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Case Report

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# Purpura fulminans and pasteurella multocida infection in an adult: a case report

## Abstract

**Introduction:** Purpura fulminans (PF) is a rare rapidly progressive disease caused by microvascular thrombosis of skin vessels manifested as characteristic skin lesions. Three different subtypes have been described: neonatal, idiopathic and acute infectious. Treatment depends on subtype and may include antibiotic therapy, supportive treatment and transfusions [mainly fresh frozen plasma (FFP)].

**Case presentation:** A fifty nine-year-old female presented at emergency department with nausea, vomit, diarrhea and abdominal pain. She was hypotensive, tachycardic, jaundiced and had mild epigastric tenderness. Analysis revealed pancytopenia, coagulopathy, renal failure and hyperbilirubinemia. Arterial blood gas analyses showed compensated metabolic acidosis and hyperlactacidemia. Patient was started on vasopressor therapy for hypotension unresponsive to fluids. Nevertheless, her condition deteriorated and severe metabolic acidosis developed. A purpuric rash developed initially at left thigh and spread through abdomen and thorax. Patient was transferred to an intensive care unit after resuscitation from a cardiorespiratory arrest. Large spectrum antibiotic therapy and renal replacement technique were started as well as transfusion with platelets, FFP and red blood cells. Susceptible Pasteurella multocida was present in two hemocultures. Despite maximal supportive treatment patient's condition deteriorated and dyed 72 hours after admission.

**Discussion:** We described a case of severe acute infectious PF presenting in an adult with Pasteurella multocida bacteriemia. The uniqueness of this case report lye on the rarity of PF in adults and on being to our knowledge the first case described of PF caused by Pasteurella multocida infection.

**Keywords:** Purpura fulminans, Adult, Pasteurella multocida

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**Abbervations:** PF, Purpura Fulminans; DIC, Disseminated Intravascular Coagulation; FFP, Fresh Frozen Plasma; PM, Pasteurella Multocida; ED, Emergency Department; NA, Noradrenaline; HDFVVC, Continuous Venovenous Hemodiafiltration

## Introduction

Purpura fulminans (PF) is a rare syndrome occurring mostly in infants.[1,2] It is a rapidly progressive disease caused by microvascular thrombosis of skin vessels leading to hemorrhagic skin necrosis manifested as characteristic skin lesions.[1,3] Three different subtypes have been described, according to etiology and pathogenesis: neonatal PF, idiopathic PF and acute infectious PF.[1,2]

Acute infectious PF occurs in the presence of severe acute infection, most commonly caused by Neisseria meningitidis, followed by Streptococcus pneumonia.[4] Early full spectrum antibiotic, supportive therapy and fresh frozen plasma (FFP) are essential in this subtype of PF with high mortality rate. We describe a case of rapidly progressive acute infectious PF presenting in an adult with Pasteurella multocida (PM) bacteriemia. With this case report we aim to illustrate the potential life threatening severity of PF and illustrate a rare presentation due to its occurrence in an adult and to our knowledge unique association with PM bacteriemia.

## Case presentation

A fifty-nine year-old white female presented to the emergency department (ED) with abdominal pain, nausea, vomiting and diarrhea (> 15 stools/day). The symptoms had begun earlier that day. Patient denied any other symptoms. Patient had past previous history of alcoholic chronic liver disease with associated pancytopenia for hypersplenism, arterial hypertension, ischemic and hypertensive cardiomyopathy, proliferative mesangial glomerulonephrytis, type 1 neurofibromatosis and scleromyxedema. There was history of alcoholic consumption until five years ago. She was previously medicated with folic acid, etoricoxib, omeprazol, estazolam and enalapril/hydroclorotiazide on standard doses.

On physical examination tympanic temperature of 36ºC, hypotension (75/45 mmHg), tachycardia (108 bpm), jaundice, mild epigastric tenderness and mild bilateral lower limb edema. The remainder physical examination was unremarkable.

Laboratory evaluation Table 1 showed deterioration of chronic pancytopenia (hemoglobin 7,6 g/L; leukocytes 3,6 x 109/L; platelets 40 x 109/L), acute renal failure (creatinine 2,6 mg/dL; urea 50 mg/dL), coagulation abnormalities (prothrombyne time 22"; APTT 52,9"), mixed hyperbilirubinemia (total bilirubin 2,98 mg/dL; direct bilirubin 1,46 mg/dL) and reactive protein C elevation (36,3 mg/L). Compensated metabolic acidosis and hyperlactacidemia (lactate 5,95 mmol/L) on arterial blood gas analyses. Chest radiography was normal.

She was admitted at observation room and started on fluid resuscitation with need of noradrenaline (NA) to a maximal dose of 100 mcg/min. Metabolic acidosis and hyperlactacidemia gradually worsened. There was deterioration of mental status and development of a petechial rash at medial side of left thigh. Patient experienced cardiopulmonary arrest (pulseless electric activity for 6 minutes)

and was resuscitated with return of spontaneous circulation. Was intubated, mechanically ventilated and transferred to an intensive care unit.

At admission she was hypothermic, hypoglycemic, hypotense despite NA (100 mcg/min) and anuric. The purpuric rash had spread through all left lower limb; it consisted, at that stage, of larger, coalescent reticulated purple lesions. Anemia, thrombocytopenia and coagulation abnormalities had worsened. Had severe metabolic acidosis with central venous oxygen saturation of 67,2%. NA was augmented to a maximum of 130 mcg/min and transfused with packed red blood cells, FFP and platelets. Transthoracic ecocardiogram had no relevant abnormalities. Blood samples were collected for microbiologic examination and started large spectrum antibiotic with piperacillin/tazobactam and clindamycin (approximately 12 hours after admission at emergency department). After started on continuous venovenous hemodiafiltration (HDFVVC) (34 ml/Kg/h) hemodynamic improvement allowed further reduction of NA to 60 mcg/min, metabolic acidosis and renal function were improved.

During the next day (day two) new hemodynamic deterioration with NA increased to 100 mcg/min. Thrombocytopenia, hyperbilirubinemia and reactive protein C also worsened (Table 1). Broadened spectrum to meropenem, HDFVVC dose was augmented to 40 ml/kg/h and was transfused with packed red blood cells and FFP. Microbiologic results revealed susceptible PM on two blood samples. Her family revealed patient had a cat. On day three purpuric rash had spread to abdomen and thorax. Despite supportive treatment and adequate antibiotic therapy the patient's condition deteriorated and she died at the end of the day.

**Table 1** Laboratory evaluation and arterial blood gas analysis

| Laboratory Evaluation | Day One | | | Day Two | Day Three |
|---|---|---|---|---|---|
| | ER | OR | ICU | | |
| **Red Blood Cells (x$10^{12}$/L)** | 2,21 | 1,95 | 1,68 | 2,29 | 2,96 |
| **Hemoglobin (g/L)** | 7,6 | 6,7 | 5,7 | 7,6 | 9,6 |
| **Hematocrit (%)** | 21,8 | 19,3 | 16,9 | 22,0 | 28,1 |
| **MCV (fL)** | 98,6 | 98,8 | 100,6 | 96,0 | 95,1 |
| **MCH (pg)** | 34,4 | 34,4 | 33,9 | 33,2 | 32,4 |
| **White Blood Cells (x$10^{9}$/L)** | 3,6 | 2,6 | 4,8 | 2,0 | 4,50 |
| **Neutrophil (%)** | 94,24 | 87,15 | 83,22 | 83,31 | 91,71 |
| **Eosinophil (%)** | 0,75 | 3,67 | 2,80 | 2,02 | 1,39 |
| **Basophil (%)** | 0,09 | 0,00 | 0,28 | 0,05 | 0,03 |
| **Lymphocyte (%)** | 4,29 | 8,97 | 10,89 | 12,93 | 5,79 |
| **Monocyte (%)** | 0,63 | 0,21 | 2,81 | 1,69 | 1,08 |
| **Platelets (x$10^{9}$/L)** | 40 | 41 | 33 | 12 | 3 |
| **PT [seconds (%)]** | 22,0 (39) | 28,4 (28) | 41,3 (18) | 27,8 (29) | 42,5 (18) |
| **INR** | 1,87 | 2,39 | 3,42 | 2,34 | 3,52 |
| **Fibrinogen (g/L)** | | | | | 1,8 |
| **aPTT (seconds)** | 52,9 | 57,8 | 112,5 | 76,9 | 71,6 |
| **Glucose (mg/dL)** | 95 | 82 | 54 | | 113 |
| **Urea (mg/dL)** | 50 | 52 | 45 | 25 | 13 |
| **Creatinine (mg/dL)** | 2,6 | 2,8 | 2,34 | 1,19 | 0,58 |
| **eGFR** | 19 | 17 | 21 | 46 | >60 |
| **Total bilirubin (mg/dL)** | 2,98 | | 2,33 | 5,60 | 9,97 |
| **Conjugated bilirubin (mg/dL)** | 1,46 | | 1,64 | 3,60 | 6,02 |
| **AST (U/L)** | 144 | | 154 | 272 | 476 |
| **ALT (U/L)** | 51 | 50 | 42 | 67 | 125 |
| **GGT (U/L)** | 299 | 223 | 163 | | 138 |
| **ALP (U/L)** | 77 | 39 | 28 | | 47 |
| **LDH (U/L)** | 196 | | 197 | 252 | 271 |
| **CRP (mg/L)** | 36,3 | 50,9 | 44,2 | 66 | 73,1 |
| **Creatine kinase (U/L)** | 383 | | 291 | 538 | 268 |
| **Myoglobin (ng/mL)** | | 1602 | | 2483 | 1341,8 |

| Arterial Blood Gas Analysis | Day One | | | | | Day Two | | Day Three | |
|---|---|---|---|---|---|---|---|---|---|
| | ER | | OR | ICU | | | | | |
| | | 12:00 | 15:53 | 17:40 | 22:40 | 10:00 | 18:30 | 11:26 | 18:41 |
| **pH** | 7,39 | 7,17 | 6,79 | 6,96 | 7,19 | 7,25 | 7,26 | 7,25 | 7,16 |
| **$pCO_2$ (mmHg)** | 21 | 17,3 | 41,4 | 20,4 | 29,4 | 32,1 | 32,6 | 34,1 | 40,3 |
| **$pO_2$ (mmHg)** | 90,1 | 99,9 | 297,8 | 550,4 | 109,9 | 101,1 | 80,7 | 91,2 | 51,3 |
| **Bycarbonate (mmol/L)** | 12,3 | 6,2 | 6,2 | 4,5 | 11,2 | 14,0 | 14,4 | 14,7 | 14,0 |
| **$sO_2$ (%)** | 96,2 | 93,1 | 96,8 | 96,7 | 95,6 | 95,7 | 94,1 | 94,8 | 81 |
| **Lactate (mmol/L)** | 5,95 | 10,34 | 13,3 | 10,13 | 8,7 | 9,17 | 9,5 | 9,73 | 10,8 |

ER, Emergency Room; OR, Observation Room; ICU, Intensive Care Unit; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Hemoglobin; PT, Prothrombin Time; INR, International Normalized Ratio; aPTT, Activated Partial Thromboplastin Time; eGFR: Estimated Glomerular Filtration Rate; AST, Aspartate Transaminase; ALT, Alanine Transaminase; GGT, Gamma-Glutamyl Transferase; ALP, Alkaline Phosphatase; LDH, Lactate Dehydrogenase; CRP, C-Reactive Protein

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## Discussion

PF is a rare syndrome and its occurrence in adults is particularly unusual. Neonatal PF, idiopathic PF and acute infectious PF are three different subtypes differing in etiology and pathogenesis.[1,2] Acute infectious PF occurs simultaneously with a severe acute infection.[4] It is considered by some authors the skin expression of disseminated intravascular coagulation (DIC).[1] Its pathogenesis is likely related to the production of inflammatory cytokines such as interleukin-12, interferon-γ, tumor necrosis factor α and interleukin-I which ultimately cause a systemic and local imbalance in coagulation and anticoagulation pathways, due to enhancement of expression of tissue factor and consequent activation of coagulation cascade, inhibition of the natural anticoagulant mechanisms involving antithrombin III, protein C, protein S and tissue factor pathway inhibitor and inhibition of fibrinolysis by increasing plasminogen activator inhibitor.[1,2,5] This eventually leads to thrombosis of small vessels of the skin.

Neonatal PF is due to congenital mutations in either protein C or protein S genes, causing a prothrombotic disorder and consequent microvascular thrombotic occlusion, usually manifested as PF lesions in first 72h of life.[3,6] Idiopathic PF includes the cases of PF without evidence of acute infection or congenital deficiency of Protein C or S. Often occurs several days or weeks after a benign infection. Some studies suggest that it may be associated with the production of antibodies against protein S.[7]

Clinical features include characteristic purpuric skin lesions which evolve through several stages. These are variable but generally begin with a dermal discomfort, edema and erythema, subsequent development of petechiae that later coalesce into larger purpuric/ecchimotic lesions. Hemorrhagic bullae may form on subepitelial tissue and necrosis and gangrene may complicate it. Other manifestations are non-specific and dependent on subtype of PF. In acute infectious PF include constitutional symptoms, signs/symptoms of the underlying infection or signs of organ failure.[1,3] Cardinal laboratory features of acute infectious PF may be indistinguishable from those of DIC. Measurement of Protein C and S levels may also be considered in all subtypes but should not delay treatment.[3] In acute infectious PF source of infection should be investigated and appropriate cultures are mandatory.

Early full spectrum antibiotic and supportive therapy are essential for sepsis associated PF. FFP is useful in all types of PF as it provides protein C and S depleted in all forms of PF, as well as other procoagulant and anticoagulant proteins depleted in DIC. Additional transfusions may be needed (platelets, fibrinogen).[2,3] Protein C concentrate is approved for the prevention of PF in neonatal subtype.[6] Other therapies requiring further investigation include antithrombin III, hyperbaric oxygen and prostacyclin/epoprostenol.[1,2] In the case described the patient developed skin purple large coalescent papules that rapidly spread through the body. The characteristics of the skin lesions along with concomitant documented acute severe infection with septic shock and the association with DIC accounted for the diagnosis of acute infectious PF.

Adequate therapeutic measures were taken namely full spectrum antibiotic, supportive measures (vasopressor therapy, HDFVVC, mechanical ventilation) as well as FFP transfusion. However the patient did not survive. PF is a poor prognosis factor in severe sepsis with a mortality rate that reaches 80% in adults.[5] In a study of Gamper et al.[8] the severities of lactic acidosis and DIC at admission were the best predictors of mortality in sepsis-associated PF. Those were major features in our patient. The time elapsed between ED admission and antibiotic administration may have also adversely affected prognosis of this patient. This case report illustrates severity of PF and also intends to evocate the importance of rapid recognition and prompt initiation of adequate treatment in order to improve prognosis.

In our patient blood cultures revealed PM bacteriemia likely acquired from her cat. PM is a gram negative coccobacillus. The infection in humans is often caused by a cat or dog bite, lick or scratch as it is a usual commensal in the upper respiratory tract of these and other animals. It may also be transmitted horizontally and vertically between humans. PM can cause a wide variety of infections including soft tissue, respiratory tract, cardiovascular, central nervous system, intraabdominal, genitourinary and ocular infections.[9] The spectrum of severity is wide, ranging from generally benign soft tissue infections, which usually resolve with antibiotic and drainage, to more serious invasive infections like Pasteurella meningitis and bacteremia that carry high mortality rates (25% and 30%, respectively).[10,11]

It is important to inquire about animal exposure and to consider Pasteurella spp infection in patients with domestic cats, since it is the main agent of infection (75% of infections) transmitted by cat bite or scratch.[12] PF is a rare disorder and it is even rarer in adults although there are cases described in the literature.[4,8] Several infections can cause this syndrome but this is to our knowledge the first case reported of PF caused by PM.

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## Conflicts of interests

Authors declare that there is no conflict of interest.

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