CASE PRESENTATION

A 75 y.o man, heavy smoker, drinker, well controlled DM with advanced atherosclerosis (CABG) 20 year ago, presented with progressive proximal muscle weakness, oliguria and hematuria one month after left subclavian stenting.

Admitted as a case of Guillain–Barré syndrome (GBS) and IV IG has been started.

Consulted to Internist

IMPRESSION AND DIFFERENTIAL DIAGNOSIS

AKD due to contrast nephropathy

Acute ischemic stroke

Acute renal artery stenosis

??????? Guillain–Barré syndrome (GBS)

MEDICATIONS AFTER SUBCLAVIAN ARTERY PCI

Zyllt 75 BID

ASA 80

Rosuvastatin 40

Nitrocantin 2.6 BID

Metformin 500 bid

Concor 2.5

PHYSICAL EXAM

V/S

Stable

Lung bilateral coarse rales

Others completely normal except for :

N/E : bilateral upper muscle power 3/5

Lower 2/5

Babinski mute

Hoffman's reflex -ve

LAB DATA

CBC: Hb 13 with mild megaloblastosis, (MCV 99.7, MCH 34, MCHC 34.2) platelets 120-140 VAIABLE, NI wbc and diff.

BUN 50, Creat. 2.8 (nl at the time of stenting)

ESR 48 CRP 12, 1 : 2

Lipid profiles: TC 71 HDL 19 LDL 40

L.Profiles at the time of stenting : TG 99 , TC 98, HDL 32, LDL 50

CPK 31480, LDH 1260

LFT: AST 790, ALT 205 Alb 3.1 Alk. P 166

UA: Blood 3+ RBC 3-4 Suger 1+ protein 1+

?? DIAGNOSIS

Myopathy

Statin induced vs malignancy associated

rhabdomyolysis

WORK UP

chest spiral CT : interstitial lung disease

Brain CT NL

Abdominal sonography completely normal

Upper Endoscopy normal , Bx. Mild chronic gastritis

Colonoscopy: Cecal pedunculated polyp 1x0.7 mm

Pathology : Adenomatous polyp, tubular type with focal low grade dysplasia, stalk is free. No malignancy

Echo; mild pulmonary hypertension otherwise normal

NCV, EMG

Normal NCV and distal latencies and amplitudes of all tested nerves

Absent Hoffmann's reflexes (Hoffmann's sign is a finding elicited by a reflex action which verifies the presence – or absence – of problems in the corticospinal tract, including myelopathy).

Myopathic process in all tested muscles.

Denervation potential and CRD (complex repetitive discharge) in almost all tested muscles.

Impression: Irritable myopathic process in both upper and lower limbs.

polymyositis vs inflammatory myopathy ???

IMMUNOLLOGY

Immunology

Test	***Result***	***Flag***	***Unit***	***Method***	***Reference Interval***
Myositis-EL Profile 3					
Mi-2	7			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
Ku	2			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
PM-SCL100	2			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
PM-SCL75	2			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
Jo-1	2			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
SRP	12			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive
PL-7	12			Immunoblot	Intensity----Class-------Explanation 0-5 o Negative 6-10 (+) Borderline 11-25 + Positive 26-50 ++ Positive 51-256 +++ Strong Positive

Checked by: **Lab Director: Dr.H.Roozbehi M.D**

Muscle biopsy had not done.

HMG-CoA reductase Abs was not available

TREATMENT AND PROGRESSION

Discontiued IV IG

Methyl-prednisolone pulse therapy

Oral steroid with fast tapering

Recovered muscle weakness, normalized CPK, LDH, LFT, and kidney function tests

HMG-COA REDUCTASE ANTIBODIES

Statins are among the most commonly prescribed medications that significantly reduce cardiovascular risk in selected individuals. However, these drugs can also be associated with muscle symptoms ranging from mild myalgias to severe rhabdomyolysis. Although statin myotoxicity is usually self-limited, in some instances statin-exposed subjects can develop an autoimmune myopathy typically characterized by progressive weakness, muscle enzyme elevations, a necrotizing myopathy on muscle biopsy, and autoantibodies that recognize 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the pharmacologic target of statins.

These antibodies are also found in some autoimmune myopathy patients without statin exposure. Importantly, anti-HMGCR antibodies are not found in the vast majority of statin-exposed subjects without autoimmune myopathy, including those with self-limited statin intolerance. Thus, testing for these antibodies may help differentiate those with self-limited statin myopathy who recover after statin discontinuation from those with a progressive statin-associated autoimmune myopathy who typically require immunosuppressive therapy.

CLINICAL POINTS OF STATIN INDUCED MYOPATHIES

1-Statins are the primary class of medication used to lower s. cholesterol for both primary and secondary prevention of CAD.

2-Statins are both effective and safe but muscle toxicity remains a concern, severe myonecrosis leading to rhabdomyolysis is unusual. 0.1%

- Muscle syndromes include: myalgias, myopathy, myositis and muscle injury

PATHOGENESIS

Mechanism I not well understood but genetic studies have provided new insights.

Statins inhibit the conversion of HMG-CoA to mevalonic acid that is an important early step in cholesterol synthesis.

Individual statins may have distinct effects on the synthesis of coenzyme Q10, ubiquinone which plays an important role in muscle cell energy productions.

A reduction in ubiquinone in skeletal muscle may contribute to statin induced muscle injury.

Long-term Rx with simvastatin (10-40 mg for>12 mo) reduced ubiquinone and decreased maximal mitochondrial oxidative phosphorylation capacity.

CLINICAL SIGNIFICANCES

Massive rhabdomyolysis with AKD was not seen in patients without other risk factors eg:

Concurrent drug Rx with niacin, macrolide Abs, digoxin, antifungal and warfarin, cyclosporin

No statistical difference in the incidence of rhabdomyolysis among atorvastatin, pravastatin or simvastatin.

Low risk: hydrophilic statins ??

Hypothyroidism, hypovitamin D, renal failure acute vs chronic