Introduction

Purple glove syndrome (PGS) is a rare complication of intravenous phenytoin use. It typically presents with pain, edema, and discoloration at the injection site that spreads to the distal limb. Treatment is supportive, and most cases resolve within days to weeks. Here we present a case of a man who developed symptoms of purple glove syndrome following acute intravenous phenytoin administration.

Case report

A 65-year-old white man with lymphoma involving his central nervous system presented after craniotomy and the excision of a tumor for his first cycle of chemotherapy. His past medical history was significant for peripheral arterial disease status post lower extremity bypass, hypertension, and hyperlipidemia. On hospital day 2 the patient experienced a generalized tonic-clonic seizure, for which he received 1mg of lorazepam and a 1.2g loading dose of intravenous phenytoin through a 20-gauge peripheral intravenous catheter in his left hand. The phenytoin dose was delivered over 80 minutes. Within 2 hours of administration, the patient’s hand became dusky and bluish in color, and the patient complained of pain and weakness. These symptoms began at the injection site but soon spread throughout the left hand. On examination, the patient’s hand was edematous, without blistering, and had a blue-purple discoloration (Figure 1). Motor strength was 3/5 with intact sensation, pulses were 1/2, and capillary refill was less than 2 seconds. The patient was diagnosed with purple glove syndrome (PGS) as a result of intravenous phenytoin and was treated with supportive care. The peripheral intravenous catheter was removed, the hand was elevated, and heat was applied to the area. By the next day the patient’s symptoms were much improved, with complete resolution within days. His serum total and free phenytoin levels were within normal limits during the entire event.

Discussion

PGS is a rare complication of intravenous phenytoin use, with prevalence ranging from 1.7% to 5.9%. It typically presents with pain, edema, and discoloration at the injection site that spreads to the distal limb. The course of PGS includes three stages. First, within 2–12 hours post-infusion, the bluish purple discoloration begins at the intravenous site. Between 12 and 24 hours post-infusion, the discoloration spreads, and edema with or without blistering develops. By the third stage, the symptoms resolve, usually back toward the intravenous site. Differential diagnosis can be broad, but includes intravenous infiltration, cellulitis, and various vasculitides (Table 1). Treatment is supportive, including limb elevation, compression, massage and gentle heat. Most cases resolve within days to weeks, with rare progression to necrosis, ischemia,
vascular compression, or compartment syndrome. Consultation with a surgeon may be warranted to evaluate the need for fasciotomy, skin grafting, or, rarely, amputation.

Several mechanisms have been proposed to explain the etiology of PGS. Some implicate the properties of phenytoin itself and the solution in which it is administered. Phenytoin is a chemically weak organic acid, insoluble in water, whose formulation includes an alkaline compound that is only soluble at a high pH. Therefore, sodium hydroxide is added to the solution. Propylene glycol and ethanol are also added for increased solubility, and this combination can induce vasoconstriction, leakage, and irritation of soft tissue. Phenytoin extravasation has also been explained as a result of vascular tears from intravenous insertion and drug precipitation upon mixing with blood. Others consider pathogenesis of PGS secondary to drug-induced vasculitis or mechanical vessel damage with microthrombi formation. Argument against this, though, has occurred from examining the histopathology of the soft tissue in these patients, where thrombotic occlusion has often been absent. However, the data do show thrombus present in earlier stages of PGS, possibly representing a correlation with time post-infusion. Other histopathologic features of PGS include edema, perivascular lymphocytic inflammation, and epidermal, dermal, and subcutaneous necrosis.

Various factors are thought to affect the incidence of PGS. For example, there is a tendency for PGS to develop in older patients with pre-existing vascular disease. This patient, though his upper extremity perfusion on admission was normal, fits both categories and thus may have had a lower threshold for developing symptoms. One also wonders if the patient’s lymphoma played a role as well. He had not started chemotherapy yet, but cancer and its treatment agents are both potential causes of vasculitides. Additionally, it has been suggested that acute administration, large doses, and/or high rates of infusion of intravenous phenytoin can affect the likelihood of PGS. While this case took place in the acute setting, the infusion rate of 15 mg/min was well within the 20 mg/min guideline set for phenytoin infusion in elderly patients. Some factors thought to decrease the probability of PGS, all of which were adhered to in this patient’s care, include the use of intravenous catheters smaller than 20-gauge, flushing with normal saline following intravenous administration, use of large-bore veins, and immediate discontinuation of the intravenous catheter upon symptom presentation. Finally, oral drug should be used whenever possible. Though there has been a report of PGS with oral phenytoin use, in this case the drug was given at larger doses than were indicated.

Some authors have suggested that the use of fosphenytoin, the pro-drug of phenytoin, may be preferred if PGS is a concern, but data regarding this indication are limited. Fosphenytoin, which is usually less toxic compared with phenytoin, is soluble at a lower pH, can be less painful upon extravasation, and can be given through either intravenous or intramuscular injection. However, the cost is substantial, and recent studies of cost-effectiveness do not support regular use. Given the low incidence and cost of treatment of PGS, fosphenytoin does not appear a prudent alternative at this time.

References

Table 1 Differential diagnosis of purple glove syndrome.

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