IVIg for Thymoma-Associated Pseudo-Obstruction: Report of Successful Treatment

David L. Greenburg^a Clifton C. Mo^a Paul A. Hemmer^b

^aUnited States Army, Walter Reed Army Medical Center, Washington, D.C., ^bUnited States Air Force, Uniformed Services University of the Health Sciences, Bethesda, Md., USA

Dear Sir,

We report the case of a 36-year-old white male from rural Alaska with severe idiopathic gastroparesis and intolerance to oral nutrition who was referred to our institution. His primary concern was for his gastrointestinal symptoms which included abdominal fullness, nausea, vomiting, and stools as infrequent as every 3 weeks. Other symptoms over the preceding 7 months included intermittent diplopia, dysgeusia, and sicca symptoms. Radiologic evaluations including chest and abdominal plain films, CT scans of the sinuses, abdomen, pelvis, and MRI of the brain had been normal. A radionuclide gastric emptying study showed 100% of the radio-tracer retained in the stomach at 90 min. EGD and colonoscopy were notable only for mild gastritis without evidence of *Helicobacter pylori*. Repetitive peripheral nerve stimulation testing and an extensive laboratory evaluation were normal. Therapies for his GI symptoms, including histamine blockers and osmotic and stimulant laxatives, were minimally effective. He lost over 50 lb and required multiple admissions for intravenous fluids and parenteral nutrition.

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At our institution ophthalmology, neuro-ophthalmology, neurology, and gastroenterology consults were initiated. A radionuclide gastric emptying study confirmed complete immotility. Evaluation of diplopia with prism testing revealed fluctuating levels of exotropia and hypertropia in the left eye. CT of the chest, abdomen, and pelvis revealed a 6 × 6 × 3 cm anterior mediastinal mass which was found to be a stage 1 thymoma. His postoperative course was complicated by a hemothorax and hypotension. Cosyntropin stimulation testing on postoperative day 1 revealed relative adrenal insufficiency for which he received intravenous hydrocortisone 100 mg three times per day for 7 days. His symptoms persisted postoperatively and he continued to require parenteral fluids and nutrition. Results of a gastric emptying examination on postoperative day 11 were unchanged. Repeat prism testing after IM injection of neostigmine 1.5 mg and atropine 2 mg resulted in mild improvement in ocular discordance. Pyridostigmine 60 mg every 8 h was started. The only improvement after 2 days was a mild reduction in diplopia.

We believed our patient had thymoma-associated pseudo-obstruction. This was first reported in 1983 in a patient presenting with altered mental status and antibodies against the nicotinic acetylcholine receptor (N-AChR) [1]. Thymectomy can

be a successful treatment for pseudo-obstruction, but recovery as late as 6 months after surgery has been reported [2–4]. Anderson et al. [5] described 2 cases of pseudo-obstruction, diplopia, dysgeusia, and antibodies against N-AChR who underwent thymectomy followed by pyridostigmine. Pseudo-obstruction resolved rapidly in one patient, but the second patient required resection of an immotile segment of duodenum prior to recovering. Histologically, the duodenum had inflammatory cell infiltrates and degenerate neurons in the myenteric plexus. Viillard et al. [6] presented a patient with thymoma-associated neuromyotonia, pseudo-obstruction and elevated titers of voltage-gated potassium channel antibodies who failed to improve with thymectomy and pyridostigmine. This patient underwent plasma exchange with resolution of the pseudo-obstruction.

Our patient was unique in that he was seronegative. Negative tests included N-AChR antibodies, voltage-gated calcium channel antibodies, type 1 antineuronal nuclear autoantibodies, ANA, ANCA, anti-Ro, anti-La, anti-double-stranded DNA, anti-RNP, Jo-1, anti-SCL-70, and anti-histone antibodies. Voltage-gated potassium channel antibodies and anti-muscle specific tyrosine kinase receptor antibody titers were not obtained. We considered the diagnosis of ocular myasthenia gravis,

as some improvement in diplopia was noted with anticholinergic agents. However, myasthenia gravis in patients with thymic hyperplasia is almost always associated with anti-N-AChR antibodies [7].

We hypothesized that our patient's ongoing pseudo-obstruction was a paraneoplastic phenomenon due to either circulating autoantibodies or chronic damage to the enteric nervous system [5, 8]. If the former were true, he would potentially respond to immunomodulatory therapy. He had already failed high-dose corticosteroids. We considered plasma exchange and intravenous immunoglobulin (IVIG) because both therapies are effective in many neurological autoimmune processes [9, 10]. We elected to treat with IVIG as our patient could be more easily retreated near his home if necessary. He received IVIG 2 mg/kg over 5 days starting on postoperative day 13. By postoperative day 22, all symptoms were markedly improved, he was tolerating a regular diet, and a third gastric emptying study was normal. He was discharged on postoperative day 23 with instructions to continue pyridostigmine but discontinued it as he had minimal symptoms. Minor complications of IVIG included transient leukopenia and

autoimmune thyroiditis [11]. Neither required therapy and both resolved spontaneously. Follow-up by telephone at 1 year revealed persistent resolution of all symptoms without further treatment. We hypothesized that his rapid recovery was due to IVIG-mediated accelerated clearance of pathogenic autoantibodies. To our knowledge, this represents the first use of IVIG to treat paraneoplastic thymoma-associated pseudo-obstruction. We feel IVIG should be considered as a potential treatment option for future cases of refractory thymoma-associated pseudo-obstruction.

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