

Medical & Clinical Research

The Importance of Hypothyroidism Screening Before Initiating Statin Therapy: A Case of Rhabdomyolysis

Vittoria Gammaldi¹, Antonietta De Sena¹, Carmine Fierarossa¹, Ludovica F. S, Grasso², Serena Ippolito², Ornella Romano², Vincenzo Nuzzo^{1,2} and Paolo Tirelli¹

¹ Department of Internal Medicine, Ospedale del Mare, ASL Napoli I Centro, Napoli	*Corresponding Author Vittoria Gammaldi, Department of Internal Medicine, Ospedale del Mare, ASL Napoli 1 Centro, Napoli.
² Unit of Endocrinology, Ospedale del Mare, ASL Napoli 1 Centro, Napoli	Submitted: 27 Dec 2024; Accepted: 03 Jan 2025; Published: 25 Jan 2025

Citation: Gammaldi, V., De Sena, A., Fierarossa, C., Ludovica, F.S., Grasso., et al. (2025). The Importance of Hypothyroidism Screening Before Initiating Statin Therapy: A Case of Rhabdomyolysis. *Med Clin Res, 10*(1), 01-03.

Abstract

Rhabdomyolysis (RM) is a clinical syndrome characterized by breakdown of skeletal muscle tissue that causes the release of various substances (such as myoglobin, creatine kinase (CK), lactate dehydrogenase (LDH), aldolase, potassium ions) into the bloodstream. It can range from asymptomatic, with isolated serum elevation of CK, to a life-threatening condition. RM can be considered a complication of hypothyroidism and can occur while taking statin medications. Given this association, it is essential to screen patients' thyroid status before initiating statin therapy. We describe the case of a 67-year-old man who had an episode of rhabdomyolysis while on statin therapy and with an undiagnosed severe hypothyroidism.

Keywords: Rhabdomyolysis, Creatine kinase, Myoglobin, Statin therapy, Hypothyroidism screening

1. Introduction

Hypothyroidism is a common pathological condition due to deficiency of thyroid hormones. Hypothyroidism is characterized by a broad spectrum of clinical findings, including muscular symptoms. Hypothyroid myopathy is most often limited to myalgia, muscle weakness and cramps, occasionally associated with mildly elevated levels of muscle enzymes [1,2]. Rhamdomyolysis (RM) is an unusual but dangerous complication of hypothyroidism. RM is a condition characterized by lysis of muscle fibers and release of substances into the bloodstream. It can be asymptomatic or a lifethreatening condition with occurrence of many complications, like compartment syndrome, acute kidney injury (AKI), disseminated intravascular coagulation (DIC) intravascular fluid depletion. RM can be traumatic (crush syndrome, injuries), and non-traumatic (alcohol consumption, hypothyroidism, medications, prolonged bedridden). The diagnosis is made by elevation of serum CK more than five-times accompanied by muscle weakness and myoglobinuria (dark urine) [3]. RM can also occur in the setting of a hypothyroidism. Although the mechanism is not so clear, it can be due the fact that triiodothyronine (T3), is involved in muscle functioning. In hypothyroidism, due to T3 deficiency, we observe a condition of muscle dysfunction due to the fact that normally T3 promote carbohydrate metabolism, utilization of glycogen in muscle tissue. The American Thyroid Association promote the screening of hypothyroidism in patients with elevation of CK or LDH within two weeks [4]. Statins, a class of drug which, by inhibiting the hydroxymethylglutarylCoA (HMG-

CoA) reductase enzyme, a key step in the sterol biosynthetic pathway, became powerful cholesterol-lowering medications. It is well known that these drugs have various side effects, especially neuromuscular ones, which can range from muscle pain/weakness to rhabdomyolysis [5]. This case report shows the importance of screening for hypothyroidism before initiating statin therapy.

2. Case Report

A 67-years-old man came to our Internal Medicine Outpatient Clinic with a severe hypercholesterolemia. In fact, his blood tests showed: total cholesterol (TC) 512 mg/dl, LDL-cholesterol (C-LDL) 392 mg/dl, HDL-cholesterol (C-HDL) 36 mg/dl, triglycerides (TG) 337 mg/dl. His past medical history included: hypertension in therapy with angiotensin-receptor blocker (ARB), and carotid atherosclerosis (he had a 30% plaque in left internal carotid artery and 35% in right internal carotid artery). According to ESC/EAS guidelines for dyslipidemias management, this patient had a very-high cardiovascular risk (SCORE2: 18.3%) [6], so his LDL target value should be <70 mg/dl. For this reason, he initiated therapy with Rosuvastatin 20 mg, Ezetimibe 10 mg and Omega-3 1000 mg two times per day. He came back few weeks later complaining of myalgia, especially during the night; at blood tests, he had CK 1123 U/l (normal values: 39-308 U/l), myoglobin 232 ng/dl (normal values: 23-72 ng/ml), and LDH 334 U/l (normal values: 135-225 U/l). C-LDL were not at target yet so he switched therapy to Alirocumab 150 mg subcutaneously every two weeks. In the following weeks C-LDL levels arrived at 130

mg/dl, instead CK and myoglobin levels remained high. He denied any precipitating cause of rhabdomyolysis, like intensive exercise, injury or alcohol consumption. The American Thyroid Association promote the screening for hypothyroidism in case of elevation of CK within two weeks [4], so we screened our patient. He had a severe hypothyroidism with no clinical symptoms: thyroid stimulating hormone (TSH) 178 U/mL (normal values: 0,55-4.78 µUI/ml), Triiodothyronine (FT3) 1,35 pg/ml (normal values: 2,30-4,20 pg/ml), thyroxine (FT4) 0,27 ng/ml (normal values 0,89-1,76 ng/ml). The thyroid peroxidase (TPO) antibody was elevated (>600 UI/ml; normal values are <34 UI/ml) and thyroglobulin (TgAb) antibody too (>4000 UI/ml; normal values are <115 UI/ml), suggestive of Hashimoto's thyroiditis. Thyroid echography was performed showing an enlarged and disomogeneous thyroid gland. L-thyroxine was prescribed. The diagnosis of rhabdomyolysis was confirmed, secondary to the synergic effects of hypothyroidism and statin therapy on muscle metabolism. Since C-LDL was not at target values yet, we switched therapy to Inclisiran 284 mg subcutaneously every three months, then every six months. Myalgia and muscle weakness progressively improved in the following weeks, as the CK and myoglobin levels decreased simultaneously to TSH. At four months laboratory tests showed: TSH 2,12UI/ml, FT4 1,50 ng/ml, FT3 3,58 pg/ml, C-LDL 71 mg/ml, TC 140 mg/dl, C-HDL 34 mg/dl, triglycerides 191mg/dl, CK 150 U/l. The patient continued his follow-up at our Outpatient Clinic.

3. Discussion

RM caused by hypothyroidism is very rare, but there are many precipitating factors taking part in its development, such as the use of statins, trauma, strenuous exercise, alcohol consumption and use of illicit drugs. Statins are the most used cholesterollowering medications for primary and secondary prevention of cardiovascular events. Although they are very well tolerated, we know that most patients observe side effects, like myalgia, muscle weakness, elevation of liver enzymes and RM [5]. RM can occur in patients with hypothyroidism, due to a mechanism of downregulation of cellular metabolism. It can range from asymptomatic to life-threatening condition. Myolysis in hypothyroidism is caused by changes in muscle fibers from fast-

twitching type II to slow-twitching type-I fibers, deposition of glycosaminoglycan, poor contractility of actin-myosin units, low myosin ATPase activity, and low ATP turnover in the skeletal muscles [2]. With hypothyroidism, there is an inhibition of mitochondrial activity in muscle cells as well as dysregulation of many metabolic pathways such as Krebs cycle, fatty acid catabolism and glycolytic energy production [2]. These metabolic anomalies may prepare patients with hypothyroidism to develop rhabdomyolysis, especially in the presence of precipitating factors that may predispose the onset of myopathy. Statins inhibit HMG-CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase, the rate-limiting enzyme in cholesterol synthesis. They may also impair other biosynthetic pathways of cholesterol, including coenzyme Q10, a component of the mitochondrial respiratory chain, resulting in a toxic, noninflammatory myopathy leading to rhabdomyolysis [5,7]. These mechanisms probably work synergistically when statins are prescribed to hypothyroid patients, with a greater likelihood of myopathy at higher statin doses. Therefore, the coexistence of hypothyroidism and statin therapy can increase the risk of RM occurrence, so, it is important to assess thyroid function before starting statin therapy, as suggested by the American Thyroid Association [4]. This case report describes the occurrence of rhabdomyolysis in a patient with an unknown severe hypothyroidism and during statin therapy. There are already various case reports describing this condition [7-11], also in patients who performed an intensive physical exercise [12,13]. Possible mechanisms for how hypothyroidism may promote statin myopathy involve decreased clearance of CK or decreased drug catabolism, resulting in higher serum statin levels [14].

4. Conclusion

With this case report we want to emphasize the screening for hypothyroidism before starting therapy with statin, moreover, hypothyroidism should be considered as a differential diagnosis of rhabdomyolysis and physicians should not delay the assessment of thyroid function tests especially in patients with no traumatic rhabdomyolysis. With prompt diagnosis and treatment of hypothyroidism before starting statin therapy we can decrease occurrence of RM's complications and the risk of mortality.

VARIABLES	Day-1	Two-months	Four-months
TSH (0,55-4.78 μUI/ml)	178	21	2,12
FT3 (2,30-4,20 pg/ml)	1,35	2,85	3,58
FT4 (0,89-1,76 ng/ml)	0,27	1,16	1,50
TPO-AB (<34 UI/mI)	>600		27
TgAB (<115 UI/ml)	>4000		98
CK (39-308 U/I)	1123	669	150
Myoglobin (23-72 ng/ml)	232	186	70
LDH (135-225 U/I)	334	294	210

Table 1. Patient's laboratory values

TSH: thyroid stimulating hormone; FT3: triiodothyroinine; FT4: thyroxine; TPO-AB: thyroid peroxidase antibody; <u>TgAB</u>: thyroglobulin antibody; CK: creatine kinase; LDH: lactate dehydrogenase

References

- Chaker, L., Bianco, A.C., Jonklaas, J., Peeters, R.P. (2017). Hypothyroidism. *Lancet*, 390, 1550-1562.
- Salehi, N., Agoston, E, Munir, I., Thompson, G.J. (2017). Rhabdomyolysis in a patient with severe hypothyroidism. *Am J Case Rep, 18*, 912-918
- Zhou, Q., Li, B., Tian, X. (2022). Rhabdomyolysis Caused by Hypothyroidism: Research Progress. *Horm Metab Res*, 54(11), 731-735.
- Ladenson, P. W., Singer, P. A., Ain, K. B., Bagchi, N., Bigos, S. T., Levy, E. G., Smith, S. A., Daniels, G. H., & Cohen, H. D. (2000). American Thyroid Association guidelines for detection of thyroid dysfunction. *Archives of internal medicine*, 160(11), 1573–1575.
- 5. Attardo, S., Musumeci, O., Velardo, D., & Toscano, A. (2022). Statins Neuromuscular Adverse Effects. *International journal of molecular sciences*, 23(15), 8364.
- Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Casula, M., Badimon, L., Chapman, M. J., De Backer, G. G., Delgado, V., Ference, B. A., Graham, I. M., Halliday, A., Landmesser, U., Mihaylova, B., Pedersen, T. R., Riccardi, G., Richter, D. J., Sabatine, M. S., Taskinen, M. R., Tokgozoglu, L., ... ESC Scientific Document Group (2020). 2019 ESC/ EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *European heart journal*, 41(1), 111–188.
- 7. Jbara, Y., & Bricker, D. (2015). Rhabdomyolysis in the setting of induced hypothyroidism and statin therapy: a case report. *European thyroid journal*, *4*(1), 62–64.

- 8. Yeter, E., Keles, T., Durmaz, T. et al. Rhabdomyolysis due to the additive effect of statin therapy and hypothyroidism: a case report. *J Med Case Reports 1, 130* (2007)
- Renteria, M., Jilani, M., Brockman, M. J., & Davis, H. E. (2023). Inflammatory Myositis Following Statin Use in a Patient With Untreated Hypothyroidism. *Cureus*, 15(11), e48463.
- Ahn, P., Min, H. J., Park, S. H., Lee, B. M., Choi, M. J., Yoon, J. W., & Koo, J. R. (2013). Rhabdomyolysis and acute kidney injury associated with hypothyroidism and statin therapy. *Endocrinology and metabolism (Seoul, Korea), 28*(4), 331– 334.
- 11. Renteria, M., Jilani, M., Brockman, M. J., & Davis, H. E. (2023). Inflammatory Myositis Following Statin Use in a Patient With Untreated Hypothyroidism. *Cureus*, 15(11), e48463.
- 12. Riggs J. E. (1990). Acute exertional rhabdomyolysis in hypothyroidism: the result of a reversible defect in glycogenolysis?. *Military medicine*, 155(4), 171–172.
- 13. Farias Moeller, R., Zecavati, N., Sherafat-Kazemzadeh, R., Aleinikoff, S., & Rennert, W. (2011). Adolescent with Rhabdomyolysis due to Undiagnosed Hypothyroidism. *Case reports in pediatrics, 2011,* 670673.
- Lando, H. M., & Burman, K. D. (2008). Two cases of statininduced myopathy caused by induced hypothyroidism. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 14(6), 726–731.

Copyright: ©2025 Vittoria Gammaldi, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.