Said et al., J Clin Case Rep 2013, 3:8
DOI: 10.4172/2165-7920.1000290

Journal of Clinical Case Reports

Case Report Open Access

Pyridostigmine-Induced High Grade SA-Block in a Patient with Myasthenia Gravis

Sarmad Said[1]*, Haider Alkhateeb[1], Chad Cooper[1], Sherif Elhanafi[1], Sayeed Khalillullah[1], Sucheta Gosavi[1] and Zainul Abedin[1,2]

[1]*Department of Internal Medicine, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, Texas, USA*
[2]*Department of Cardiology and electrophysiology, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, Texas, USA*

Abstract

Myasthenia gravis requires a long-term treatment with a parasympathomimetic agent, which may result in bradycardia and asystole. Pharmacologic treatment with a reversible inhibitor of Inosine Monophosphate Dehydrogenase (IMPDH) and Methylprednisolone are seen to improve the muscular symptoms but may reinforce potential bradyarrhythmias. This potential side effect can be treated with the levo isomer of atropine, Hyoscyamine, or Glycopyrollate in an intact conduction system.

Case presentation: A 70-year old Caucasian female patient with a family history of myasthenia gravis presented with mild weakness of the bilateral facial muscles, moderate dysarthria, dysphagia, diplopia predominantly on the right side and difficulty tracking ocular movements bilaterally. The treatment with pharmacological agents was initiated. Subsequently she developed asymptomatic bradycardia and SA-block. An improvement on Hyoscyamine failed to appear. A dual chamber pacemaker was placed.

Conclusion: In symptomatic bradycardia or asymptomatic, however, significant high grade SA-block in patients with myasthenia gravis the insertion of a permanent pacemaker can be the definitive solution.

Introduction

Myasthenia gravis is an autoimmune neuromuscular disease that causes muscle weakness and fatigability with activity. The circulating antibodies block nicotinic acetylcholine receptors at the postsynaptic neuromuscular junction [1] causing an inhibitory effect.

Myasthenia gravis is treated medically with acetylcholinesterase inhibitors and/or immunosuppressants, and with thymectomy especially in patients with thymoma. Bradyarrythmias have been reported in patients treated with Acetylcholine esterase inhibitors for myasthenia gravis [2].

We present a case of a 70-year-old Caucasian female with myasthenia gravis, who developed bradycardia and significant SA-block with the initiation of pyridostigmine.

Case Presentation

Seventy-year-old Caucasian female without significant past medical history presented with 3-year history of weakness, diplopia, dysphagia and fatigue. She reported a family history of Myasthenia Gravis (MG) in her mother and two brothers.

Physical examination revealed bilateral facial paresis, moderate dysarthria, dysphagia and diplopia. Muscle power was 3/5 in lower extremities without upper extremities, sensory or sphincter involvement. Reflexes were normal. Taking the family history into consideration a tensilon test was performed using 1 mL of edrophonium (10 mg/mL) on this patient with rapid improvement after the infusion of the drug. We observed a significant improvement in her ptosis and jaw weakness. Acetylcholine Receptor Antibodies (AChR-Ab) and MuSK-protein antibodies were detected.

A diagnosis of MG was confirmed. Thymoma was excluded by CT-chest. Cardiac catheterization and coronary angiography were reported to be normal.

Pyridostigmine 30 mg orally Q 4 hrs and methylprednisolone 1000 mg daily were administered. Her clinical symptoms began to improve after the third day. On the 4th/5th day, patient developed asymptomatic bradycardia and 5.9 second asystole consistent with the diagnosis of SA-block.

To further avoid increase in the Pyridostigmine dose the treatment with mycophenolate mofetil could be extended. However due to its delayed onset of action in relation to the subacute developed bradycardia mycophenolate mofetil was not given. In contrast Glycopyrrolate was added to counteract the pyridostigmine side effects; however, it did not improve bradycardia. To minimize acute complications and to counteract the progressive Pyridostigmine-induced bradycardia, although no myasthenic crisis was observed, a five-day-course of IVIG (IgG) 400 mg/kg daily was given. Additionally Hyoscyamine 0.125 mg was initiated.

Despite these measures significant bradycardia and pauses continued (Figure 1). A dual chamber permanent pacemaker was implanted on eleventh day and pyridostigmine dose was increased. Neurologic symptoms continued to improve.

Myasthenia gravis is an autoimmune neuromuscular disorder with generalized muscle involvement resulting in weakness and fatigue [2].

Figure 1: Telemetry tracings on the 5th day of the hospitalization showing SA-block of 5.9 seconds.

***Corresponding author:** Sarmad Said, MD, Department of Internal Medicine, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, Texas, 4800 Alberta Ave, El Paso, TX, 79905, USA, Tel: 310-956-0107; E-mail: sarmad.said@ttuhsc.edu

Received June 27, 2013; **Accepted** July 08, 2013; **Published** July 11, 2013

Citation: Said S, Alkhateeb H, Cooper C, Elhanafi S, Khalillullah S, et al. (2013) Pyridostigmine-Induced High Grade SA-Block in a Patient with Myasthenia Gravis. J Clin Case Rep 3: 290. doi:10.4172/2165-7920.1000290

The incidence is approximately 1:40000 per year with a maximum prevalence in the 3rd and 4th decade in women and in the fifth decade in men [3]. There is a slight genetic predisposition associated with different HLA types. About 60-70% of the patients have an abnormality of the thymus and 20% have a thymoma [4].

Discussion

The main stay in MG treatment is acetylcholinesterase-inhibitors and/or immunosuppressants, and with thymectomy in patients with thymoma. Bradyarrythmias have been reported in patients treated with Acetylcholine-esterase-inhibitors [1,2].

The association between myasthenia gravis and cardiovascular diseases has been known for many years, but no specific etiologic link has been established. Most of the data has been derived from either case series or case reports [3].

Guglin et al. have shown cardiac involvement in patients with myasthenia gravis [4]. In 16% of the patients an atrial fibrillation, atrioventricular blocks, asystole, and sudden death were attributed to possible myocarditis from the autoimmune involvement. Cardiovascular involvement occurred more in patients with thymoma (50%), compared to those without thymoma (12%). Arrhythmias were common clinical manifestations and these patients were noted to be at an increased risk of sudden death. However, some of the patients in these studies were not tested for coronary artery disease; their EKG changes could not be attributed to cardiac involvement due to myasthenia gravis.

In 2008 Gehi et al. [5] reported case of myasthenia gravis with a pyridostigmine-induced high grade AV block with episodes of syncope. This patient was subsequently treated with hyoscyamine and the AV block disappeared completely without further syncope, and therefore a permanent pacemaker was avoided. However, our patient despite therapy with hyoscyamine continued to have significant pauses thus requiring permanent pacemaker.

Following a similar presentation from a case report the addition of Immunoglobuline (IVIG) in our patient was a part of the treatment. In this reported case in 2004 Vats et al. [6] treated a patient with atrioventricular block from myasthenia gravis, with a favorable course, with immunosuppressive therapy and plasmapheresis.

To our knowledge, pyridostigmine-induced high grade AV block has been reported, yet pyridostigmine SA-exit block and sinus-arrest-block resulting in prolonged pauses in a patient with MG has not been reported previously.

It is possible that the same autoimmune process that causes MG also affects the SA-node resulting in clinical manifestations of sick-sinus-syndrome and this effect might be aggravated by the use of pyridostigmine as in our patient. Nonetheless, pyridostigmine as a significant part of the myasthenia gravis therapy can be continued after the insertion of a permanent pacemaker, if that complication was to occur.

References

1. Fulton B, Markham A (1996) Mycophenolate mofetil. A review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in renal transplantation. Drugs 51: 278-298.
2. McGrogan A, Sneddon S, de Vries CS (2010) The incidence of myasthenia gravis: a systematic literature review. Neuroepidemiology 34: 171-183.
3. Conti-Fine BM, Milani M, Kaminski HJ (2006) Myasthenia gravis: past, present, and future. J Clin Invest 116: 2843–2854.
4. Guglin M, Campellone JV, Heintz K, Parrillo JE (2003) Cardiac disease in myasthenia gravis: a literature review. J Clin Neuromuscul Dis 4: 199-203.
5. Gehi A, Benatar M, Langberg J (2008) Treatment of pyridostigmine-induced AV block with hyoscyamine in a patient with myasthenia gravis. J Cardiovasc Electrophysiol 19: 214-216.
6. Vats HS, Richardson SK, Pulukurthy S, Olshansky B (2004) Pericarditis in myasthenia gravis. Cardiol Rev 12: 134-137.