

Focal myositis with extraordinary late onset after the combined antilipidemics therapy: Risk factors management

Bartosz Bujan, Elmar Ginzburg

ABSTRACT

Introduction: Statins and other antilipidemics are frequently described medications for the treatment of hypercholesterolemia to prevent cardiovascular events like heart infarctions or strokes. Statins are, conform to the German neurological guidelines, administered often independent of initial cholesterol level after stroke to prevent new relapses. Hence, we can observe in the clinical practice in our Neurologic Rehabilitation Department permanent increase in number of patients with long-term statin therapy. Although statins have side effects like deleterious effect on skeletal muscle. The most serious complications are myositis or rhabdomyolysis with kidney failure.

Case Report: We present a case report of a 51-year-old Caucasian woman with combined antilipidemics therapy who developed a focal myositis with extraordinary late onset after the cessation of drug therapy. The patient received simvastatin 40 mg per day for a couple of weeks. Due to the persistent high cholesterol level the patient received an add-on therapy with ezetimibe for 2–3 weeks. She complained about generalized muscle pains and her high

level of creatine kinase 373 U/l (normal range, 0–167 U/L). The patient showed initially a good recovery with less intense pain. Nevertheless, the muscle pain did not disappear completely and six months after the cessation of statin therapy the patient revealed again an intense muscle pain and tenderness notably femoral on the right side with the very high level of CK 2694 U/l. The femoral magnetic resonance imaging (MRI) demonstrated an accentuated vascular network right and a congestion of subcutaneous and endomysial lymphatic vessels, hence this configuration implicated a focal inflammatory reaction. We diagnosed a focal myositis in view to the clinical characteristics and MRI-tests. We initiated a steroid therapy (prednisolon 1 mg/kg on total body weight). Thereby the CK level decreased dramatically. At discharge CK level decreased to 548 U/l and ESR revealed normal values 3 mm in the first hour. After three weeks of therapy with steroids we could not register any femoral induration or local tenderness any more. **Conclusion:** Hence, it should be a prime concern to evaluate risk factors for statin-induced myopathy or myositis by intensive rehabilitation training.

Keywords: Antilipidemics, Exercise training, Myositis, Risk factors, Side effects, Statin

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INTRODUCTION

Statins and other antilipidemics are widespread, frequently described medications for the treatment of hypercholesterolemia to prevent cardiovascular events like heart infarctions or strokes. According to the German neurological guidelines, statins should be prescribed independently of initial cholesterol level after stroke in order to prevent new episodes. Hence, we can observe in our Neurorehabilitation Department an increase in number of patients with long-term statin therapy. Although some side effects profile are reported for statins, a long-term use can promote deleterious effects on skeletal muscles. The most serious complications are myositis or rhabdomyolysis with kidney failure. Hence, it should be a prime concern to evaluate risk factors for statin-induced myopathy or myositis by intensively rehabilitation training. Previous studies suggest promoting effects of antilipidemics for myositis [1–4] but the etiology remains unknown. A study by Mikus et al. and Thompson et al. have identified intensive exercise training as a potential risk factor for deleterious effect on skeletal muscles [5, 6].

We present a case report of a patient with combined antilipidemics therapy who developed a focal myositis with extraordinary late onset after the cessation of drug therapy. Hence, it should be a prime concern to evaluate risk factors for statin-induced myopathy or myositis by intensive rehabilitation training.

CASE REPORT

A 51-year-old Caucasian female with the wide cardiovascular risk spectrum, hypothyroidism and high cholesterol level 336 mg/dl (normal range: <200 mg/dl) received simvastatin 40 mg per day for a couple of weeks. Due to the persistent high cholesterol level the patient received an add-on therapy with ezetimibe for 2–3 weeks. She complained about generalized muscle pains and her high level of creatine kinase 373 U/l (normal range, 0–167 U/L). Hence, the treatment was terminated by her general practitioner. The patient showed initially a good recovery with less intense pain. Nevertheless, the muscle pain did not disappear completely and six months after the cessation of statin therapy the patient consulted a neurologist. On grounds of persistent muscle pains, high level of creatine kinase (CK) and EMG changes a statin-induced myopathy was diagnosed. During the first weeks after termination of statin therapy has been observed a good recovery. After this temporary good recovery period the patient revealed again an intense muscle pain and tenderness notably femoral on the right side with the

very high level of CK 2694 U/l. Furthermore it has been noticed a light elevation of the erythrocyte sedimentation rate (ESR) with values up to 26 mm in the first hour. The C-reactive protein showed normal values (1.2 mg/l). The femoral magnetic resonance imaging (MRI) demonstrated an accentuated vascular network right and a congestion of subcutaneous and endomysial lymphatic vessels (Figure 1), hence this configuration implicated a focal inflammatory reaction.

To recovery and re-establishment of motor function the patient was admitted to our Neurologic Rehabilitation Center. The neurological examination revealed a local muscle pain of the musculus quadriceps right. There was no evidence for manifest paresis or manifest muscle atrophy. However, due to femoral muscle pain the patient revealed a gait disorder and reported weakness with limited functional capacity and activities of daily life. Focal neurological symptoms, which could implicate an involvement by central or periphery neural system, could not be identified. Considering the characteristics of clinical symptoms and the ancillary tests (MRI, EMG and light ESR-elevation) we diagnosed a focal myositis of quadriceps muscle. We cannot provide histological proofs, because the patient refused to have a muscle biopsy. In such cases support a MRI is an important diagnostic instrument and can facilitate the path to an appropriate therapy [3]. We diagnosed a focal myositis in view to the clinical characteristics and MRI scans. We initiated a steroid therapy (prednisolone 1 mg/kg on total body weight). Thereby the CK level decreased



Figure 1: Femoral magnetic resonance imaging (MRI). T1-weighted sequence with contrast demonstrated a high accentuated vascular network right (arrows) and a moderate congestion of the subcutaneous and endomysial lymphatic vessels.

dramatically. At discharge CK level decreased to 548 U/l and ESR revealed normal values 3 mm in first hour. After three weeks of therapy with steroids we could not register any femoral induration or local tenderness any more. Steroid therapy led to almost complete remission of the patients complains. Thereby it has been confirmed an inflammatory etiology.

In regard to the wide cardiovascular risk spectrum and a persistent cholesterol elevation 255 mg/dl it has been recommended low cholesterol diet, weight reduction and moderate sport activation. In addition due to long-term side effects of the cortisone therapy should be considered a therapy with azathioprine as a long-term drug. However, this decision should be considered after a completely clinical recovery and CK level stabilizing.

DISCUSSION

To our knowledge, this is the first described case of the focal myositis with extraordinary late onset by 10 months after the cessation of therapy with antilipidemics.

Some publications suggest the frequency of statin myopathy between 9% and 20% [7] and a 5.5-fold higher frequency compared with statin use as monotherapy [8]. The etiology of synergic side effects is still unknown. Hence, patients with combined antilipidemics therapy should be monitored intensively regarding to muscle functioning. In normal, case has to be noticed that between 2 and 4 months after stopping statin therapy (mean 2.3 months) there no evidence for myalgia and other muscle complains [9]. In our case, this duration of muscle complains was extraordinary long and late onset of focal myositis to our knowledge has not published before.

Previous studies considered promoting effects of antilipidemics for myositis induction [1–4] but the etiology remained still unknown. As mechanisms for statin mediating myopathy have been supposed inter alia decreased sarcolemmal or endoplasmic reticulum cholesterol, reduced fat catabolism, increased myocellular concentration of cholesterol or vitamin D deficiency [6]. Some studies revealed that hypothyroidism, hypertension, type 1 diabetes and chronic liver disease could be considered as risk factors for statin-induced myopathy [10].

As concurrent risk factor for statin-induced myopathy should be taken in account the intensive exercise training. The results reported by Sinzinger et al. [11] that only 20% of 22 professional athletes with familial hypercholesterolemia could tolerate any of statins.

In addition, has recently been reported that simvastatin could attenuate increase in skeletal muscle mitochondrial content when combined with exercise training [5, 6]. The results reported by Mikus et al. showed that in the simvastatin-plus-exercise group could not be

noticed a increase of skeletal muscle citrate synthase activity [5].

CONCLUSION

In summary, focal myositis is a rare complication after statins or other antilipidemics therapy. It is to conclude, that future observations of similar cases should contribute to more understanding of pathological pathways by antilipidemics induced focal myositis. In addition, future reports should examine concomitant promoting effects by intensive exercise training. Consequently we could minimize the risk for the development of dangerous complications on skeletal muscles after antilipidemics therapy.

Author Contributions

Bartosz Bujan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Elmar Ginzburg – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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