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PURPLE GLOVE SYNDROME IS NOT ALWAYS PURPLE AT THE INITIAL PRESENTATION: A Case Report and Literature Review

Abdulaziz Al-Dhubaib, Saqqer Al-Mulhim, Mohammed Al-Ghamdi, Zeead Al-Ghamdi, Atef Elhag

Department of Surgery, King Fahad University Hospital, University of Dammam.

ABSTRACT

Background: Purple glove syndrome (PGS) is a rare complication of intravenous phenytoin use that typically presents with pain, edema, and discoloration at the injection site that spreads to the distal limb.

Case Presentation: A 25-year-old female patient presented to Kind Fahad University hospital's emergency department (ER) following a seizure episode, on admission to the hospital she was found to have profound tonic-clonic seizures, flexed limbs, uprolling eyes and frothy secretion from her mouth. The patient received IV fluid 0.9 NS and diazepam 5 mg IV injection followed by Phenytoin 1g was IV administrated on 100cc NS over 3 hours with a dose of 50 mg IV/min, and was admitted to the medicine service. Soon, the patient felt pain, swelling, Erythema and abnormal movement from the site of the IV cannula over the left forearm while Phenytoin was being injected, however no purple discoloration was detected and the patient was diagnosed with purple Glove syndrome (PGS). Accordingly, Phenytoin was held and replaced by carbamazepine for Seizure control, Brain MRI and EEG were ordered simultaneously. Patient symptoms were alleviated 2 days later and was ready for discharge. Follow-up visits were scheduled until the patient was fully recovered and aware of the implications of Phenytoin on her case.

Conclusion: Since PGS is a rare complication of IV phenytoin therapy, it's not common to link the clinical symptoms of PGS to Phenytoin adverse reactions at the first prognosis especially when discoloration - which is a profound symptom of PGS -is missing. The risk of PGS for this patient may have been abated at the very early stage by decreasing the phenytoin infusion rate from 50 mg/min to less than 25 mg/min.

Keywords: Phenytoin, PGS, seizures, extravasation, adverse reactions.

INTRODUCTION

One of the most poorly understood and potentially serious local complications of intravenous phenytoin administration is the purple glove syndrome, which is characterized by progressive limb edema, discoloration, and pain. In the only reported systematic study of this syndrome at the time (1998) had the incidence of purple glove syndrome was 5.9% (nine of 152) in patients receiving intravenous phenytoin [(1)].

Phenytoin is an anticonvulsant licensed for the management of generalized tonic-clonic (grandmal) seizures and complex partial (psychomotor, temporal lobe) seizures [(2)].It is also approved by the United States Federal Drug Authority for the prevention and treatment of seizures occurring during or after neurosurgery [(3)].

A more recent study – in 2000- a case of PGS was reported following oral administration of phenytoin which provides supporting evidence that PGS may occur with or without phenytoin extravasation. This has raised the question as to whether phenytoin itself, irrespective of route of administration, may induce PGS in patients due to phenytoin doses and serum levels that are higher than recommended therapeutic doses or levels. [(4)]

The presence of thrombi in the early-stage lesion of PGS also suggests that thrombosis plays a role in the initial pathogenesis of this condition. [(5)]

In this study, the authors prospectively concluded that LCR is common in routine hospital practice, but are generally mild and benign.

CASE PRESENTATION

A 25 years old female - who was accompanied by her sister and wasn't known to have any previous medical illness -was presented to ER with a tonic-clonic seizures, flexed limbs, uprolling eyes and frothy secretion from her mouth. It was discovered later on that she had similar episode one month ago.

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At the time of presentation, the patient was given IV fluid 0.9 NS and diazepam 5 mg IV with close and continuous monitoring and a CT brain scan was ordered. The patient was free of seizures for 5 min then seized again. Following that, another dose of diazepam 5 mg IV was given, then the patient was free of seizure again for 5 min but seized for the 3rd time.

After that, Phenytoin 1g was IV administrated on 100cc NS over 3 hours with a dose of 50 mg IV/min at maximum , only then the patient has started to regain consciousness, however, she felt pain, swelling and abnormal movement while drug is being injected. The Pain, Erythema and swelling manifestations were extended distally from the site of the IV cannula over the left forearm (picture A).

Tenderness has extended from the cannulation site to the full hand and forearm. Moreover, she was fully conscious and alert and with normal vital signs and pulse. Patient was hence diagnosed with purple Glove syndrome (PGS).

A follow-up visit schedule were setup for the patient to ensure full support provided for the proper management of the case.

Management plan

The assigned study team received the patient and started the supportive treatment (hand elevation, warm compression, analgesia and physiotherapy). A Vascular surgeon and a neurologist were also consulted. Phenytoin was held and replaced by carbamazepine. For Seizure and neurological assessment, we ordered Brain MRI and EEG.

Progression: day 2 post admission patient was feeling better; swelling and erythema decreased gradually, sensation and peripheral pulse were intact yet the left hand pain and restriction of movement remained.

For social reasons, the patient insisted on clinical discharge- as soon as her condition was partially improved – however follow-up visits were scheduled by the study team in order to provide the appropriate care and guidance and keep track of the case progression. The first follow-up visit was scheduled two weeks later, significant improvement was observed, however total recovery was not yet obtained. Two weeks later, the patient was clinically checked again, she was totally recovered and discoloration receded back toward the original IV site.

Finally, the condition and precautions were explained thoroughly to her and was advised to follow up with a neurologist with special attention to her left upper limb condition (Patient was clear that symptoms recurrence demands an immediate ER visit).

DISCUSSION

The extravasation theory suggests that the highly alkaline IV phenytoin solution (pH = 12) contributes to the development of PGS when it infiltrates extravenously into surrounding tissues. Phenytoin is a weak organic acid and is very insoluble. Sodium hydroxide is added to IV phenytoin solution to increase its alkalinity. Propylene glycol and ethanol are also added to IV phenytoin solution to increase its solubility. [6] These 3 pharmaceutical additives (sodium hydroxide, propylene glycol, and ethanol) are well-known soft tissue irritants; when they are infused extravenously, they may produce PGS. [1,7]

It is found that with early detection and intervention with non-pharmacologic therapy after the discontinuation of IV phenytoin (such as limb elevation, application of dry, gentle heat, physiotherapy, pain control and patient reassurance) , mild cases may resolve spontaneously [1], whereas in rare severe cases the condition has led to On very rare occasions, PGS may progress to necrosis, ischemia, vascular compression, or compartment syndrome, which may require surgical interventions such as fasciotomy, skin grafting, or amputation. [8]

In this study, the patient hasn't manifested the typical purple/blackish discoloration of the skin when she was first presented at the hospital.

The patient has gone through all PGS phases except for the discoloration manifestation as explained in **Table 1**. The differential diagnosis includes, but is not limited to,intravenous line malfunction and drug toxicity, arterial occlusion, venous thrombus, thrombophlebitis, Raynaud phenomenon, Buerger disease, cellulitis, and polyarteritis nodosa **[8]**.

Table 1 shows the progression stages of PGS.

Stages	Appearance
Stage (1)	Blue or purple discoloration around IV site 2-12 hours post infusion
Stage (2)	Progression: 12-16 hours post infusion, spreading discoloration, edema, skin blistering, and sloughing and possible ulceration. Further extension distally and proximally may occur
Stage (3)	Resolution: may take weeks to months, discoloration recedes back toward original IV site

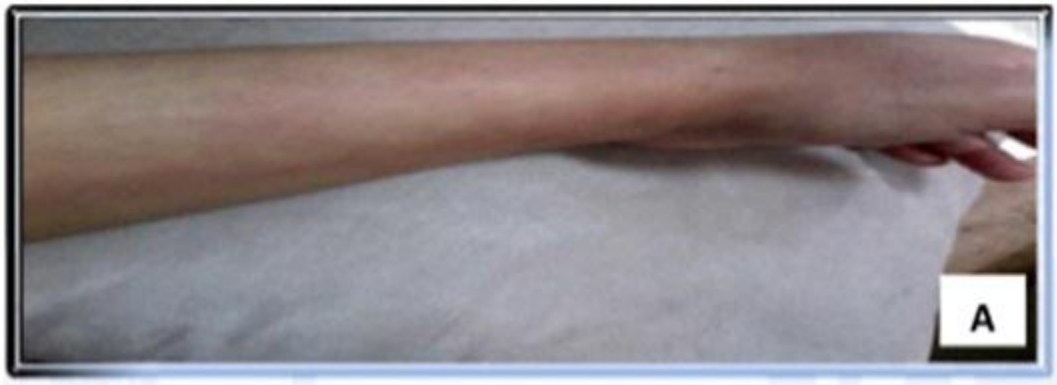

Figure A: a picture showing Patient's left arm with mild erythema and swelling with bluish discoloration of the wrest and dorsum of hand.

CONCLUSION

Purple gloves syndrome should not only be distinguished by the purple or blackish discoloration as the primary presentation of the case as commonly practiced. Typically, a standard differential diagnosis should be in place which needs to include phenytoin- as the main rootcause of PGS- has been administrated. Physicians must have high suspicion for this syndrome even if the clinical picture of this syndrome not appear completely

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