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Case report

Acute infectious purpura fulminans with *Enterobacter aerogenes* post-neurosurgery

Shinya Yamamoto*, Ryoji Ito

Department of Internal Medicine, Shonan Kamakura General Hospital, 1370-1, Kamakura, Kanagawa, 247-8533, Japan

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ABSTRACT

Acute infectious purpura fulminans (AIPF) is a rare, life-threatening disease commonly caused by *Neisseria meningitidis* and *Streptococcus pneumoniae*. Gram-negative rods are rarely involved. We described a case of AIPF associated with *Enterobacter* bacteremia in a 48-year-old man admitted for subarachnoid hemorrhage treatment. After surgical clipping for intracranial aneurysms, septic shock, multiple organ failure, and extensive purpura on the skin developed. *Enterobacter aerogenes* bacteremia was detected and AIPF was diagnosed. His condition progressively worsened and he died on day 19. Autopsy showed multiple abscesses and thrombosis in the lung, intestinal tract, and kidney.

Introduction

Acute infectious purpura fulminans (AIPF) is a rare life-threatening disease, which rapidly progresses with small vessel microthrombosis and extensive purpura associated with disseminated intravascular coagulation (DIC) and acute circulatory failure [1]. This disorder was reported in various age groups from neonates to adults [2,3], however, Childers et al reported that the majority of patients were under the age of seven in the USA [4]. AIPF is commonly caused by *Neisseria meningitidis* and *Streptococcus pneumoniae,* however, Gram-negative rods are less commonly involved. AIPF is an emergency condition, and the associated mortality is high despite appropriate treatment and intensive care management. This report describes a case of AIPF with *Enterobacter aerogenes*.

Case report

A 48-year-old man presented to the Emergency Room with a headache and was diagnosed with subarachnoid hemorrhage by computed tomography. His past medical history only involved untreated hypertension. The patient had no smoking history and no family history of thrombotic disease. He was admitted to our hospital the same day. After admission, surgical titanium clipping for left intracranial aneurysms was performed. The surgery was completed without any complications. Three days post-operation, he was transferred from the intensive care unit to the general ward and was receiving rehabilitation (walking and brain training).

Five days post-operation (day 1 of illness), High grade fever with chills and nausea developed. Ceftriaxone and vancomycin were initiated for possible meningitis. The next day, the patient was hypotensive with tachycardia. His vital signs at the time revealed temperature, 37.4 °C; blood pressure, 62/52 mmHg; heart rate, 110/min; respiratory rate, 26 breaths/min; and oxygen saturation, 68% at 3 L/min supplemental oxygen. A physical examination showed cold limbs, cyanosis, and tachypnea. Laboratory data revealed leukocytosis (white blood cell count 20,900/μL), elevated liver enzymes (AST 103 U/L, ALT 106 U/L), elevated serum creatinine (3.71 mg/dL), and C-reactive protein (29.33 mg/dL). The protein C level was in the normal range. Urine test showed pyuria and bacteriuria. Contrast-enhanced computed tomography showed acute focal bacterial nephritis (Fig. 1). We diagnosed the patient with septic shock due to nephritis and started intravenous fluid resuscitation and antimicrobials (meropenem [1 g 12 h], vancomycin [1 g q 24 h], and metronidazole [500 mg q 8 h]) in combination with vasopressors (norepinephrine and vasopressin), methylprednisolone 200 mg/day, anticoagulant therapy (recombinant thrombomodulin) for DIC and started continuous hemodiafiltration.

On the subsequent day, *Enterobacter aerogenes* grew in multiple sets of blood cultures that were obtained. The organism showed sensitivity to antimicrobials including meropenem and piperacillin/tazpbactum. However, he continued to have high-grade fever and DIC despite of the treatment. Platelet transfusion was performed until the platelet level rose. Moreover, the patient's skin developed extensive purpura (Fig. 2, day 3), which was diagnosed by the dermatologist as purpura fulminans due to infection. The extensive purpura progressively became worse. Skin

* Corresponding author at: Department of General Internal Medicine, Shonan Kamakura General Hospital, Kamakura, 247-8533, Japan.
E-mail address: shiyamamoto-ehi@umin.ac.jp (S. Yamamoto).

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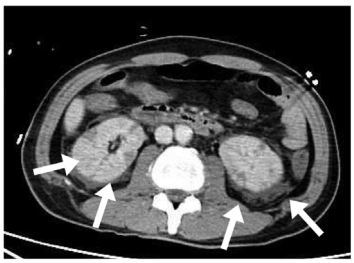

Fig. 1. Computed tomography of abdomen: Kidney with intravenous contrast shows multiple low density lesions and surrounding dirty fat sign. (white arrow).

biopsy showed necrosis and bullae, and thrombosis, compatible with purpura fulminans. (Fig. 3 A, B) We planned to perform limb amputation after the patient's condition improved.

Hypotension and low platelet levels improved temporarily on day 9. However, he still had high-grade persistent fever with chills. All devices (central venous catheter, arterial line, vascular access) were changed and performed two sets of blood cultures, which revealed persistent bacteremia with *Enterobacter aerogenes*. Moreover, the patient became transfusion dependent because of the progressing anemia and low platelet levels. In total, the patient received 100 units of platelets and 10 units of red blood cells. His condition progressively worsened and he died on day 19. Autopsy was performed and revealed findings of multiple abscesses and thrombosis in the lung, intestinal tract, and kidney.

Discussion

We present a case of infectious purpura fulminans due to *Enterobacter aerogenes* which is rarely associated with purpura fulminans. Prior studies reported that the most common organism of AIPF is *Neisseria meningitidis*, followed by *S. pneumoniae* and *Haemophilus influenzae* [1]. Kubo et al showed that *S. pneumoniae* was the most common organism of AIPF in Japan in their case-review [5]. Other microorganisms, such as *Streptococcus* species [6,7], *Staphylococcus aureus* [8], and *Capnocytophaga canimorsus* have also been reported [9]. On the contrary. *Enterobacteriaceae* are very seldomly associated with AIPF. To date, only three cases of purpura fulminans due to *Enterobacter* have been reported [10,11]. We reviewed each case as well as our case (Table 1) with patients' ages ranging from neonates to adult. Two neonates had low protein C plasma activity. In all patients, the microorganism was *Enterobacter cloacae*. Therefore, we described the first case of purpura fulminans with *Enterobacter aerogenes,* which is known to cause nosocomial infections including urinary tract infections, pneumonia, and bloodstream infections [9].

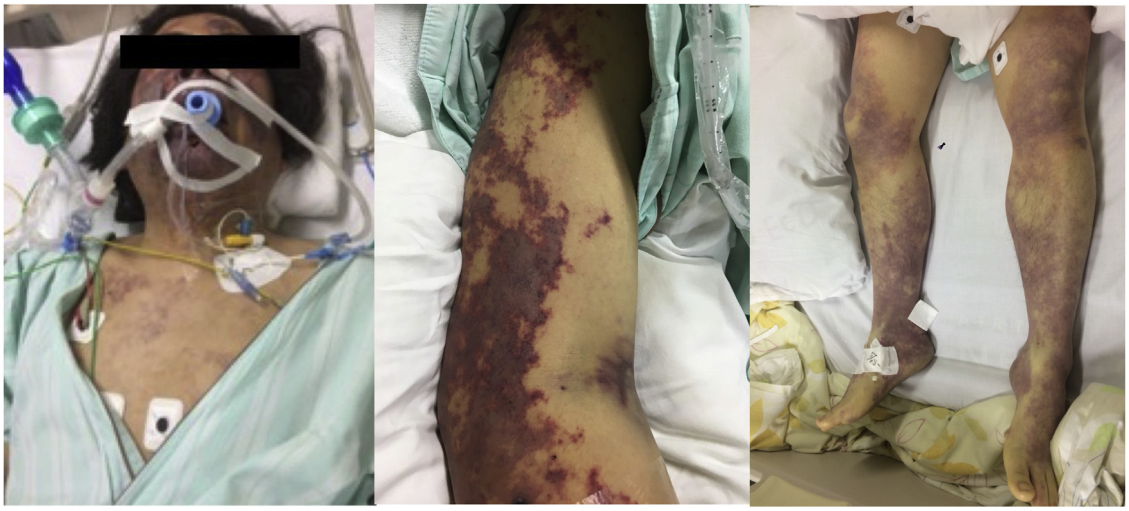

Fig. 2. Skin purpura and necrosis: The skin purpura presented from the face to the feet.

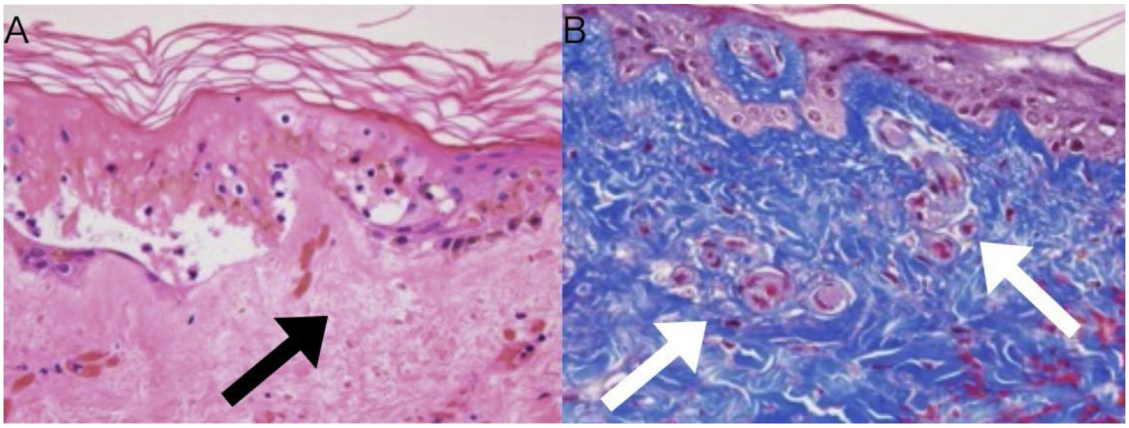

Fig. 3. A. Hematoxylin-Eosin stain (scale x400), Black arrow shows necrosis of the skin and capillary without inflammatory cellular infiltration. B Masson trichrome stain (scale x400), White arrows show thrombosis of capillary vessel.

Table 1
Summary of the published literature on purpura fulminans due to *Enterobacter species.*

Case	1	2	3	4
Reference number	10	10	11	Present case
Patient age (years)	0	0	79	48
Underlying disease	Low PC plasma activity	Low PC plasma activity	Lung cancer	Hypertension
Site of purpura fulminans	Feet, abdominal wall	Limb	Limb	Face, Limb
Causative agent	*E. cloacae*	*E. cloacae*	*E. cloacae*	*E. aerogenes*
Outcome	Survived	Survived	ND	Dead

PC: Protein C; ND: No Data.

AIPF is a rare complication of sepsis, which rapidly progresses to ischemic changes in the extremities and septic shock, DIC, and multiple organ failure. AIPF is therefore associated with high mortality. Most such cases require amputation for survival after recovering from AIPF. Contou D et al. showed that the rates of mortality associated with AIPF, at 54% (78/144 patients), and limb amputation, at 32% (12/37), were high in a multicenter retrospective cohort study in France [1]. Protein C deficiency is a known risk factor for AIPF. However, our patient had normal plasma protein C activity level and no asplenia.

In the present case, the infection could not be controlled successfully. We speculated that this could be attributable to the presence of abscesses in multiple organs, and thus, surgical debridement including limb amputation was considered to treat persistent bacteremia. Moreover, this patient was transfusion dependent. Laboratory data showed no evidence of hemolytic anemia and hemophagocytic syndrome. Autopsy of bone marrow showed no myeloproliferative disorder and CT scan showed no splenomegaly. Therefore, we concluded that the requirement of transfusion was caused by sepsis-induced DIC.

Conclusion

We described an uncommon case of AIPF associated with *Enterobacter* bacteremia. Further accumulation of similar cases is needed.

Conflict of interest

The authors state that they have no conflicts of interest.

Author contributions

SY cared for the patient and wrote the manuscript. RI cared for the patient and contributed to revising the manuscript.

Credit author statement

Shinya Yamamoto: Conceptualization, Data Curation, Formal Analysis, Investigation, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft

Ryoji Ito: Formal Analysis, Methodology, Project Administration, Supervision,Writing – Review & Editing

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