

# Acute Iatrogenic Rhabdomyolysis and Guillan-Barre' Syndrome: A Dangerous Association

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## Abstract

Guillan-Barré Syndrome (GBS) is an acute, symmetrical polyneuropathy with a clinical manifestation of flaccid paralysis with areflexia and variable sensory disturbance. GBS has an incidence of 1-2 cases/100.000 inhabitants for year. The pathological spectrum of GBS includes Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN). We report a case of an 81-year-old man with GBS (subtype AMSAN), secondary to a previous *Mycoplasma Pneumoniae* infection, who presented with an elevation of Creatin Kinase (CK) serum levels, and worsened by a co-administration of statins and clarithromycin. By our knowledge there are few cases in the literature in which the association of these drugs contributed to worsening GBS.

**Keywords:** Guillan-Barré syndrome; Simvastatin; Clarithromycin; Rhabdomyolysis; AMSAN

## Introduction

GBS is an acute demyelinating disease of peripheral nerves, which usually follows viral or bacterial illness. There is considerable evidence that GBS is an immune-mediated disease often due to a gastrointestinal or, more rarely, to a lung infection [1]. However, the exact pathogenesis remains unclear. In this case report, we describe a patient in which a preceding lung infection, associated with a co-administration of simvastatin and clarithromycin, resulting in rhabdomyolysis and acute inflammatory demyelinating polineuropathy.

## Case Report

An 81-year-old Caucasian man presented to the emergency department complaining of dyspnea, chest and abdominal pain and severe and progressive weakness for the last 30 days.

His medical history was significant for hypertension, BPCO, diabetes type 2, gout, mild renal failure, heart failure after myocardial infarction (ejection fraction 54%) and coronary heart disease. Two weeks before admission in our department, the same patient had been admitted to for dyspnoea, chest pain and elevated temperature. This clinical condition has due to pneumonia, and was treated with clarithromycin 500 mg twice a day. He had been taking, among other drugs, simvastatin 20mg/once/day for almost one year before.

The patient, after 14 days of discharge returned to the hospital, with classical signs of rhabdomyolysis. Laboratory chemistry revealed a significant elevation of CK (maximum dosage detected 3956 U/l; normal range 60-190 UI/l), myoglobin (maximum 5049 ng/ml; normal range  $\leq$  90 ng/ml) and myoglobinuria (maximum 1010 mg/L; normal range 4 mg/L); also GPT-ALT (maximum 142 UI/l; normal range 9-63 UI/l), GOT-AST (maximum 77 U/l; normal range 13-41 UI/l) and GGT (maximum 175U/l; normal value  $\leq$  55U/L) levels were raised. Neurological examination showed a moderate tetraparesis, muscles very painful to pressure, and tendon reflexes unremarkable in the upper extremities; instead, in the legs, tendon reflexes could not be elicited. Needle electromyography (EMG) did not reveal a typical myopathic pattern, but during the routine F-wave evaluation we

recorded the presence of A-wave. The electroneurography displayed a motor-sensitive predominantly axonal poliradiculoneuropathy. The examination of cerebro-spinal fluid (CSF) showed a moderate damage of emotion-encephalic barrier with an albumin-citologic dissociation and systemic production of 6 oligoclonal immunoglobulins. The simvastatin was stopped and treatment with forced urine alkalinization was started. A diagnosis of GBS syndrome was made and the patient was started intravenous immunoglobulins therapy with prompt improvement: the paresis improved and the serum CK and myoglobin dropped to normal levels ( $<$ 159U/l and  $<$ 85 ng/ml respectively).

## Discussion

Usually, one-half to two-third of GBS patients report antecedent infections, and *Campylobacter jejuni*, Cytomegalovirus (CMV), Epstein-Barr virus (EBV) and *Mycoplasma pneumoniae* are recognised triggering agents of GBS [2]. Moreover, *Mycoplasma Pneumoniae* infection appears to be associated strongly with GBS cases (15%) [3]. Moreover, marked raised levels of CK has been recognized and documented in GBS, correlating with occurrence of pain, [4] which was a presenting symptom in this patient. Raised level of CK can be a feature of the early course of GBS, and may cause diagnostic confusion with other conditions, particularly if the clinical picture is not typical. In fact, rhabdomyolysis is also a rare side-effect of 3-hydroxy-3-methylglutaryl coenzyme A (HMGA-CoA) reductase inhibitors. Co-medication with inhibitors of the CYP34A pathway-as Clarithromycin- may increase this risk of rhabdomyolysis [5]. In our case, the patient, 3 weeks before

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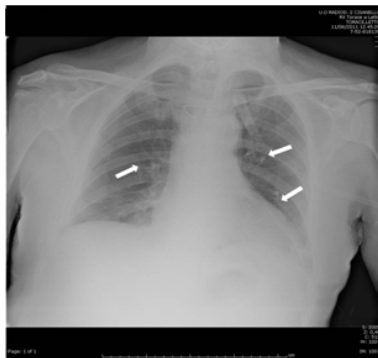
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the first admission to the hospital, had presented dyspnea and chest pain, so atypical pneumonia was suspected and diagnosis of pneumonia was made based with clinical and instrumental texts (including chest X-ray (Figure 1), High Resolution Computer Tomography (HRCT) (Figure 2), tracheo-bronchial endoscopy with bronchial aspirated for cytologic and bacteriological examination). In addition, our patient started having symptoms of increased fatigue, shortness of breath, progressive and severe diffuse myalgia, cramps, exercise intolerance weakness, functional disability (inability to raise arms and legs) with the beginning of clarithromycin therapy. Clarithromycin, has been implicated in other many reports of statin-induced rhabdomyolysis [6,7] but was used only after signs and symptoms had developed. In the literature several reports show an important rhabdomyolysis following the co-administration of statins and macrolide antibiotics (such as clarithromycin or erythromycin), or other drugs that inhibit the cytochrome CYP3A4 pathway, but most of patients described in these studies were treated with high doses of statins (i.e. simvastatin 80 mg/die). Our case demonstrates that even low-dose therapy with statins may result in severe side effects, when combined with CYP3A4-inhibiting drugs, especially in patients with kidney failure. Moreover, the previous pneumoniae could be triggering the GBS that was exacerbated by the use of dangerous concurrent medication with simvastatin and clarithromycin. In fact, the electromiographic pattern as considered the presence of rhabdomyolysis, but it was consistent with an AMSAN. The EMG in fact showed a nerve damage with a widespread denervation activity in progress on both left and right tibial anterior muscles, on the right side of the diaphragm and on the I first dorsal interosseous, suggestive of a motor-sensitive predominantly axonal polyradiculoneuropathy (Figure 3).

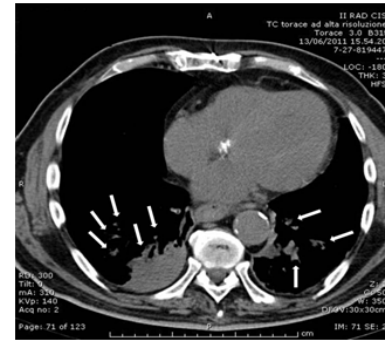
In addition to neurophysiological examinations, that confirm this clinical picture, we have the result of CSF's analysis. From a simple point of view, a sudden muscle denervation could account for release of muscle enzymes in acute axonal polyradiculoneuropathies, up to seven times of the upper limit of normal; however, in a previous report Scott and colleagues [8] highlighted a relative sparing of small autonomic fibres in early phases of illness in a patient presenting with acute rhabdomyolysis and later developing an atypical Guillain-Barré axonal neuropathy. That makes unlikely an elevation of muscle enzymes as epiphenomena of severe denervation in progress.

## Conclusion

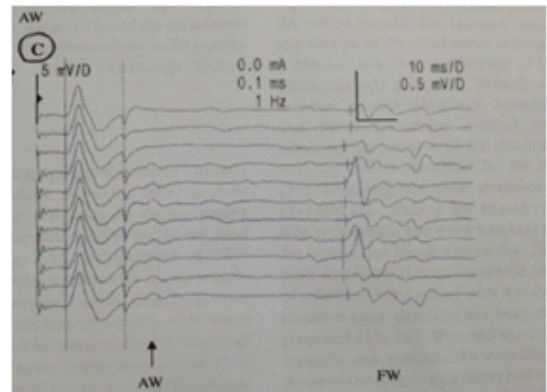
In conclusion, by our knowledge, this is the first case in which GBS, due to a preceding lung infection, was strongly exacerbated by a severe rhabdomyolysis for a co-administration of simvastatin at low



**Figure 1: Chest X-ray.** Consolidation in the right emithorax and interstitial spread thickening.



**Figure 2: High Resolution Computer Tomography (HRCT).** Inflammatory-flogistic finding. Note the thickening of bronchial walls, the signs of phlegmatic infarction and soft mass with nodular and ramified morphaology.



**Figure 3: A-waves records.** Set of A-waves recorded in our case of acute form of polyradiculoneuropathy.

dose, and clarithromycin. Moreover, our case shows how is important to evaluate the use of statins in association with others CYP3A4 (Cytochrome P450 3A4) inhibiting drugs, particularly in patients with prior infective conditions, renal insufficiency or other risk factors such as diabetes, heart failure, age>80 years. It is crucial, in particular among physicians, to have an awareness of the interaction's risk associated with these conditions because the early diagnosis and aggressive therapy may reduce the comorbidity and mortality and could result in rapid improvement, as shown in the present patient. In particular it is important to make an early diagnosis, through the use of laboratory tests and neurophysiological tests, and it's also important to know the medical history of the patient and his treatment history to suspend or avoid, in case of suspected rhabdomyolysis, any dangerous associations.

## References

1. Pritchard J, Hughes RA (2004) Guillain-Barré syndrome. *Lancet* 363: 2186-2188.
2. Hadden RD, Karch H, Hartung HP, Zielasek J, Weissbrich B, et al. (2001) Preceding infections, immune factors, and outcome in Guillain-Barré syndrome. *Neurology* 56: 758-765.
3. S Sinha, KN Prasad, D Jain, CM Pandey, S.Jha (2007) Preceding infections and anti-ganglioside antibodies in patients with Guillain-Barré syndrome: a single centre prospective case control study. *Clinical Microbiology and Infection. Clin Microbiol Infect* 2007: 334-337.
4. Ropper AH, Shahani BT (1984) Pain in Guillain-Barré syndrome. *Arch Neurol* 41: 511-514.
5. Wagner J, Suessmair C, Pfister HW (2009) Rhabdomyolysis caused by co-medication with simvastatin and clarithromycin. *J Neurol* 256: 1182-1183.

6. Schreiber DH, Anderson TR (2006) Statin-induced rhabdomyolysis. J Emerg Med. 2006: 177-180.
7. Molden E, Andersson KS (2007) Simvastatin-associated rhabdomyolysis after coadministration of macrolide antibiotics in two patients. Pharmacotherapy 27: 603-607.
8. Scott AJ, Duncan R, Henderson L, Jamal GA, Kennedy PG (1991) Acute rhabdomyolysis associated with atypical Guillain-Barré syndrome. Postgrad Med J 67: 73-74.

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