

# Asymmetrical Peripheral Gangrene Due to Norepinephrine Injection

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## ABSTRACT

Norepinephrine (NE) is commonly recommended as a first-line vasopressor treatment for the majority of adult patients with acute circulatory failure. Critically ill patients with circulatory shock may need rescue treatment with high doses of NE, which can be associated with a poor outcome due to excessive vasoconstriction. Herein we present a patient of post-partum hypovolemic shock who developed gangrenous changes in the digits of her hands after norepinephrine administration.

**Keywords:** Norepinephrine; Vasoconstriction; Gangrene.

## INTRODUCTION

A 34 year old female with no known co-morbidities presented to the trauma centre with persistent vaginal bleeding following an explorative laparotomy under spinal anaesthesia after a full term normal delivery (3 kg male child) with episiotomy. On presentation the patient had hypotension (Blood Pressure-70/50 mmHg) and was given fluid resuscitation with 10 cryoprecipitate. The patient was immediately

shifted to the operation theatre for emergency obstetric hysterectomy and was given 4 fresh frozen plasma, 4 Platelets, 10 cryoprecipitate and 4 packed cell volume for the 700 ml blood loss intra-operatively. The patient was shifted to the critical care centre and given intravenously noradrenaline 2 amp in 50cc of normal saline at 4ml/ hour infusion rate for 4 days.

After 3 days, the patient developed painful reddish lesions over both hands. The patient also complained of blackening of left hand ring finger and fluid filled lesions over both hands and feet. On examination gangrenous changes of size approximately 2 x 3 cm over left hand ring finger were noted. (Fig. 1 & b) Erythematous, tender, inflamed plaques of size approximately 1 x 2 cm in size over right hand (Fig. 2) and few erythematous macules and bullae over both dorsum of feet was present. (Fig. 3) The patient did not have history of any topical application before appearance of lesions or any food or drug allergy. No similar complaints in the past were noted. The patient had a Full term normal delivery of a 2.5 kg male child 11 years ago but did not have any blood transfusions or similar

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**Fig. 1:** Gangrenous changes of size approximately 2 x 3 cm over left hand ring finger

a) Palmar aspect

b) Dorsal aspect



**Fig. 2:** Erythematous, tender, inflamed plaques of size approximately 1 x 2 cm in size over right hand.



**Fig. 3:** Few erythematous macules and bullae over both dorsum of feet



episodes during that delivery. No history of hair loss or Raynaud's phenomenon was elicited. The patient was started on Inj Enoxaparin 0.4 ml SC once daily for 7 days followed by tab Apixaban 5 mg twice a day, tab Aspirin 75 mg once daily and local application of silver sulphadiazine and zinc sulphate cream twice a day. She gradually showed improvement in the form of resolution of blisters which was replaced by gangrenous changes over left ring and little finger. (Fig. 4a & b)

## DISCUSSION

Intravenous norepinephrine (NE), an alpha-receptor stimulator, with vasoconstrictor properties, is used in patients with septic shock and hypotensive states, but on occasion it may produce extreme local vasoconstriction resulting in necrosis of tissues.<sup>1</sup> It also has some  $\beta_1$  receptor



Fig. 4: Gangrenous changes over left ring and little finger after treatment

a) Palmar aspect

b) Dorsal aspect

agonist activity that results in a positive inotropic effect on the heart at higher doses.<sup>2</sup>

The precise pathophysiology of vascular occlusion remains unclear. Low-flow state is commonly associated with hypercoagulable vasospastic condition, leading to microcirculatory occlusion. The pathogenesis of symmetrical peripheral gangrene may involve bacterial endotoxin release and platelet plugging in peripheral arterioles due to vascular collapse and disseminated intravascular coagulation.<sup>1</sup>

Our patient lacked risk factors for peripheral vascular disease and diabetes mellitus. Treatment

with inotropes was not prolonged or in high doses, so it can be suggested an idiosyncratic response.

Digital necrosis caused by NE tends to be bilateral and symmetrical and usually affects a patient's toes.<sup>3,4</sup> However, as seen in our case, asymmetrical presentation and finger gangrene has been described which is uncommon. It is believed that the necrosis of tissue is due to intense prolonged arteriolar vasoconstriction produced by high local concentration of noradrenaline.<sup>5</sup> The development of gangrene was subsequent to Inj Noradrenaline at the infusion rate of 4 ml/hour for 4 days in our case with asymmetrical involvement.

Since the vasospastic effects of NE may be more intense in the digital vascular beds, low blood pressure could certainly have contributed to her digital gangrene.

The three stages leading up to symmetrical peripheral gangrene are sepsis, ischaemia and gangrene. Treatment can be administered at each stage to prevent, slow or reverse the course.

The therapies that slow or reverse ischaemia are sympathetic blockers, intravenous vasodilators, local injection of alpha-blockers, intravenous alpha-adrenergic antagonists such as chlorpromazine hydrochloride and infiltration of the ischaemic areas with phentolamine hydrochloride and phosphodiesterase inhibitors.<sup>3</sup> Locally nitroglycerine ointment and epoprostenol have been reported as beneficial.

Inj Enoxaparin a low molecular weight heparin binds to and potentiates antithrombin 3 to form a complex that irreversibly inactivates factor Xa inhibiting thrombus formation. Apixaban inhibits free and clot bound factor Xa and prothrombinase activity, thus decreases thrombin generation and thrombus formation. Aspirin impairs platelet aggregation via inhibition of platelet thromboxane A<sub>2</sub> synthesis thus reducing thrombus formation.<sup>6</sup>

The only definitive treatment for gangrene is amputation of the necrotic digits after development of a clear line of demarcation. Autoamputation of the gangrenous digits may also occur. Local wound care consist of interdigital padding to protect the gangrenous or ischaemic extremities, antiseptic dressings, debridement and antibiotics.

Microvascular spasm is a rare complication of inotrope use which must be considered especially

in patients with pre-existing peripheral vascular disease.

## CONCLUSION

We report this rare case of asymmetrical peripheral gangrene following prolonged inotrope administration. Microvascular spasm is a rare complication of inotrope use which must be considered especially in patients with pre-existing peripheral vascular disease.

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