevation (<5× ULN) and limited functional impairment. Conversely, rhabdomyolysis—typically presenting with severe CK elevation (>100× ULN), myoglobinuria, and acute kidney injury—was excluded here due to the absence of systemic features [3,14].

Diagnosing statin-induced myopathy remains challenging due to its heterogeneous presentation and overlap with age-related comorbidities. While immunoprecipitation remains the gold standard for diagnosing IMNM, newer techniques like ELISA and immunoblotting are increasingly accessible. Additionally, pharmacogenomic factors—such as SLCO1B1 and CYP3A5*3 polymorphisms may influence individual susceptibility, though their integration into clinical practice requires further validation [8,9].

Older adults and individuals with diabetes are particularly vulnerable to statin-induced muscle toxicity [10,11,15]. Moreover, emerging data suggest statin use may impair postural control and increase fall risk—highlighting the importance of comprehensive risk-benefit assessment in geriatric populations [12,13].

Management centres on symptom-driven statin discontinuation or dose modification, with alternative lipid-lowering strategies considered when intolerance persists. This case underscores the need for individualised clinical assessment, early recognition of statin toxicity, and a structured diagnostic approach to prevent misdiagnosis and facilitate timely recovery [1,4,16].

Conclusion

Statin-induced myopathy remains a significant yet frequently under-recognized complication of statin therapy, particularly in older adults and individuals with comorbidities. This case illustrates the clinical presentation, diagnostic reasoning, and effective management of self-limited toxic statin myopathy, marked by progressive proximal muscle weakness, functional decline, and recurrent falls in an older patient. The striking improvement following prompt statin withdrawal and supportive care reinforces the need for vigilance in recognising reversible causes of frailty and immobility especially in populations where such symptoms may be mistakenly attributed to age-related decline or neurodegenerative disease.

By highlighting the diagnostic challenge and rapid reversibility of symptoms, this report serves as a timely clinical reminder of the importance of individualized risk–benefit assessment in statin therapy. It also underscores the critical value of careful medication review when evaluating nonspecific symptoms in older adults. In doing so, it contributes to the growing body of evidence advocating for more nuanced, patient-centred prescribing practices, and may aid clinicians in avoiding unnecessary investigations or delays in appropriate care.

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