

A 62-Year-Old Woman with Muscle Weakness

Laurens Dobbels,¹ Philip Van Damme,¹ Michael Mahler,² and Xavier Bossuyt^{3,4*}

Departments of ¹ Neurology and ³ Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium; ² Inova Diagnostics, Inc., San Diego, CA; ⁴ Department of Microbiology and Immunology, Katholieke Universiteit Leuven, Leuven, Belgium.

* Address correspondence to this author at: Laboratory Medicine, University Hospitals Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium. Fax +32-16-34-79-31; E-mail: xavier.bossuyt@uzleuven.be.

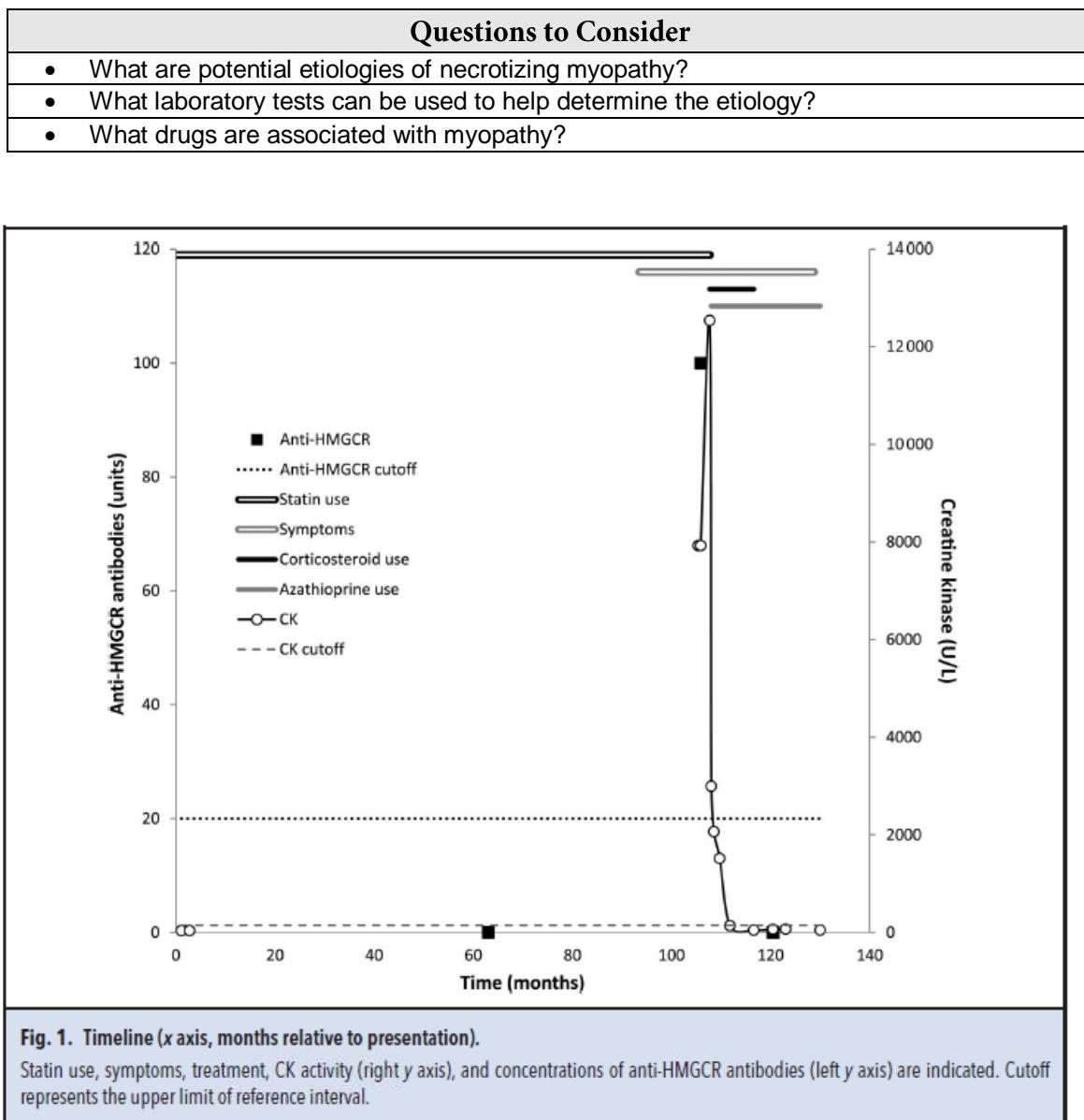
CASE DESCRIPTION

A 62-year-old woman noticed muscle weakness in the right leg, which was followed a few months later by weakness in the left leg. Over a 6-month period, the muscle weakness progressed to the upper limbs. One year after onset, the patient was referred to a neurologist with a suspected diagnosis of amyotrophic lateral sclerosis. She was taking atorvastatin 40 mg (started approximately 6 years earlier) and L-thyroxine 125 µg (for hypothyroidism after nuclide therapy for Graves disease). Clinical examination revealed a proximal paresis in the arms and legs. Creatine kinase (CK) activity was 7925 U/L (reference interval <145 U/L). Electromyography showed myogenic changes (small and polyphasic motor units). A toxic statin myopathy was considered, although the time span between the start of the statin and onset of the symptoms was long. Late-onset Pompe (glycogen storage) disease was excluded by α -glucosidase activity testing. Further laboratory testing was unremarkable. A biopsy of the right quadriceps muscle was performed and revealed polygonal muscle fibers of varying diameter (and an increase of internal nuclei). There was some evidence of endomysial fibrosis without inflammatory infiltration. Individual muscle fibers showed necrosis with myocyte phagocytosis and without HLA-ABC upregulation.

PATIENT FOLLOW-UP

The muscle weakness was progressive and also affected distal hand muscles and bulbar muscles. The use of statins was discontinued, and high-dose intravenous methylprednisolone was given, followed by oral tapering. Ten days later, there was only minor improvement of the muscle weakness, and azathioprine 100 mg per day was added. Ezetimibe and fenofibrate were started for hypercholesterolemia. The weakness improved, CK activity decreased, and oral methylprednisolone was stopped. The patient fully recovered and was stable at 1-year follow-up after discontinuation of azathioprine. The CK activity normalized.

Quantification of antibodies to 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) was not available at the time the patient presented but was performed later (with approval of the local ethics committee) by use of ELISA (Quanta Lite HMGCR, Inova Diagnostics) on 3 banked serum samples obtained (*a*) before onset of symptoms, (*b*) when the patient presented with muscle weakness, and (*c*) after treatment. Anti-HMGCR antibodies were absent before symptoms and increased to 100 U (cutoff 20 U) when the patient presented with symptoms. The antibodies decreased to 0.8 U after immunosuppressive treatment. Fig. 1 shows a timeline of symptoms, treatment, CK, and anti-HMGCR antibodies.



Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the September 2015 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol61/issue9> and follow the link to the Clinical Case Study and Commentaries.

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Clinical Case Study

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