



## Gangrenous Purpura Fulminans Associated with *Influenza A* Infection

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### Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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### ABSTRACT

**Background and Purpose:** Purpura fulminans (PF) is a rapidly progressive disease of small-vessel thrombosis and hemorrhagic skin infarctions with high mortality and morbidity. Three forms of disease exist; neonatal, idiopathic and infectious. Infectious one usually appears secondary to gram-negative bacteremia and rarely secondary to viral infections.

**Case Description:** In this paper, we present a 27-year-old female patient with diagnosis of purpura fulminans secondary to *Influenza A* septicemia which is the first case reported in the literature.

**Discussion:** Several kinds of infection may cause purpura fulminans including rare viral infections so the clinician should be alert to diagnose and to treat purpura fulminans in case of purpuric and hemorrhagic lesions in patients with infectious diseases.

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## 1. INTRODUCTION

Purpura fulminans (PF) is a rapidly progressive situation characterized by thrombosis in small-vessels leading to hemorrhagic skin infarctions and tissue necrosis accompanied by disseminated intravascular coagulation [1]. It is mostly encountered after an infectious disease and usually involves extremities. Survived patients generally undergo surgical interventions where extremity amputations are heading [2]. We describe a case of PF secondary to *Influenza A* infection which to our knowledge is the first reported case in the literature.

## 2. CASE

A twenty-seven-year old obese (body mass index: 35) female patient with Type I diabetes mellitus applied to the state hospital with dyspnea, fever and confusion. She was admitted to the level 2 intensive care unit (ICU) with the diagnosis of pneumonia-associated sepsis. The patient, then, developed hypotension, thrombocytopenia, convulsion, acute kidney injury and respiratory failure, and was intubated. The patient had cardiac arrest while intubated and cardiopulmonary resuscitation was done for less than five minutes (as the physician declared). The patient had dopamine infusion (maximum 10 mcg/kg/minute) via central line for two days. During hypotensive period, molted-skin changes with some purple discoloration on her both hands were observed. Although the skin changes on the left hand resolved, petechial

rashes, hemorrhagic blebs and necrotic patches were added on right hand's lesions (Fig. 1). The patient received piperacillin-tazobactam, linezolid, clarithromycin and oseltamivir phosphate. Five days later, although vasopressor infusion was stopped, the patient's clinic did not improve and was transferred to our ICU. On arrival, the patient had the Glasgow coma scale of 5, thrombocytopenia (platelet:  $27000/\text{mm}^3$ ), elevated INR (1.6), acute kidney injury requiring renal replacement therapy (RRT), moderate ARDS ( $\text{PO}_2/\text{FiO}_2$ : 156) and recurrent seizures but no need for vasopressor infusion. There were erosive patches and hemorrhagic small blebs on the right wrist and hand dorsum with gangrenous changes located mostly on the first and second fingers. Other parts of the hand were erythematous. Cranial computed tomography (CT) did not show any frank cranial pathology except for the evidence of left eye vitreous bleeding that was verified by ultrasonography. Thorax CT displayed bilateral lung infiltrations. Arterial doppler ultrasonography of the right hand and echocardiography were normal. The right hand lesions were diagnosed as PF. Ilomedine and pentoxifylline infusions were prescribed for five days and daily fresh frozen plasma was infused for PF treatment. Heparin therapy could not be started due to thrombocytopenia and the newly diagnosed vitreous bleeding. After these treatments, the lesions became limited to the first and second fingers and dorsum of the right hand with necrotic changes mostly located on the first finger and radial half of the second finger.



**Fig. 1. Petechial rashes, hemorrhagic blebs and necrotic patches on right hand dorsum**

Blood, urine and tracheal aspirate cultures taken on the state and our hospital were negative, except for positive PCR results for *Influenza A*. The patient was stabilized and the platelet count normalized on follow-up. The demarcation lines of gangrenous lesions became clear two weeks later and an amputation was planned (Fig. 2). The patient was lost because of ventilator associated-pneumonia while on a weaning program. The patient had RRT during ICU stay, did not become conscious, and had a tracheotomy procedure on the fifteenth day of intubation. We did not study anti-thrombin III, Protein C and Protein S levels as the patient's clinic was compatible with disseminated intravascular coagulation [DIC] and these anticoagulants would most probably be measured to be low due to DIC.

### 3. DISCUSSION

PF is a potentially disabling and life-threatening skin disorder. It includes tissue necrosis, small vessel thrombosis with DIC and multi organ

failures. Three types of PF exist; inherited [neonatal], idiopathic and infectious PF. Inherited one is mostly encountered in neonates with protein C or S deficiency [3]. Idiopathic one, a diagnosis of exclusion, is an autoimmune manifestation seen after normally benign infections and usually presents with a less severe clinic [3,4]. Infectious type is the most common form of PF in adults and its mortality rate ranges from 10-50% [1].

In infectious PF, coagulation is deteriorated by sepsis where DIC and protein C and S consumption result in intravascular thrombosis and tissue infarction [1,2]. Primary lesions are tender areas of purpura surrounded by an erythematous halo followed by purplish black areas of hemorrhagic cutaneous necrosis [5]. Necrosis can extend to deep tissues including muscle and bone, and auto-amputation of digits may occur [6]. While any part of the body can be affected, distal extremities are mainly involved [1,2,7].



**Fig. 2. Lesions limited to the first and second fingers and dorsum of the right hand with necrotic changes**

Although infectious PF has been mostly reported in children with *Neisseria meningitis*, infection with other microorganisms including *Staphylococcus aureus* [8], *Varicella zoster* [3,4], *Streptococcus pneumonia* [9], *Plasmodium falciparum* [2], *Escherichia coli* [10], *Leptospira* [3] have also been demonstrated. Gram negative bacteria are predominantly encountered because of the endotoxins in the outer membrane of their cell walls that stimulate inflammatory cytokines which then consume anti-thrombin III, protein C and protein S, leading to intravascular thrombosis [2,11]. On the other hand, the reports of gram-positive bacteria associated with PF have been increasing. Konda et al. [9] added a new case to 19 documented pediatric patients with PF in the setting of *S. pneumonia* septicemia. Kravitz et al. [8] described 5 cases of *S. aureus* and recommended that patients who present with PF should receive antibiotic therapy active not only against gram negative but also against gram-positive bacteria. Infectious PF secondary to systemic leptospirosis described by Tanwar et al. [3] and secondary to *Pseudomonas* bacteremia described by Harikrishna et al. [12] are the two uncommon reasons limited with case reports in the literature.

Nonbacterial PF has also been documented, mostly following *Varicella zoster* infections [3,4]. There were rare cases of PF reported after hantavirus, dengue virus and human herpesvirus-6 infections [6,13,14]. Herein, we mentioned a PF secondary to *Influenza A* which is also, to our knowledge, the only PF case associated with *Influenza A* infection in the literature.

Early recognition and immediate initiation of therapy including early empirical antimicrobial therapy is life-saving in the treatment of PF. If lesions become necrotic, surgical approach partakes in the treatment of survived patients [2]. Amputations of distal extremities are commonly performed. Unfortunately, more proximal amputations above knees and elbows are also carried out. In general, these patients need a long rehabilitation period [7].

We have focused on the infectious type that our patient was affected by. Since DM is associated with an increased susceptibility to sepsis [15] and diabetic patients are prone to vascular complications, having type I DM since her childhood and being obese, a risk factor for DM and cardiovascular diseases [16], rapid deterioration of our patient's clinic might be caused by her comorbidities.

#### 4. CONCLUSION

PF is a devastating state and mainly encountered after infectious diseases. Several kinds of infection may cause it including rare viral infections. Therefore, the clinician should be alert to diagnose and to treat PF in case of purpuric and hemorrhagic lesions in patients with infectious diseases.

#### CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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