

Statin Myopathy

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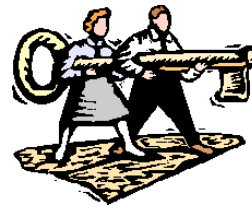
Learning Objectives

- Correlate anatomy and the patients' signs and symptoms in order to locate the neuromusculoskeletal lesion(s) and properly record the findings.
- Elicit a neuromusculoskeletal patient history and record the subjective findings in order to perform differential diagnosis procedures and determine use of objective testing.

Learning Objectives

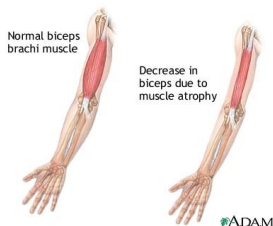
- Perform neuromusculoskeletal evaluation procedures and record the objective findings in order to make an assessment/diagnosis of piriformis syndrome.
- Organize a clinical thought process while performing a neuromusculoskeletal evaluation of a patient with statin myopathy and piriformis syndrome.

Opening Statement ...



- Diagnosis is the key to successful treatment!

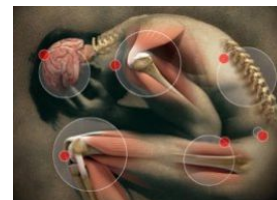
Myopathy



- The myopathies are neuromuscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber.


Myopathy

- Other symptoms of myopathy can include muscle cramps, stiffness, and spasm.



Myopathy

Myopathies can be inherited (such as the muscular dystrophies) or acquired (such as common muscle cramps).




NIH: National Institute of Neurological Disorders and Stroke. What is Myopathy. <http://www.ninds.nih.gov/disorders/myopathy/myopathy.htm>.

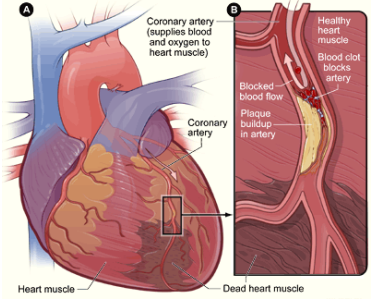
- **Statins (or HMG-CoA reductase inhibitors)** are a class of drugs used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver, which produces about 70 percent of total cholesterol in the body.
- Lewington S, Whitlock G, Clarke R et al. (December 2007). "Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths". *Lancet* **370** (9602): 1829–39.

Cholesterol and Cardiovascular Disease

- Increased cholesterol levels have been associated with cardiovascular disease (CVD).
- Lewington S, Whitlock G, Clarke R et al. (December 2007). "Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths". *Lancet* **370** (9602): 1829–39.


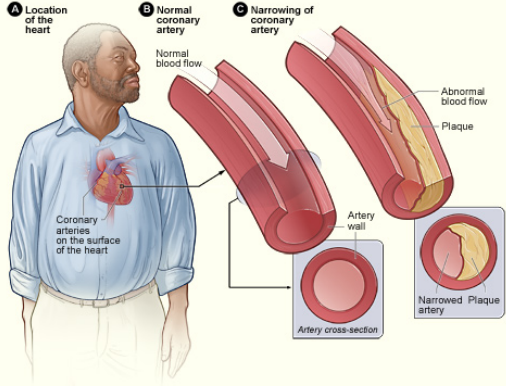


Coronary Artery Disease

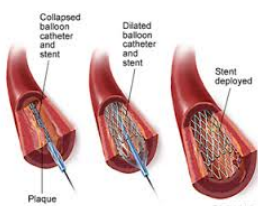


Coronary Heart Disease

- Hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors represent the most successful class of drugs for the treatment of hypercholesterolaemia and dyslipidaemia implicated in the pathogenesis of coronary heart disease and atherosclerosis.

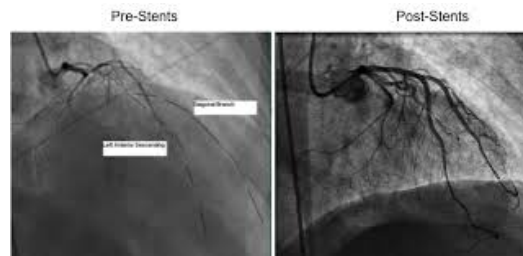



Angioplasty



- Angioplasty can restore blood flow to the heart. During the procedure, a thin, flexible catheter (tube) with a balloon at its tip is threaded through a blood vessel to the affected artery. Once in place, the balloon is inflated to compress the plaque against the artery wall. This restores blood flow through the artery.

Pre and Post Stent Images



Benefits of Statins

- *Statins appear to drive down the risk of heart attack or stroke by lowering the levels of fatty deposits circulating in the bloodstream. Research suggests that the drugs dampen inflammatory processes that can prompt deposits of plaque to break away from blood vessel walls and cause sudden blockages of arteries leading to the heart or brain.*
- JOHN D. ABRAMSON. Harvard School of Medicine

Adverse Drug Reactions

- However, the popular profile of statins in terms of efficacy has been maligned by its adverse events. The myotoxicity, ranging from mild myopathy to serious rhabdomyolysis, associated with HMG-CoA reductase inhibitors, during treatment of hypercholesterolaemia is of paramount importance.
- Tiwari A, Bansal V, Chugh A, Mookhtiar K. Statins and myotoxicity: a therapeutic limitation. *Expert Opin Drug Saf.* 2006 Sep;5(5):651-66.

Caveat Emptor

- Perhaps more dangerous, statins provide false reassurances that may discourage patients from taking the steps that actually reduce cardiovascular disease.
- According to the World Health Organization, 80 percent of cardiovascular disease is caused by smoking, lack of exercise, an unhealthy diet, and other lifestyle factors.
- Statins give the illusion of protection to many people, who would be much better served, for example, by simply walking an extra 10 minutes per day.

JOHN D. ABRAMSON and RITA F. REDBERG. Don't Give More Patients Statins. *NYT.* Published: November 13, 2013

Physician Denial

Eighty-seven percent of patients reportedly spoke to their physician about the possible connection between statin use and their symptom.



Physician Denial

- Patients reported that they and not the doctor most commonly initiated the discussion regarding the possible connection of drug to symptom (98% vs 2% cognition survey, 96% vs 4% neuropathy survey, 86% vs 14% muscle survey; $p < 10^{-8}$ for each).
- Physicians were reportedly more likely to deny than affirm the possibility of a connection.

Physician Denial CONCLUSIONS

- Since low reporting rates are considered to contribute to delays in identification of adverse drug reactions (ADRs), findings from this study suggest that additional putative cases may be identified by targeting patients as reporters, potentially speeding recognition of ADRs.
- Golomb BA, McGraw JJ, Evans MA, Dimsdale JE. Drug Saf. 2007;30(8):669-75. Physician response to patient reports of adverse drug effects: implications for patient-targeted adverse effect surveillance.

Muscle-Related Adverse Effects(MAE)

- Three hundred fifty-four patients (age range 34-86 yrs) who self-reported muscle-related problems associated with statin therapy.



- Pharmacotherapy. 2010 Jun; 30(6):541-53.

Muscle-Related Adverse Effects(MAE)

- Patients with perceived statin-associated MAEs completed a survey assessing statin drugs and dosages; characteristics of the MAEs; time course of onset, resolution, or recurrence; and impact on quality of life (QOL).

Quality of Life


- The best way of approaching quality of life measurement is to measure the extent to which people's 'happiness requirements' are met (those requirements which are a necessary, although not sufficient, condition of anyone's happiness) those 'without which no member of the human race can be happy.'
- McCall, S.: 1975, 'Quality of Life', Social Indicators Research 2, pp 229-248.

Muscle-Related Adverse Effects(MAE)

- Higher potency statins reproduced MAEs in 100% of 39 rechallenges versus 73% (29/40) with lower potency rechallenges ($p < 0.01$).
- Time course of onset after statin initiation varied (median 14 wks); some MAEs occurred after long-term symptom-free use.
- Cham S, Evans MA, Denenberg JO, Golomb BA. Statin-associated muscle-related adverse effects: a case series of 354 patients. Pharmacotherapy. 2010 Jun;30(6):541-53.

Muscle-Related Adverse Effects(MAE)


- Recurrence with rechallenge had a significantly shorter latency to onset (median 2 wks).
- The MAEs adversely affected all assessed functional and QOL domains.



Muscle-Related Adverse Effects(MAE)

CONCLUSION:

- This study complements available information on the properties and natural history of statin-associated MAEs, affirming dose dependence and strong QOL impact.



Cham S, Evans MA, Denenberg JO, Golomb BA. Statin-associated muscle-related adverse effects: a case series of 354 patients. *Pharmacotherapy*. 2010 Jun;30(6):541-53.

Muscle-Related Adverse Effects(MAE)

CONCLUSION:

- The data indicating a dose-dependent relationship between MAE risk and recurrence suggest lower potency statins or discontinuation may bear consideration for ameliorating symptoms.
- Cham S, Evans MA, Denenberg JO, Golomb BA. Statin-associated muscle-related adverse effects: a case series of 354 patients. *Pharmacotherapy*. 2010 Jun;30(6):541-53.

Case Report

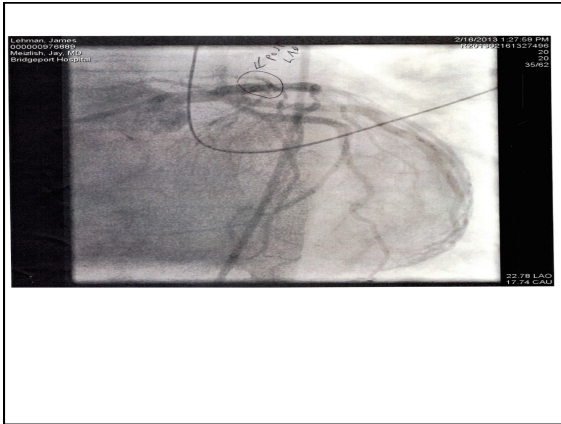
- A 63 year-old professor experienced a myocardial infarct on February 16, 2013. He endured severe chest and upper thoracic pain for a period of 3 hours due complete occlusion of the left anterior descending coronary artery, which is known as the “widow maker.” Aspirin and nitroglycerine in the ER did not reduce the pain and morphine reduced the pain from 10/10 to 9.7/10.



Case Report

Angioplasty (One stent implant) restored circulation and the patient recovered without signs of permanent heart damage.

Fluoroscopic angiogram showing restored blood flow after stent placement. The image displays the coronary artery system with a stent implanted in the left anterior descending artery, restoring blood flow. Technical details in the top left corner include: 'Lithium 24000', '020000078695', 'Newark, NJ 07102', 'Bridgeport Hospital'. Technical details in the top right corner include: '27F000012', '100 550 100', 'P5097500', '10 132 74300', '2000'. Technical details in the bottom right corner include: '70.50 LAC', '10.00 CAL', '2000'.



Muscle Pain and Piriformis Syndrome

Approximately 2-4 weeks post surgery the patient experienced severe muscle pains and piriformis syndrome

©MMIG 2005

Clinical Challenge

- Please list the subjective and objective findings that would differentiate lumbar radiculopathy and piriformis syndrome due to piriformis compression of the sciatic nerve.

Piriformis Syndrome

- Piriformis syndrome is a neuromuscular condition characterized by a constellation of symptoms that includes hip and buttock pain. The pain is often referred down the back of the leg, sometimes into the medial foot.

Kirschner JS, Foye PM, Cole JL. Piriformis syndrome, diagnosis and treatment. Muscle Nerve. 2009;40(1):10-18. doi: 10.1002/mus.21318.

Symptoms of Piriformis Syndrome

- Pain in buttocks and affected limb with sitting and rising to stand from seated or squatting position
- Pain and/or paresthesias from sacral area to affected limb
- Change of position does not relieve pain completely
- Increasing pain after sitting for longer than 15-20 minutes (most common symptom)

Symptoms of Piriformis Syndrome

- Weakness in ipsilateral lower extremity
- Contralateral SIJ pain
- Headaches
- Neck pain
- Abdominal, pelvic, and inguinal pain
- Dyspareunia in women
- Pain with bowel movements

Signs of Piriformis Syndrome

- Tenderness in region of SIJ, greater sciatic notch, and piriformis muscle
- Palpable mass in ipsilateral buttock
- Asymmetrical weakness of affected limb
- Presence of Pace, Piriformis, Frieberg, Lasegue, and Beatty signs
- Ipsilateral leg length inequality
- Gluteal atrophy (chronic cases only)

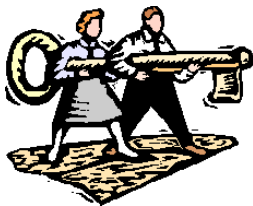
Evaluation and Management of Drug Induced Myopathy and Piriformis Syndrome

- Statin holiday and determine response
- Resume statin medications with reduced dosage and determine response
- Change from one statin medication to another and determine response
- If patient is allergic to statins it might be necessary to discontinue and switch to niacin
- Dietary changes, regular exercise, and stress control is mandatory

Discussion

- Describe your experiences with the evaluation and management of patient's presenting for painful neuromusculoskeletal conditions and taking statin medications...

Closing Statement ...



- Diagnosis is the key to successful treatment!

