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Pulmonary Embolism Associated with Intravenous Immunoglobulin Therapy

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TO THE EDITOR: Intravenous immunoglobulin (IVIG) therapy has gained popularity for the treatment of neuromuscular diseases (i.e., myasthenia gravis, inflammatory myopathy, chronic inflammatory demyelinating polyneuropathy), although adverse events are associated with high-dose IVIG infusions.^{1,2} Common adverse reactions to IVIG therapy are anxiety, headache, fever, chills, chest pain, dyspnea, nausea, and abdominal pain.³ More serious adverse events include anaphylaxis, hemolytic anemia, hepatitis C, and thrombosis.³ Studies have shown documented effects of IVIG on blood rheology. It increases plasma viscosity in a dose-related response and may also activate platelets.²⁻⁴ High-dose IVIG therapy is approximately 24–54 g/d.⁴

Case Report. A 55-year-old white man presented to the emergency department (ED) complaining of chest pain and shortness of breath for 5 days in mid-2002. The patient's past medical history included sleep apnea, hypertension, deep-vein thrombosis (DVT), peripheral neuropathy, and immunosuppressive syndrome. He had no history of diabetes or heart or lung disease, and his family history was noncontributory. Current medications included warfarin for treatment of DVT caused by Port-A-Cath and IVIG for peripheral neuropathy. He also used oxycodone/acetaminophen and amitriptyline as needed. The patient used continuous positive airway pressure for sleep apnea. His last IVIG infusion had been administered 7 days prior to the ED visit. Abnormal laboratory test findings in ED were international normalized ratio (INR) 1.73 (normal 2–3), partial thromboplastin time 45.7 seconds (21–35), pH 7.47 (7.36–7.44), and pO₂ 60 mmHg (90–100). A computed tomography scan of the chest discovered bilateral pulmonary embolism in the right lower and left upper lobes. He was admitted to the hospital with severe stenosis extending to the occlusion of the left subclavian vein, and his left innominate vein was thrombosed by >5 cm.

The patient had a history of thrombosis, and now bilateral pulmonary emboli were noted without obvious triggering factors. Upon further investigation, we found that the patient had been evaluated at another institution for peripheral neuropathy of unknown origin in 2000. He suffered from severe burning, tingling, numbness, and pain in his extremities that was incapacitating when he was not receiving IVIG. He had developed his first DVT in late 2001. At that time, the patient started IVIG infusions twice weekly. Due to cost issues, the infusions were decreased to once a week at the beginning of 2002. After evaluating all potential causes for thrombosis, including the subtherapeutic INR upon admission, IVIG was determined to be the most probable cause of pulmonary embolism according to the Naranjo probability scale,⁵ and the patient was advised to discontinue IVIG therapy. Inpatient treatment for pulmonary embolism included enoxaparin and warfarin and, on discharge, the patient was prescribed subcutaneous enoxaparin 100 mg twice daily for 7 days and warfarin 7.5 mg 1 day per week and 5 mg on all other days, adjusted to an INR goal of 2.5–3.5.

Discussion. To date, there have been <15 cases reported concerning thrombotic events related to IVIG therapy.² Caution should be used when considering IVIG therapy in the geriatric population and patients with known risk factors such as history of pulmonary embolism, DVT, stroke, myocardial infarction, cardiac valve replacement, or low cardiac output.^{1,3}

References

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