# Rare fatal case of purpura fulminans due to pneumococcal sepsis in a child, associated with multiorgan failure

*Gheorghiță Jugulete*[1], *Maria Mădălina Merișescu*[2,*], *Carmen Pavelescu*[3], *Monica Luminița Luminos*[4]

## Abstract

**Introduction** ***Streptococcus pneumoniae*** **is one of the associated bacteria that can cause the rare but high mortality hematological pathology known as purpura fulminans (PF) in both adults and children. Pediatric patients with PF can progress quickly to sepsis and multiorgan failure, especially immunocompromised individuals and young children. Due to the thrombotic blockage of blood arteries in PF, there is diffuse intravascular thrombosis and hemorrhagic infarction of the skin, which evolves from ecchymosis to skin necrosis, risk of limb sequelae, sepsis and fatality.**

**Case report We present a case of a previously healthy 1-year and 9-months old female who was admitted to the Intensive Care Unit of the National Institute of Infectious Diseases "Prof. Dr. Matei Balş"- Bucharest, Romania. On physical examination, she was febrile, hypotensive, tachycardic, and had erythematous patches on her left upper limb and trunk. Initial blood work was significant for creatinine 4.45 mg/dL, aspartate aminotransferase 112 U/L, alanine aminotransferase 130 U/L and fibrinogen 596 mg/dL. Hematological workup showed a white blood cells count of 34 × $10^9$/L, hemoglobin 9.7 g/dL, platelets 23000/L, D-dimers 89000 µg/L, and elevated PT and aPTT. Broad-spectrum antibiotics vancomycin and ceftriaxone were administrated. A lumbar puncture was performed for cerebrospinal fluid (CSF) analysis and culture grew *Streptococcus pneumoniae* serotype 1A. She required peritoneal dialysis due to acute kidney injury (AKI) and surgeries for affected skin areas. After multiple organ system failures, our patient evolved rapidly to irreversible tissue necrosis and death.**

**Conclusions We aim to report a rare case of PF associated with pneumococcal meningoencephalitis in an immunocompetent child, to better appreciate the risk of fatal evolution when managing this disease in children.**

**Keywords** ***Streptococcus pneumoniae*****, purpura fulminans, sepsis, shock, children, multiple organ and system failures, mortality.**

## Introduction

PF is a rapidly progressive fatal syndrome characterized by purpuric lesions and is often associated with ecchymosis and necrosis due to diffuse thrombosis and disseminated intravascular coagulation.[1-3] About 90% of the cases that have been described in the pediatric literature have been fatal. Three forms of PF are described as follows: neonatal, idiopathic and acute infection. First is the patient with abnormalities of the protein C or protein S anticoagulant course.[3,4] The second condition is

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[1]MD, PhD, Faculty of Dentistry, Carol Davila University of Medicine and Pharmacy, No. 37, Dionisie Lupu Street, 020021 Bucharest, Romania, and National Institute for Infectious Diseases "Prof. Dr. Matei Balş", No. 1 Dr. Calistrat Grozovici street, Bucharest, 021105, Romania; [2]MD, PhD, Faculty of Dentistry, Carol Davila University of Medicine and Pharmacy, No. 37, Dionisie Lupu Street, 020021 Bucharest, Romania, and National Institute for Infectious Diseases "Prof. Dr. Matei Balş", No. 1 Dr. Calistrat Grozovici street, Bucharest, 021105, Romania; [3]MD, PhD, Faculty of Dentistry, Carol Davila University of Medicine and Pharmacy, No. 37, Dionisie Lupu Street, 020021 Bucharest, Romania; [4]MD, PhD, Faculty of Dentistry, Carol Davila University of Medicine and Pharmacy, No. 37, Dionisie Lupu Street, 020021 Bucharest, Romania, and National Institute for Infectious Diseases "Prof. Dr. Matei Balş", No. 1 Dr. Calistrat Grozovici street, Bucharest, 021105, Romania.

*Corresponding author: Maria Mădălina Merișescu, madalina.merisescu@umfcd.ro


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the rarest form of the disease, and the third form is the most common type, and it manifests as hemorrhagic necrosis due to thrombosis of the microvascular system of the skin.[2-6] *Streptococcus pneumoniae* can cause different kinds of infections, including invasive pneumonia, and can also be associated with a more severe disease course and can cause PF.[1,4-6] Pneumococcal infections are dangerous and often require hospitalization, with mortality rates between 8 to 15%.[7-10] As of clinical presentations, PF first develops cutaneous macules, which become indurated and then evolve into irreversible necrosis of the skin, sepsis, and secondary infections that may occur as gangrene. As necrosis extends to deeper tissues, it is associated with a high incidence of amputations, and skin grafts and decreases in survival rate.[11-15] We herein report a rare case of PF due to acute infection caused by *S. pneumoniae*, in a healthy and completely vaccinated child.[15,16]

## Case report

This previously healthy one-year-old nine-month-old girl, pneumococcal vaccine immunized, with a two-day history of fever, nasal obstruction, mucopurulent rhinorrhea, otorrhea, and productive cough developed a high-grade fever (39.8°C) and became lethargic and presented to the Pediatric Intensive Care Unit at the National Institute for Infectious Diseases, „Prof. Dr Matei Balş", Bucharest, Romania.

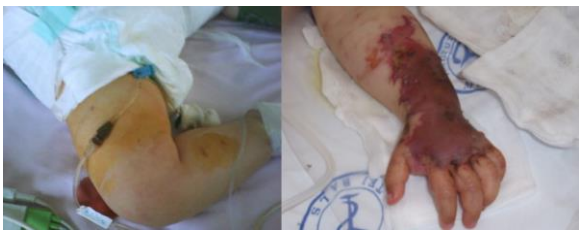

**Figure 1. Petechial rash on both arms**

From the initial examination in our Pediatric department, she was very ill-appearing, dehydrated, hypotensive (55/30 mmHg), tachycardic (188 beats/min), had delayed capillary refill, and petechial rash on both her arms and trunk (Figure 1). The presumptive diagnosis was purpura fulminans.

On auscultation, there were crepitations at both bases of the lungs. The abdominal examination did not reveal peritoneal signs. Abnormalities in laboratory studies included tests as follows: elevated C reactive protein 97 mg/L, leukocytosis 34.000/µL, anemia (Hb 9.7 g/dL), thrombocytopenia – platelets 23000/µL, impaired renal function (creatinine 4.45 mg/dL), hyponatremia and hyperkalemia. She also presented serum procalcitonin (PCT-Q), hepatic cytolysis syndrome, increasing values of serum urea. Coagulation tests showed disseminated intravascular coagulation (DIC) with prolonged prothrombin time (international normalized ratio >5.59), activated partial thromboplastin time over 160 s, thrombin time over 140 s, and increased D-dimer levels 8.9 mg/dL). Follow-up laboratory tests revealed deterioration of coagulopathy, with increased prothrombin time, (Table 1). The blood cultures were sent for incubation and no growth was detected. Urine culture tests were negative. Nose and throat swabs showed the absence of adenovirus, influenza A, B, and respiratory syncytial virus. Chest radiograph revealed pneumonia and a diagnosis of sepsis due to streptococcal infection was suspected and prompted broad-spectrum antibiotics: vancomycin (60 mg/kg/day) and ceftriaxone (100 mg/kg/day) were administrated. Standardized sepsis therapy was applied according to the surviving sepsis guidelines. On the second day of admission, the lumbar puncture revealed cloudy, purulent cerebrospinal fluid (CSF), latex agglutination positive for *Streptococcus pneumoniae* serotype 1A. Purpura fulminans was confirmed as a diagnostic when evidence of a severe infection, shock liver, and DIC was associated. The areas of ecchymoses on the left hand lesions became necrotic after 3 days and required surgical debridement, and the patient was transferred to the plastic surgery clinic (Figure 2). After 14 days, the patient developed anuria and required peritoneal dialysis.

Despite all therapeutic efforts, antibiotic therapy and aggressive supportive care in an intensive care unit, the patient did not recover and multi-organ failure (cardio-respiratory, hematological, hepatic, neurological, renal) developed since day 15 throughout her

**Table 1. Laboratory values during hospitalization of the pediatric patient with PF**

| Parameter | 1st week | 2nd week | 3rd week | 4th week | Reference range |
|---|---|---|---|---|---|
| White blood cells (WBC) $\times 10^9$/L | 34 | 31.5 | 23.3 | 33.8 | 4-11 |
| Platelets $\times 10^9$/L | 23 | 28 | 29 | 24 | 150-400 |
| Hemoglobin g/dL | 9.7 | 9.6 | 10.8 | 9.4 | 12-15 |
| Fibrinogen mg/dL | 596 | 697 | 331 | 440 | <400 |
| Prothrombin time (PT) seconds | 140 | 81 | 90 | 134 | 11-15 |
| Aspartate aminotransferase (AST) U/L | 112 | 96 | 64 | 102 | 14-50 |
| Alanine aminotransferase (ALT) U/L | 130 | 122 | 120 | 110 | 0-50 |
| Serum creatinine mg/dL | 4.45 | 4.40 | 3.00 | 2.90 | <0.7 |
| D-dimers mg/L | 8.9 | 9 | 9.3 | 10 | 0-0.50 |

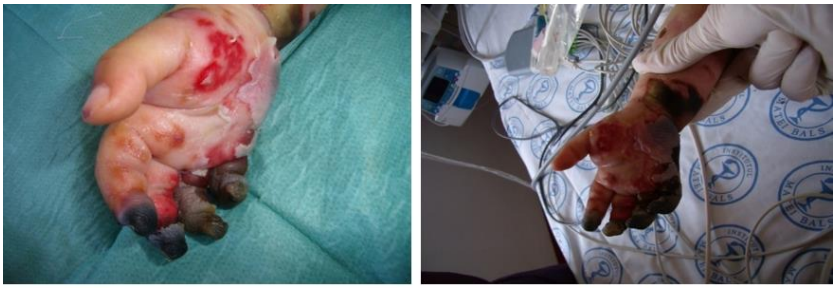

**Figure 2. Necrotic lesions on the hand**

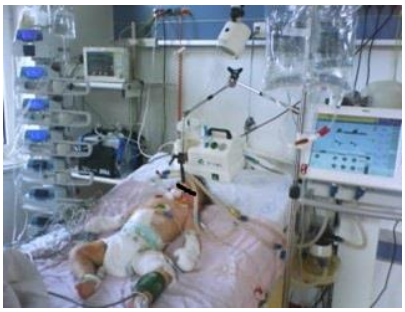

**Figure 3. Patient was intubated and mechanically ventilated**

hospitalization. On the 16th day of hospitalization, the child was intubated, and mechanically ventilated, and complex therapy was administered, supporting vital functions, hydro-electrolytic and acid-base rebalancing, pathogenic methylprednisolone 1 mg/kg/day pulse therapy), antibiotic vancomycin (60 mg/kg/day) and ceftriaxone (100 mg/kg/day), symptomatic therapy, and peritoneal dialysis. (Figure 3). Heparin administration could not be started due to thrombocytopenia. The patient succumbed within 30 days of admission, despite early recognition of purpura fulminans, septic shock and complex therapy administration.

## Discussion

Purpura fulminans, also known as purpura gangrenous, is a rare and life-threatening disorder, and it manifests as a widespread purpuric rash that develops hemorrhagic necrosis. It occurs in both adults and children and is accompanied by vascular collapse, fever

and DIC.[11-13,16] In our case, the clinical symptoms are indicative of microangiopathic thrombosis with hemolysis related to DIC. PF lesions can be distinguished from other purpuric lesions by their distinctive appearance. Rapidly following erythema are black hemorrhagic necrosis centers surrounded by an erythematous border, as our patient developed.[16-18] Recent observations include the development of hard eschar and the production of vesicles and bullae, which indicate the progression of hemorrhagic necrosis. Usually, the most seriously affected are the distal extremities. Henoch-Schönlein bullous purpura was first thought to be a differential diagnosis because of the palpable purpura and blisters.[13-15] Deep tissue may be compromised by extensive skin necrosis, necessitating surgical debridement and fasciotomy. For this reason, early diagnosis and prompt rehabilitation depend on a multidisciplinary patient follow-up involving plastic surgery healthcare teams. The prognosis for this age category is poor once soft tissue ischemia evolves to necrosis because it is associated with arterial and venous thrombosis leading to serious events and death.[19]

We found *S. pneumoniae* associated with the course of sepsis and PF. The Center for Disease Control (CDC) advises pneumococcal vaccinations for young children (less than 5 years old), as part of regular prophylaxis. Routine vaccination with 13-valent pneumococcal vaccine with 3 doses at ages 2, 4, and 11 months is the indicated active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae*, in children aged 6 weeks and older.[12-14] Unfortunately, vaccination does not fully eliminate the risk of invasive infection in our case report. Sepsis resulting from pneumococcal infection typically presents so dramatically that immunosuppression is involved. Most examples that have been documented in the literature include people who have some kind of immunodeficiency. This dramatic presentation in a healthy pediatric patient has only been described in a small number of cases. We compared our data with similar articles published on children with PF and the condition was complicated by hemodynamic collapse with skin involvement necrosis of the skin.[20-22]

Follow-up laboratory tests revealed deterioration and coagulopathy, elongated prothrombin time and dimerized fragment D and fibrinogen. Several differential diagnoses, including drug-related skin reactions like Steven-Johnson syndrome, toxic epidermal necrolysis, cryoglobulinemia as well as autoimmune vasculitis and immunological tests were unspecific in our patient.[24] Other etiologies of infections were found to be negative, and this workup confirmed the cause of PF was *Streptococcus pneumoniae* serotype 1A. In an intensive-care environment, patients with purpura fulminans and severe bacterial infections should be treated with strong fluid resuscitation, correction of electrolytes, inotropic support if necessary and early delivery of antibacterial medications. Vancomycin is active against strains of *S. pneumoniae* for the treatment of meningitis and should be administrated with cefotaxime or ceftriaxone to severely sick or immunocompromised children who may have pneumococcal pneumonia, until information on the organism's susceptibilities is available.[25,26]

Lerolle and colleagues studied patients with PF, and included patients with severe sepsis. They observed the occurrence of multiple organ failure, with a higher mortality rate.[27] Patients with PF had a low number of platelets, and high levels of D-dimers, but similar levels of fibrinogen. In our situation, the patient status is associated with multiple systems organ failure, but the fibrinogen is increased in the dynamics. It is known that certain infectious diseases are later complicated by PF, after the initial disease has resolved.[28]

## Conclusions

We think that it's important for clinicians to be knowledgeable of this diagnosis and to have a considerable level of suspicion when disseminated intravascular coagulation and thrombocytopenia are present in conjunction with PF, as this dermatological finding is uncommon among patients in the critical care setting. This clinical case reveals the severity of

systemic infection with *Streptococcus pneumoniae* serotype 1a, in a pediatric patient who developed septic shock, and multiorgan failure. PF can cause irreversible tissue necrosis and, in severe cases, death.

**Authors' contributions statement:** Conceptualization, GJ, MLL, CP, MMM; Validation, GJ, MLL, CP, MMM; Formal analysis, GJ, CP; Investigation, GJ, CP; Resources, GJ, MLL; Data curation, GJ, MMM; Writing–Original draft preparation, GJ; Writing–Review & Editing, GJ, MLL, CP, MMM; Visualization, GJ, CP; Supervision, GJ; Project administration, GJ, MLL, CP, MMM. All authors read and approved the final version of the manuscript.

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