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A Rare Case Report of Retrograde Air Embolism and Phenytoin Extravasation Causing Acute Superficial Venous Thrombosis and Purple Glove Syndrome of the Upper Limb.

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Abstract

Background: 26-Year-old female patient admitted with pseudocyst of pancreas with systemic lupus erythematosus,Evans syndrome,known case of epilepsy on treatment was admitted for Elective cystogastrostomy. Postoperatively patient was on IV Phenytoin infusion. On postoperative day 3 patient developed sudden Purple glove syndrome of the left upper limb within 15 minutes of IV phenytoin infusion. On examination at 15 mins patient had deep blue cyanosed left hand with cold clammy hand and forearm. Patient complained of excessive pain in the hand and forearm. Radial artery pulsations were feeble. Within 30 mins of the incident patient developed wrist drop and sensory loss extending till the elbow. Capillary refill was not appreciated in the hand. Doppler ultrasound revealed cephalic and basilica vein thrombosis with biphasic waveform of the arteries of the upper limb with shouldering on systolic downstroke. Emergency vascular surgery consult was taken and conservative line of management with IV heparin, Dextran, nifidipine was started. Patient had to undergo 13 serial fasciotomies for compartment syndrome of the upper limb. Patient also had bone marrow failure on day 2 due to predisposing Evans syndrome and lupus. Here is one case where a routine elective abdominal procedure became a nightmare for the surgeon. Later complete recovery and hand function was achieved.

Keywords: Phenytoin, Purple glove syndrome [PGS], Retrograde air embolus, Acute venous thrombosis.

Introduction

Purple glove syndrome (PGS) is a rare complication of intravenous (IV) phenytoin administration that is characterized by delayed soft tissue injury of the skin adjacent to the site of IV phenytoin infusion.[1,2] PGS may occur with or without extravasation of IV phenytoin.[3] The clinical manifestation of PGS includes pain, edema, and purple-blue discoloration of skin tissue adjacent to the site of IV phenytoin infusion.[4] In her 1992 publication, Hanna named a delayed, soft tissue injury of the hand and forearm following IV administration of phenytoin purple glove syndrome (PGS) [5, 6]. Increasing reports of this condition have recently emerged, some involving permanent tissue damage or loss, leading to questions regarding the safety and risk-

benefit profile of IV phenytoin [7]. Phenytoin sodium (Dilantin®, Pfizer Inc., NY, NY) is an anticonvulsant drug used for the treatment and prevention of seizures since 1956 [8]. It is recommended by the Epilepsy Foundation of America (EFA) and European Federation of Neurological Societies (EFNS) practice guidelines as the second-line agent for treatment of status epilepticus after IV benzodiazepines [9]. Phenytoin has been associated with a number of serious adverse drug reactions (ADR) including hypotension and arrhythmias with rapid IV administration, dermatologic reactions ranging from rashes to StevensJohnson syndrome or toxic epidermal necrolysis, severe hepatotoxicity, and other hypersensitivity events [10]. Extravasation or soft tissue injuries following administration of IV phenytoin have been reported or documented since 1950s. In 1984, Comer et al. first described the association between IV phenytoin administration and rapid onset of discoloration, pain, and tissue necrosis affecting the distal limb through which the drug was administered.

Case Report

26-Year-old female patient admitted with pseudocyst of pancreas with systemic lupus erythematosus,Evans syndrome,known case of epilepsy on treatment was admitted for Elective cystogastrostomy. Postoperatively patient was on IV Phenytoin infusion. On postoperative day 3 patient developed sudden Purple glove syndrome of the left upper limb within 15 minutes of IV phenytoin infusion. On examination at 15 mins patient had deep blue cyanosed left hand with cold clammy hand and forearm. Patient complained of excessive pain in the hand and forearm. Radial artery pulsations were feeble. Within 30 mins of the incident patient developed wrist drop and sensory loss extending till the elbow. Capillary refill was not appreciated in the hand. Doppler ultrasound revealed cephalic and basilica vein thrombosis with biphasic waveform of the arteries of the upper limb with shouldering on systolic downstroke. Emergency vascular surgery consult was taken and retrograde air embolus causing cephalic and basilic vein thrombosis with phenytoin extravasation causing digital arteriovenous vasospasm was diagnosed.

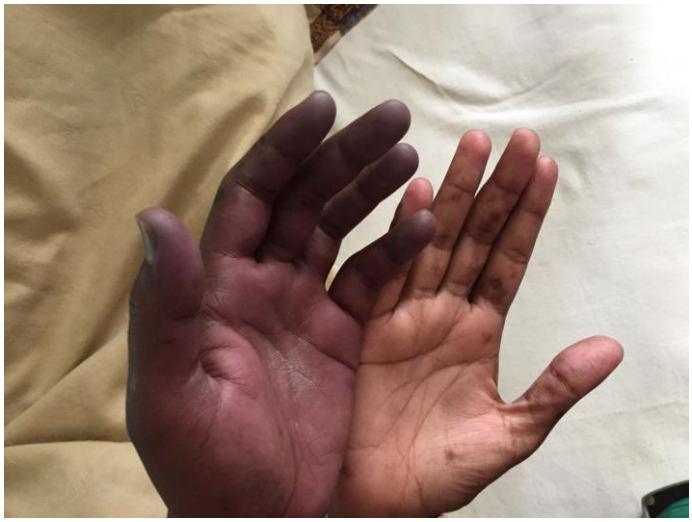

Figure 1: Purple Glove Syndrome At 15 Mins.

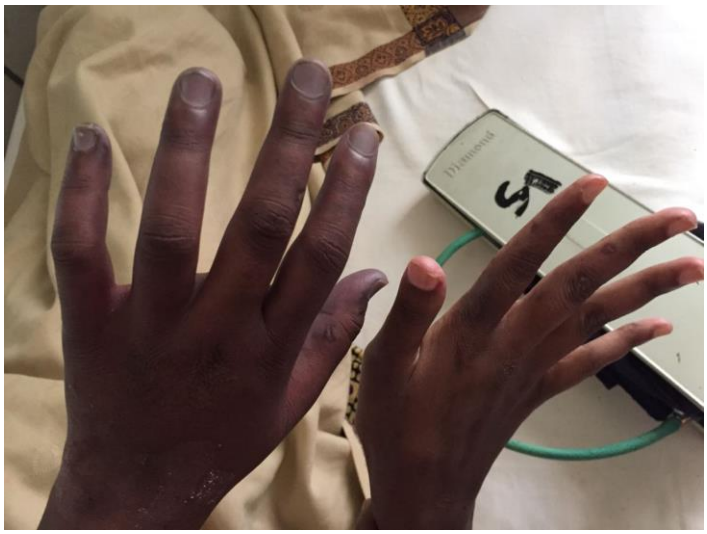

Figure 2: At 15 Mins Bluish Discoloration Of Nails.

Doppler of the Upper Limb

Cephalic and basilic veins are non compressible showing no colour uptake.Echogenic content within the lumen of the veins was noted- likely suggestive of thrombosis. Deep veins are normal and show colour uptake. Arteries of the upper limb show bipasic waveform with

shouldering on systolic downstroke- pulsewave reflection from distal disease.

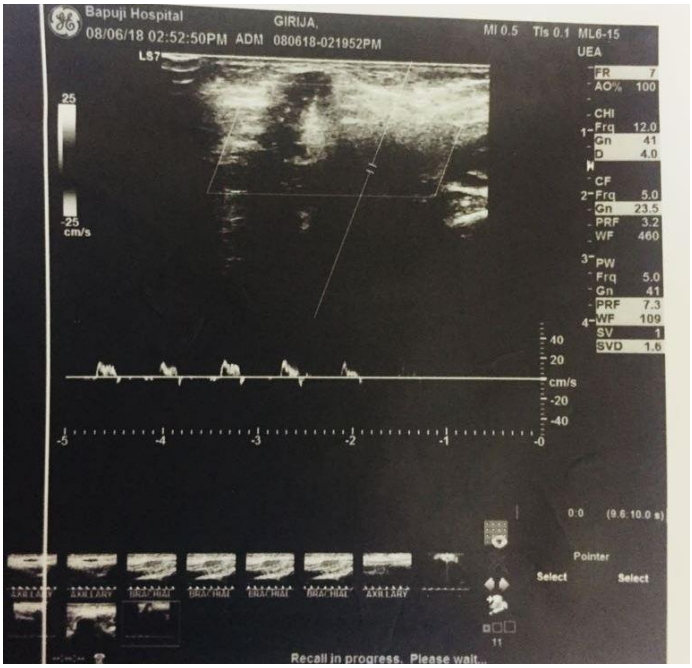

Figure 3: Echogenic Thrombus In Cephalic And Basilic Vein.

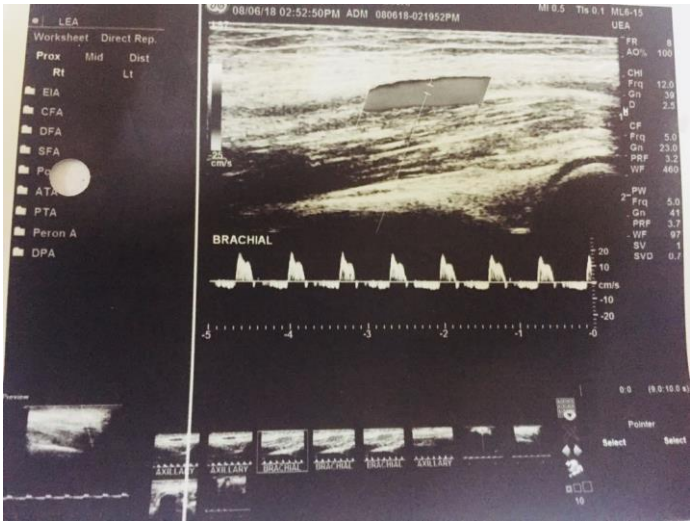

Figure 4- Biphasic Arterial Waveform.

Treatment

Conservative line of management was advised. 5000IU of IV Heparin 8th hourly with IV Dextran infusion Once daily was started. Calcium channel blockers were strated orally. Within 6 hours patient developed severe edema and compartment syndrome of the hand with absent radial and ulnar pulsations. Patient was taken for serial fasciotomies of the hand. 13 fasicotomy incisions were placed. On each phalanx, thenar, hypothenar eminence and back incisions were placed and pressure was released. Even after tight compression banding bleeding was not stopped due to IV heparin. Patient developed severe anemia hypovolemic shock with Hb- 2.0g/dl and bone marrow failure due to predisposed lupus and Evans syndrome. Patient was managed aggressively with blood and plasma transfusions and IV dexamethasone 8th hourly. Patient improved gradually with return of wrist function on day 3. Daily debridement with dressing was done for 21 days and patient regained full function of the hand. Estimated loss of the distal phalanx was also avoided and all finger movements were normally regained.

Figure 5: Day 3 Wound Status Post Fasciotomy.

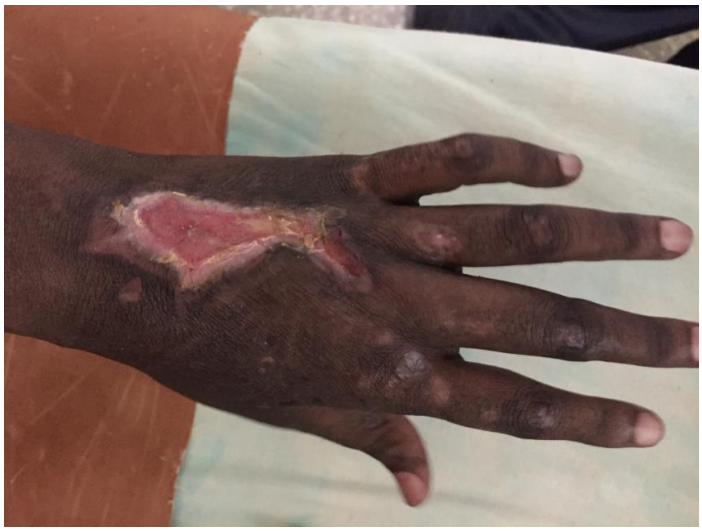

Figure 6- Wound Status On Day 21.

Figure 7 – Wound Status on Day 21.

Discussion

Here is one such rare case admitted for elective cystogastrostomy became a nightmare to manage postoperatively because of IV phenytoin and the predisposing factors like systemic lupus erythematosus and Evans syndrome. Patient was kept Nil per oral post cystogastrostomy so the need for IV phenytoin had arisen. Aggressive early intervention helped regained full function of the hand and amputation was avoided. Limb salvage was successful owing to the emergent administration of IV antibiotics, heparin and dextran with calcium channel blockers. Bone marrow failure and severe anemia was detected early and treated with transfusions and IV steroids. The pathophysiology of PGS is poorly understood. However, it may be related to the crystallization of phenytoin upon contact with blood and extravasates into the interstitial tissue.[11] Another mechanism is due to the disruption of the endothelial–intercellular junctions following leakage of phenytoin and irritation of soft tissue. To obscure the assumption on the etiology even more, the report on PGS occurring after an oral dose[12] of phenytoin suggests that this event may be due to phenytoin itself and not directly related to the infusion. 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.[4,8] 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.[1,3] Extravasation of phenytoin may also occur due to a microtear of the vein during the IV cannulation procedure.[1]

Conclusion

PGS may be prevented by adjusting modifiable established risk factors that are associated with the development of PGS, namely the use of higher phenytoin infusion rates and the administration of multiple doses of IV phenytoin. It is prudent to use IV phenytoin infusion rates less than 25 mg/min and to convert patients to oral phenytoin, when appropriate, to prevent the occurrence of PGS. Here is one such rare case of phenytoin extravasation and infusion causing purple glove syndrome complicated by superficial venous thromboses and a suspected retrograde air embolus. Evans syndrome with lupus complicated the scenario further.

Declarations

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Conflict of interest: None.

Ethical approval: Not required.

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