Case Report

Necrotizing autoimmune myopathy: Muscle weakness due to atorvastatin

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Abstract

Statins are medications with great use. One of the side effects of medications is myopathy. In some case, statins switch on, a process of autoimmune system which will not terminate with discontinuation of statins. Necrotizing autoimmune myopathy (NAM) is a subgroup of inflammatory myopathies characterized pathologically by necrotic muscle fibers with absent or minimal inflammation. The purpose of this study was to describe NAM in a patient undergoing treatment with atorvastatin for an extended period, diagnosis of the disease process, treatment, and resolution of symptoms. The case presented in this paper is about 72-year-old woman who showed continued general weakness even though she stopped taking atorvastatin. This patient also had elevated creatine kinase and aldolase. Myopathy confirmed by muscle biopsy. She was treated with intravenous immune globulin (IVIG) and pulse of methyl prednisolone and followed with high dose of steroid and azathioprine. Our case report illustrates the importance of early recognition of NAM and that the treatment with immediately administer IVIG, pulse of methylprednisolone, and high dose of steroid can result in complete recovery.

Keywords: Atorvastatin, Autoimmune myopathy, Necrosis

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INTRODUCTION

The idiopathic inflammatory myopathies (IIMs) are combination of a group of autoimmune disorders that target skeletal muscle. Such disorders are characterized by typical laboratory and clinical features including muscle weakness, elevated muscle enzymes, characteristic histopathology of muscle biopsies, as well as electromyography abnormalities.[1]

Necrotizing autoimmune myopathy (NAM), inclusion body myositis, dermatomyositis, polymyositis, and nonspecific myositis can be subcategory of the inflammatory myopathies and are characterized by muscle cell infiltrations and specific alterations of the muscle fibers.[2]

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Relatively, newly recognized subgroup of IIMs which despite diverse causes have the common histopathological features of myocyte necrosis without significant inflammation is the purpose of reviewing NAM.

Presented patients had subacute severe symmetrical proximal myopathy, associated with a markedly elevated creatine kinase level.[3]

Recognized risk factors for NAM include statin exposure, connective tissue disease (CTD), cancer, and rarely, human immunodeficiency virus infection.[4,5]

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Statin exposure may associate with necrotizing myopathy. It is thought that the statin may induce an autoimmune process that persists despite withdrawal of the statin.[6] This is in contrast to a statin-induced myopathy that improves over weeks to months when the statin is discontinued[7] and requires therapy with immunosuppressive agents.[3,8] Specific autoantibodies have been noted in those with necrotizing myopathy, including anti-3-hydroxy-3-methylglutaryl-coenzyme a reductase antibody and signal recognition particle.[9,10] NAM is a rare side effect of statins. Various studies have been done in this regard that will address the importance of the subject.[11,12]

In this study, we report a case. The purpose of this study was to describe NAM in a patient undergoing treatment with atorvastatin for an extended period of time, diagnosis of the disease process, treatment, and resolution of symptoms.

CASE REPORT

History

This study was conducted in the year 2015, at Razi Hospital in Qaemshahr (located in the north of Iran).

This case is about a 70-year-old woman presented for evaluation of proximal muscle weakness mostly in lower extremities.

This woman was not able to get up without using her hands 2 years ago. There was no progress in her disabilities since then, until 3 months ago which she experienced progression in muscle weakness that led to complete disability.

Her medical history shows type 2 diabetes; hypothyroidism and 10 months ago, she underwent coronary artery bypass graft (CABG). After CABG surgery, she has taken atorvastatin 20 mg/day for 6 months. She was advised to stop taking atorvastatin after she experienced muscle weakness. Her muscle weakness progressed to the point that she could not walk anymore.

She did not have weight loss, night sweats, fever, joint and muscle pain, no abnormalities observed on her skin, and no recent trips.

Physical examination

The patient was alert. In neurological examination, muscle force: 2/5 power in both upper extremities and 1/5 power in lower extremities, weakness in neck flexor muscle, intact sensation, and absent ankle and knee reflex bilaterally.

Diabetes and thyroid function in this patient were controlled. As it is presented in Table 1, tests carried out on this patient ruled out the CTDs. However, it showed elevated aldolase.

Table 1: Laboratory test results

Tests	Results	Normal range
Hemoglobin A1C	6.5%	Good diabetic control <7
TSH	4.5 μIU/ml	0.27-4.5
Aldolase	18 U/L	0-7.6
ANA	0.7	Up to 1.5
C3	117 mg/Dl	90-180
C4	31 mg/dl	10-40
CH50	100 mg/dl	70-150
Anti-ds-DNA	5 IU/ml	Up to 20
Anti MPO (P-ANCA)	1 U/ml	Up to 5
Anti PR3 (C-ANCA)	2 U/ml	Up to 5
Anti SCL-70	0.1 RU/ml	> 20 positive
ACE	21 IU/L	8-5
Anti jo-1 Ab	1.6 RU/ml	Up to 20

TSH: Thyroid-stimulating hormone, ANA: Antinuclear Antibodies, Anti MPO: Anti Myeloperoxidase, ANCA: Anti-neutrophil cytoplasmic antibodies, Anti SCL-70: Anti-topoisomerase I , ACE: Angiotensin-converting enzyme

Given accelerated muscle weakness in extremities and weakness in neck flexor muscle, it was decided to prescribe intravenous immune globulin) IVIG ((2 mg/kg) divided into five doses. Then, the patient immediately went through electromyography (EMG) and nerve conduction velocity (NCV). EMG_NCV and muscle biopsy. EMG_NCV showed myopathy.

Preliminary result of muscle biopsy indicated necrotizing myopathy. Based on this result and the patient history, atorvastatin was suspected as a cause of muscle weakness.

Drug history

- Tablet glibenclamide: 2.5 mg/day
- Tablet metformin: 500 mg/day
- Tablet ASA: 80 mg/day
- Tablet levothyroxine: 0.1 mg/day.

To eliminate other cause of myopathy following procedure was carried out as follows:

- Abdomen and pelvic computed tomography (CT) scan: normal
- Lung and mediastinum CT scan: normal
- Thyroid function: normal
- Mammography performed showed no abnormality
- The patient refused to take colorectal screening
- Variation of bowel habit and stool examination: Normal.

After muscle biopsy, sample was extracted 1 gram of methyl prednisolone infused for 3 days. After IVIG and methyl prednisolone infusion, progression of muscle weakness

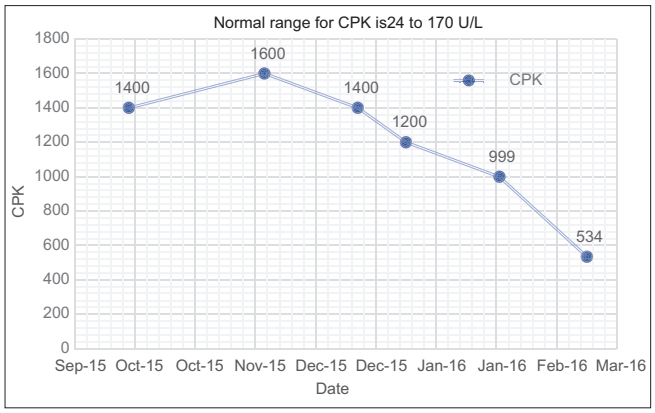

Figure 1: CPK variation with date

stopped, and as it is presented in Figure 1, her CPK stared to reduce. Muscle biopsy result indicated myopathy atrophy with many necrotic and degenerative/regenerative fibers as well as some ragged red fibers with no inflammation. After muscle biopsy result indicated necrotizing myopathy, the patient was advised to continue prednisolone 60 mg/day and azathioprine 100 mg/day.

Four months of treatment gradually reduced muscle enzyme to normal level.

Since antisignal recognition particle (anti-SRP) and 3-hydroxy-3-methylglutaryl-coenzyme a reductase (HMGCR) tests were not available in this location, these laboratory tests were not performed on this patient.

After taking these, medications patient's muscle power returned in 6 months to almost normal level. So much that she did not require waking aid. During this 6-month period, the patient also received physical therapy.

Ethical consideration

To collect data and report this case, the researcher, while introducing himself and expressing the purpose of the research, received informed consent from the patient for participate in the research.

DISCUSSION

In this article, we present a very rare case of a 72-year-old female who presented continued general weakness even though she stopped taking atorvastatin. This patient also had elevated creatine kinase and aldolase. Myopathy confirmed by muscle biopsy. She was treated with IVIG and pulse of methyl prednisolone and followed with high dose of steroid and azathioprine.

Statin exposure has been associated with necrotizing myopathy. It is thought that the statin may induce an autoimmune process that persists despite withdrawal of the statin. This is in contrast to a statin-induced myopathy that improves over weeks to months when the statin is discontinued.[2]

For this patient also myopathy started after the use of statin and despite the discontinuation of atorvastatin, myopathy not only did not stop but also progressed.

Malignancy or autoimmune among other diseases is causes of necrotizing myopathy.[13]

Laboratory tests and diagnostic procedures ruled out other causes of necrotizing myopathy such a malignancy or autoimmune diseases.

In two-thirds of the cases, anti-SRP and HMGCR have been described as having an association with NAM,[3] but these laboratory tests were not available in Iran therefore were not performed on this patient.

Two years ago, this patient experienced low-level weakness in the proximal muscle of lower extremities, and her condition remained unchanged. Three months ago, she was then referred to hospital. During this 2-year period, her muscle enzyme remained almost normal level. Diabetes and hypothyroidism are risk factor for NAM, and this patient showed both of them. If a patient with a history of muscle weakness be exposed to atorvastatin, she may develop NAM. Therefore, in these cases, precautionary measure must be taken in prescribing statins.

NAM causes chest muscle weakness which in turn could lead to respiratory failure and death. Early diagnosis and treatment of this disease is very important.[14]

Strength improvement and favorable outcome are associated with early use of IVIG or plasmapheresis.[3] Therefore, in this case, it was preferred to immediately administer IVIG, pulse of methyl prednisolone, and high dose of steroid.

CONCLUSION

Our case report illustrates the importance of early recognition of NAM and that the treatment with immediately administer IVIG, pulse of methyl prednisolone, and high dose of steroid can result in complete recovery.

Conflicts of interest

There are no conflicts of interest.

Author contribution

All authors contributed to this research

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