Unexpected outcome (positive or negative) including adverse drug reactions

Purple glove syndrome: a dreadful complication of intravenous phenytoin administration

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Summary

Purple glove syndrome is an uncommon but dreaded complication of intravenous phenytoin administration characterised by pain, oedema and purple-blue discolouration of the limb distal to the site of injection. We describe a 37-year-old gentleman having the characteristic purple glove appearance after phenytoin loading, and discuss the salient features of this syndrome highlighting the pathophysiological and preventive aspects.

BACKGROUND

Purple glove syndrome (PGS) is characterised by pain, oedema and purple-blue discolouration of the limb distal to the site of phenytoin injection.¹ The evolution of this syndrome may range from simple discolouration to development of blisters and necrosis of the involved area. It may account for 1.7–5.9% of all phenytoin administrations depending upon the recognition as well as adverse drug event reporting.² Administration of higher than recommended concentration/dose, extravasation, chemical irritation by solvents (sodium hydroxide, propylene glycol and ethanol), drug-induced vasculitis and drug-induced vasoconstriction are the important pathophysiological mechanisms postulated, to explain the occurrence of PGS. We herein describe a 37-year-old gentleman developing PGS after phenytoin administration and discuss the salient features, differential diagnosis, pathophysiology and preventive aspects involved.

CASE PRESENTATION

A 37-year-old gentleman was referred to our department, a tertiary care neurology centre, as a case of refractory seizures for further management. He had been admitted at the primary care facility with complaints of high-grade fever associated with chills and rigours, accompanied by frequent generalised tonic-clonic seizures for 3 days. A provisional diagnosis of acute encephalitis syndrome was made in view of the history and presence of signs of meningeal irritation. The patient was administered intravenous phenytoin (20 mg/kg body weight, given over 60 min; details of concentration were not available) following 4 mg of lorazepam intravenously. The patient was additionally loaded with half-dose phenytoin (10 mg/kg body weight, given over 30 min) in view of continuing seizure activity. The seizures ceased for 2 h but the patient remained unconscious; a referral was made after recurrence of seizures. The patient was received at our department in status epilepticus, with respiratory distress and hypotension. His right hand and forearm were swollen and congested, with purple-blue discolouration; multiple

blisters were observed towards the radial end of the lower forearm near the anatomical snuff box, where the 20-gauge intravenous catheter had been placed. (figure 1) Radial pulse was feeble and the capillary refill time was less than 2 s. Approximately 10 h had lapsed between phenytoin administration and receipt of patient in our department.

INVESTIGATIONS

Electroencephalography, at the time of admission, revealed generalised tonic discharges without any significant right-left asymmetry; postictal suppression was evident after cessation of seizures. Doppler study of the right upper limb did not reveal any vascular compromise.

TREATMENT

After administering intravenous lorazepam (4 mg), the patient was loaded with intravenous valproate (30 mg/kg body weight) and shifted to the intensive care unit. The affected limb (right) was elevated and a central venous

Figure 1 Photograph of the right distal forearm and hand depicts swollen and congested skin with purple-blue discolouration; multiple blisters are observed over the anatomical snuff box, the site of venous access.

access was secured. Care was taken to avoid any secondary infection.

OUTCOME AND FOLLOW-UP

The seizure activity terminated but the patient developed fulminant aspiration pneumonia followed by multiorgan dysfunction syndrome. He succumbed to his illness on the third day of admission.

DISCUSSION

PGS is characterised by pain, oedema and purple-blue discoloration of the limb distal to the site of phenytoin injection.¹ It is an uncommon but dreaded complication of intravenous phenytoin use accounting for 1.7–5.9% of all administrations.² Although the cutaneous adverse manifestations of intravenous phenytoin administration were individually described by Comer³ and Kilarski *et al*⁴ in 1984, it was in 1992 that the features were likened to and named PGS by Hanna.¹ The syndrome has been described to evolve in three stages: in the initial stage, 2–12 h after injection, there is pain and purple-blue discoloration around the site of administration. The second stage involves development of oedema, varying degrees of discoloration, blister formation or necrosis. The third stage is the phase of resolution of pain, oedema and discoloration.^{1–5} This condition needs to be differentiated from local infiltration/extravasation, cellulitis and manifestations of peripheral vascular disease or a collagen vascular disorder. Characteristic purple-blue discoloration and evolution of the features beyond the infusion time, and absence of fever or purulent discharge clinically negate the possibility of local effect and cellulitis, respectively. Prior history of a vascular illness in the form of Raynaud's phenomenon, acrocyanosis, multiple organ afflictions or other cutaneous changes may help to provide contributory evidence of such an illness; such finding were not present in our case.

Several pathophysiological mechanisms have been proposed to explain the occurrence of PGS.

The most plausible ones include administration of higher than recommended concentration/dose, extravasation, chemical irritation by solvents (sodium hydroxide, propylene glycol and ethanol), drug-induced vasculitis and drug-induced vasoconstriction. Not all patients who receive intravenous phenytoin develop PGS, and therefore a patient's susceptibility (?genetic predisposition) seems to be a possibility; the single most important preventable factor determining the development of PGS appears to be

the lack of adherence to the guidelines for intravenous administration of phenytoin. Use of an appropriate catheter (20-gauge or more), dedicated access through a large-bore vein preventing admixture with other injectables especially glucose, correct dose (15–20 mg/kg body weight) and rate (25–50 mg/min) and postinfusion flush with normal saline can help in preventing this dreaded adverse event associated with intravenous phenytoin. The infusion should be discontinued immediately at the very first appearance of PGS.^{5–6} The nursing staff and the other personnel involved should be advised to follow the guidelines to minimise avoidable errors. The treatment of PGS involves elevation of the affected limb, avoiding further venous access through the limb, and preventing secondary infection through the site of initial access. Fasciotomy may be done to relieve the pressure if vascular compromise is evident.

Learning points

- ▶ Purple glove syndrome is an uncommon but dreaded complication of phenytoin administration.
- ▶ Administration of phenytoin in accordance with the established guidelines may help in preventing the development of this syndrome.
- ▶ The nursing staff and the residents should be sensitised towards the minimisation of such preventable errors of administration of medication.

Competing interests None.

Patient consent Obtained.

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