Case Report

Statin-associated rhabdomyolysis: an exemplary case report and a mini-review of therapeutic management

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Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Familial hypercholesterolemia (FH) is a genetic disorder that significantly increases low-density lipoprotein cholesterol (LDL-C) levels. Statins are commonly prescribed to minors to improve overall cardiovascular outcomes. Despite their well-documented efficacy in lowering lipid levels, statins can cause adverse side effects, including myopathy and, in rare cases, rhabdomyolysis.

Case Description: A 17-year-old male adolescent presented with acute muscle pain in both arms. The patient had a history of FH and was undergoing treatment with rosuvastatin. Laboratory results revealed a marked elevation in creatine kinase (CK), myoglobin, cystatin C, and hepatic enzymes. Urinalysis did not show any abnormalities. Given the suspicion of statin-associated rhabdomyolysis, rosuvastatin was promptly discontinued. Further, the patient was administered intravenous fluids (3 L/m^2/day) for renal protection. Nine days after admission, levels of CK, myoglobin, and creatinine returned to normal. Hepatic enzymes and cystatin C remained elevated. The patient was advised to discontinue statin therapy for a total of 6 weeks. For further treatment, the patient was referred to a pediatric lipid clinic.

Conclusions: While the use of statins is generally safe, rare side effects including rhabdomyolysis must be detected and therapy promptly initiated to prevent long-term health effects. Patients that experienced statin-associated rhabdomyolysis should be monitored closely and referred to a pediatric lipid clinic for further treatment.

Keywords: Rhabdomyolysis; statins; familial hypercholesterolemia (FH); case report

Submitted Jan 13, 2025. Accepted for publication Mar 31, 2025. Published online Apr 24, 2025.
doi: 10.21037/tp-2025-30
View this article at: https://dx.doi.org/10.21037/tp-2025-30

Introduction

Familial hypercholesterolemia (FH) is a genetic disorder severely increasing low-density lipoprotein cholesterol (LDL-C) concentrations from a young age (1). Globally, approximately one in 311 people is affected by FH (1). Individuals with FH are faced with an elevated risk for developing atherosclerotic cardiovascular disease early in life (1). To improve overall cardiovascular outcome, aggressive lipid-lowering treatment starting in childhood is recommended (2). Statins are considered "the cornerstone" of pediatric FH management (2). Despite statins' well-documented lipid-lowering efficacy, adverse side affects including myopathy, and, rarely, rhabdomyolysis, have been reported (3). During rhabdomyolysis, skeletal muscle cells are destroyed which leads to the release of intracellular components such as myoglobin or creatine kinase (CK) (3). While set criteria for the diagnosis of rhabdomyolysis do not exist, a CK >5 times the normal upper limit is often considered as diagnostic (4). Symptoms of rhabdomyolysis

can include muscle pain, weakness, tea-colored urine, and most worrisome, acute renal failure (3). Data on the incidence of statin-associated rhabdomyolysis in minors is scarce, however, large-scale studies in adult patients suggest an average incidence of 0.44 per 10,000 person-years for statin monotherapy (5).

In the following, we present a case report of a 17-year-old adolescent with FH and statin-associated rhabdomyolysis. In addition, special emphasis is put on reviewing risk factors and therapeutic management of statin-associated rhabdomyolysis. We present this case in accordance with the CARE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-2025-30/rc).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration and its subsequent amendments. Written informed consent was obtained from the parents of the adolescent for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

A 17-year-old adolescent presented with acute muscle pain in both arms, which had been persisting for 1 week, at our pediatric emergency unit. Patient's history revealed that the boy suffered from FH and was taking rosuvastatin (5 mg per os/day) for the past 6 months. No further medications nor drugs were taken. The boy was physically active and regularly engaged in strength training. Physical examination showed tenderness of both arms and limitation of forearm extension. No swelling or skin discoloration were noted. Vital parameters were normal, and the boy presented with a regular body temperature. The presence of an infectious disease was ruled out. A nasopharyngeal swab for respiratory viruses was negative. Moreover, infectious blood parameters (e.g., white blood cell count, C-reactive protein) were not elevated. Urinalysis did not reveal abnormalities. The initial blood test revealed a marked elevation of CK, myoglobin, cystatin C, hepatic enzymes, and phosphate (*Table 1*). Glomerular filtration rate cystatin C was reduced (*Table 1*). LDL-C at admission was 114 mg/dL (reference value <130 mg/dL).

As statin-associated rhabdomyolysis was suspected, rosuvastatin was promptly paused. Further, the adolescent received intravenous fluids (3 L/m^2/day) for renal protection. During inpatient care, the adolescent presented with normal vitals and regular urine output. The muscle pain resolved and analgetic medications were not required. Four days after admission, the adolescent was discharged with already declining CK, myoglobin, hepatic enzymes, and phosphate. Post stationary blood testing 9 days after admission revealed normal levels for CK, myoglobin, creatine, and phosphate (*Table 1*). Levels for hepatic enzymes, cystatin C, and glomerular filtration rate cystatin C improved but were still abnormal (*Table 1*).

The patient was asked to pause statin medication for a total of 6 weeks. For further treatment, the patient was referred to a pediatric lipid clinic.

Highlight box

Key findings

- This case report presents a 17-year-old adolescent with familial hypercholesterolemia and statin-associated rhabdomyolysis. Special emphasis is put on risk factors and therapeutic management.

What is known and what is new?

- Rhabdomyolysis is a rare but severe side effect of statins.
- Risk factors and therapeutic management of statin-associated rhabdomyolysis during childhood is discussed in this manuscript.

What is the implication, and what should change now?

- Statin-associated rhabdomyolysis is rare but must be detected and therapy promptly initiated to prevent long-term health effects. Patients that experienced statin-associated rhabdomyolysis should be monitored closely and referred to a pediatric lipid clinic for further treatment.

Discussion

Statin-associated rhabdomyolysis is rare, particularly within the pediatric population. We reported a case of statin-associated rhabdomyolysis in a 17-year-old adolescent with FH who was taking rosuvastatin.

Previous literature reports on statin-associated rhabdomyolysis

Pediatric case reports on statin-associated rhabdomyolysis are sparse. In a letter to the editor, Buonuomo *et al.* reported a 10-year-old boy with FH who presented with severe myalgia, generalized weakness, darkened urine as well as high CK (1,951 U/L) and myoglobin levels (1,201 ng/mL) approximately 10 days after the start of atorvastatin therapy (10 mg per os/day). As rhabdomyolysis was presumed, fluid

Table 1 Laboratory parameters

Laboratory parameters	Reference value	Value at admission	Value 9 days after admission
CK (U/L)	30–200	20,108	196
Myoglobin (µg/L)	<155	1,959	31.3
Creatinine (mg/dL)	0.7–1.2	0.6	0.6
Cystatin C (mg/L)	0.31–0.79	1.13	1.08
Glomerular filtration rate cystatin C (mL/min)	80–160	70	74
Aspartate transaminase (U/L)	<35	277	134
Alanine transaminase (U/L)	<45	81	69
Phosphate (mmol/L)	0.74–1.52	1.95	1.02

CK, creatine kinase.

therapy was initiated and atorvastatin was discontinued resulting into a quick recovery of clinical status and laboratory results (6). Vijayakanthi *et al.* presented a case of a 13-year-old female diagnosed with rapid-onset obesity, hypothalamic dysfunction, hypoventilation, and autonomic dysregulation syndrome, along with panhypopituitarism, dyslipidemia, type 2 diabetes mellitus, and non-alcoholic fatty liver disease. Two weeks after switching from lovastatin to rosuvastatin (40 mg per os/day), the girl developed rhabdomyolysis and acute kidney injury. The patient presented with dizziness, malaise, polyuria, polydipsia, and hematuria. Laboratory studies demonstrated hypernatremia, hyperchloremia as well as increased creatinine (2.16 mg/dL), hepatic enzymes, and CK level (53,000 U/L). Moreover, myoglobinuria was present. Aggressive fluid therapy was initiated and rosuvastatin as well as metformin were stopped. Five days after admission, CK and creatinine levels returned to nearly normal. The girl was discharged with healthy lifestyle instructions, hormone replacement medications, and amlodipine. A non-statin lipid-lowering agent was considered in this patient as a future therapeutic option (7). Conte *et al.* investigated adverse drug reactions of statins in children and adolescents recorded in the World Health Organization global database of individual case safety reports. The authors identified 311 individual case safety reports associated with statins. In total, 11 cases of rhabdomyolysis were detected, eight reported a statin as the only suspected drug and one reported the simultaneous intake of multiple statins. Two cases reported the concomitant exposure (ribavirine, telaprevir, peginterferon alfa-2a, prednisolone) potentially associated with rhabdomyolysis (8).

Pathophysiology and risk factors of statin-associated rhabdomyolysis

The precise pathophysiology behind statin-associated rhabdomyolysis has not been fully understood yet, however, an altered mitochondrial function, idiopathic inflammatory mechanisms, and a genetic susceptibility are presumed (9). Statins lower LDL-C concentration in the blood by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. The HMG-CoA pathway is also involved in the synthesizes of coenzyme Q, a mitochondrial electron transport facilitator. By inhibiting HMG-CoA reductase, statins may decrease coenzyme Q production impairing cellular energy metabolism and ultimately leading to myocyte apoptosis (10). Further, experimental studies suggest that statins may reduce contractile function of skeletal muscles by lowering Ca^{2+} release from the sarcoplasmic reticulum and by downsizing ATP levels in myofibers potentially leading to cell death (10,11). Moreover, a study by Hanai *et al.* revealed that lovastatin induces the expression of atrogin-1, a gene associated with skeletal muscle atrophy (12). The gene *SLCO1B* encodes the organic anion-transporting polypeptide OATP1B1, which is involved in the hepatic uptake of statins (13). Variants of the gene *SLCO1B* lead to an increased statin

plasma level and are linked with statin-associated muscle symptoms (13). Statin-associated muscle symptoms are more prevalent in subjects receiving intense-dose statin therapy compared to those with standard-dose therapy (14). The literature suggests that more hydrophilic statins (e.g., pravastatin, fluvastatin) display a lower prevalence of statin-associated muscle symptoms presumably due to less muscle penetration (15). Moreover, potential drug-drug interactions need to be addressed as statins are primarily metabolized by cytochrome P450 2C9 and cytochrome P450 3A4. In addition, drug-habit interactions (e.g., alcohol consumption, excessive exercising) as well as drug-disease interactions (e.g., hypothyroidism, hereditary metabolic muscle diseases) can increase the risk for statin-associated muscle symptoms (16).

Despite our patient being physically active and regularly engaging in strength training, no further risk factors for statin-associated rhabdomyolysis were present. However, a genetic susceptibility for statin-associated rhabdomyolysis can not be ruled out as corresponding testing was not initiated.

Acute management of statin-associated rhabdomyolysis

Guidelines on the management of pediatric rhabdomyolysis do not exist (4). After reviewing the literature, the following acute therapeutic algorithm is proposed (4,9,17): If statin-associated rhabdomyolysis is suspected, prompt pausing of statin intake is recommended (17). Serum CK level, a comprehensive metabolic panel, microscopic urinalysis and complete blood cell count should be assessed (4). If CK is >5 times the normal upper limit, intravenous fluids (e.g., initial bolus of 20 mL/kg normal saline followed by twice the maintenance rate) should be administered for renal protection (4,9). The additional use of sodium bicarbonate and/or mannitol might help in preventing acute kidney failure (4). In addition, urine output should be monitored (4). A urine output goal of 3–4 mL/kg/h is hypothesized (4). CK level, electrolytes and creatine should be regularly assessed during acute therapy (4). In case of acute kidney failure and/or decreased urine output, the consultation of a pediatric nephrologist is recommended (4). Patients might be discharged if asymptomatic, display normal levels of creatine and electrolytes, declining CK levels and sufficient oral intake as well as normal urine output (4). *Figure 1* visualizes the proposed acute therapeutic algorithm for statin-associated rhabdomyolysis.

Lipid-lowering therapy following statin-associated rhabdomyolysis

Patients that have experienced statin-associated rhabdomyolysis should be referred to a lipid expert (9,17). In adult patients, a 6-week statin washout period is recommended after rhabdomyolysis until normalisation of symptoms, CK, and creatine levels (9). For the pediatric population, statins might be restarted once laboratory abnormalities as well as symptoms have resolved (17). The same statin at lower dosage or a different statin should be reintroduced (9). Lipid-lowering medication is adjusted depending on clinical symptomatic (e.g., myopathy), LDL-C (minimal target <130 mg/dL), and aspartate transaminase/alanine transaminase level (<3 times the reported normal upper limit) (9,17). This includes the up- or down-titration of statins, alternate day or twice-weekly dosage of statins as well as the addition of alternative LDL-C lowering agents (e.g., bile acid sequestrant or cholesterol absorption inhibitor) (9,17).

Conclusions

While the use of statins is generally safe, rare side effects including rhabdomyolysis must be detected and therapy promptly initiated to prevent long-term health effects. Patients that experienced statin-associated rhabdomyolysis should be monitored closely and referred to a pediatric lipid clinic for further treatment.

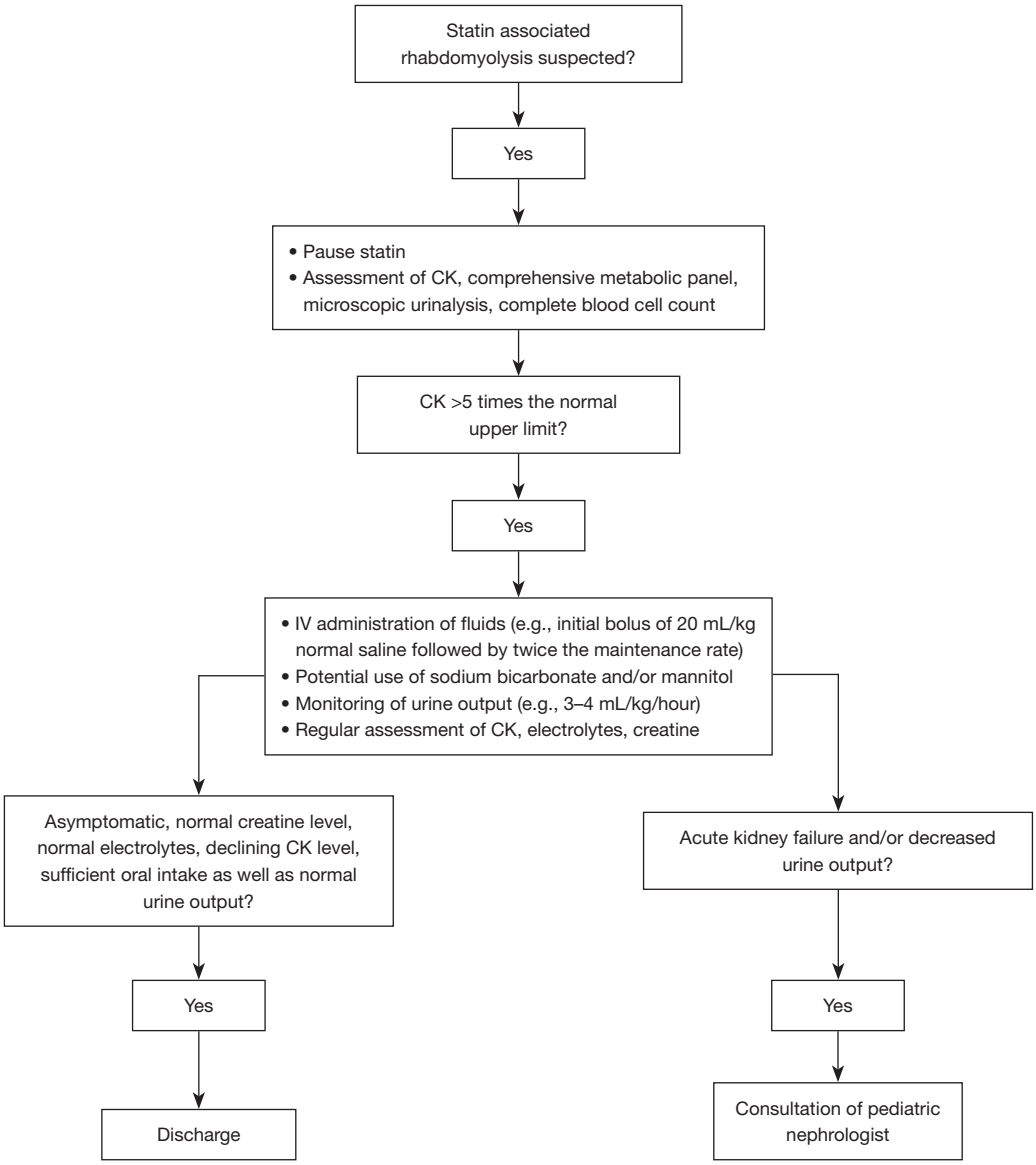

Figure 1 Proposed acute therapeutic algorithm for statin-associated rhabdomyolysis. CK, creatine kinase; IV, intravenous.

Acknowledgments

We would like to thank Megan Crouse for her editorial assistance.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-2025-30/rc

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-2025-30/prf

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-2025-30/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration and its subsequent amendments. Written informed consent was obtained from the parents of the adolescent for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Oberhoffer FS, Rieger E, Schenk S, Hauer J, Chmiel R, Steinhauser M. Statin-associated rhabdomyolysis: an exemplary case report and a mini-review of therapeutic management. Transl Pediatr 2025;14(4):763-768. doi: 10.21037/tp-2025-30