

**PURPURA FULMINANS IN PROGRESS OF ACUTE MENINGOCOCCAL SEPSIS IN A  
24-YEAR OLD WOMAN, ENDED WITH RECOVERY**Pekova L.<sup>1\*</sup>, P. Parousheva<sup>1</sup> and D. Petrov<sup>2</sup><sup>1\*</sup>Clinic of Infectious Diseases, University Multiprofile Hospital of Active Treatment, Stara Zagora, Bulgaria.<sup>2</sup>Deptm. of Social Medicine and Health Management, Medical Faculty, Trakia University, Stara Zagora, Bulgaria.**\*Author for Correspondence: Dr. Pekova L.**

Clinic of Infectious Diseases, University Multiprofile Hospital of Active Treatment, Stara Zagora, Bulgaria.

Article Received on 11/01/2016

Article Revised on 31/01/2016

Article Accepted on 21/02/2016

**SUMMARY**

We present a case of acute meningococcal sepsis in a 24-year old female. She presented with a 12 hours history of fever, asthenia, headache and vomiting. Just an hour before the admission a petechial rash on the lower extremities appeared. On admission there was a clinical manifestation of septic shock and cardiovascular collapse - temperature, RR 50/20, heart rate 140-160 per minute, respiratory rate 4 per minute. Her skin was greyish, cyanotic with a typical hemorrhagic-necrotic rash widely distributed over the lower extremities. Enlarged liver and spleen presented. The neurological examination revealed brisk tendon and periosteal reflexes and mild signs of meningeal-radicular injury (MRI). Blood tests showed leukocytosis with a left shift, hemostasis disorders. The cerebrospinal fluid (CSF) changes were consisted with those of purulent bacterial meningitis. Microbiological blood and CSF tests proved *N. meningitidis* serogroup C. A provisional diagnosis of meningococemia associated purpura fulminans (PF) was considered. Initial treatment with Medaxon and Penicillin with corticoids was started immediately. In the next days the patient's condition deteriorated. The skin lesions progressed to involve the whole body, areas of hemorrhagic necrosis appeared. Auto-amputation of the distal phalanges of II, III, IV and V toe of the right leg and the heel of the left leg occurred. The patient was discharged after a hospital stay of 28-day stay and transferred to the plastic surgery unit. Six years later after 16 reconstructive surgical procedures she was in invalid wheel-chair, a mother of a 2-year-old child.

**KEYWORDS:** acute meningococemia, adult patient, clinical course.**INTRODUCTION**

Purpura fulminans is an acute, often fatal, thrombotic disorder which manifests with hemorrhagic necrotic skin lesions and clinical features of disseminated intravascular coagulation (DIC).<sup>[1]</sup> It has been first described by Guelliot in 1884 as hemorrhagic condition usually associated with either benign infection of severe sepsis. Clinical feature include hypotension, DIC and purpura leading to tissue necrosis with small vessel thrombosis.<sup>[2,3]</sup> PF is a rare syndrome of intravascular thrombosis and hemorrhagic infarction of the skin that is rapidly progressive and is accompanied by vascular collapse and DIC. PF is classified into the following 3 types:

1. Neonatal.
2. Idiopathic.
3. Acute infections.

PF most commonly occurs in babies and small children, but it can also affects young adults. Severe clinical course is typical for the least age group.<sup>[4]</sup>

The most common type of PF is acute infections. Gram-negative bacilli are most often associated with this form of PF.<sup>[5]</sup>

The 4 primary clinical features of this syndrome are as follows:

- Large purpuric skin lesions
- Fever
- Hypotension
- DIC.<sup>[1]</sup>

Sepsis-induced PF is a rare but life-threatening disorder. Meningococcal sepsis accompanied with multiple organ failure is associated with more than 50% mortality. Meningococcal sepsis is the most common cause followed by pneumococcal sepsis. Meningococemia is a disease with a potentially devastating consequences. It is complicated by PF in 10-20% of cases among children.<sup>[6,7,8,9]</sup> PF is often accompanied by microvascular thrombosis and hemorrhagic infarction in the lungs, kidneys, central nervous system and adrenal glands leading to multiple organ failure and causes initial high mortality.

**CASE REPORT**

A previously healthy 24-year-old female was admitted to the Department of Infectious diseases with a 12-hour history of asthenia, severe headache, vomiting and fever – 37,6°C. Some hours before admission she had severe pains in her legs, where a petechial rash developed. Her past medical history was unremarkable. Ten days prior to admission her 1-year-old son had an acute respiratory infection. He was treated symptomatically assuming a viral illness diagnosis and soon recovered.

On admission the patient was in a generally very bad condition, drowsy, but conscious.

There are a clinical manifestation of septic shock and vascular collapse – RR 50/20, heart rate 140-160 per minute, temperature 35,5°C. Her skin was greyish, cyanotic with characteristic polygonal hemorrhagic-necrotic rash. It began distally-from the lower extremities an thighs – progressed proximally and in several hours involved the whole body forming large blue-black necrotic areas. **Fig 1.** On lung auscultation basal decreased vesicular breathing with the crackles were heard. There was a moderate hepatosplenomegaly continuous bleeding from vascular access sites, nosebleeds and macroscopic hematuria presented.

Neurological examination revealed exaggerated tendon and periosteal reflexes and mild MRI. On admission hematological findings include mild leukocytosis with a left shift, increased erythrocyte speed rate (ESR) and coagulation disorders. In the next days leukocytosis increased, anaemia appeared, coagulation disorders deteriorated.

**Tab. 1.**

A lumbar puncture was performed some hours after the entry. CSF was clear and colorless, under normal pressure with normal cellularity and normal levels of glucose and proteins. Gram stain examination of CSF identified the causative agent – *Neisseria meningitidis*. Latex agglutination testing was positive for *N. meningitidis* as well CSF cultures confirmed *N. meningitidis* serogroup C. Despite aggressive treatment her cardiovascular state remained bad in the following two days, skin lesions progressed rapidly affecting the whole body surface and forming large necrotic areas.

**Tab. 1. Laboratorial findings in blood in a patient with PF.**

Variable (unit)	Reference range	Admission	1-st day	5-th day	15-th day	28-th day
Hemoglobin (g/L)	120-155	140	135	103	105	97
White blood cells (x10 <sup>9</sup> /L)	3,5-10,5	17,3	24,3	44,6	15,5	11,4
Metamyelocytes	/	15	5	3	0	0
Band-neutrophils (%)	3-6	30	33	6	1	3
Neutrophils (%)	51-67	47	55	80	71	64
Lymphocytes (%)	22-40	4	4	7	24	25
Monocytes (%)	4-8	2	1	4	4	8
Trombocytes (x10 <sup>9</sup> /L)	140-440	140	54	11	144	444
Urea (mmol/L)	1,67-8,2	8,2	4,7			7,3
Creatinin ( )	44-134	124	76			84

On the third hospital day the patient exhibited symptoms of MRJ – severe neck stiffness, Brudzinski neck sign, Brudzinski symphyseal sign, Kernig's sign, Babinski sign. Temperature was 40°C, i.e. a clinical manifestation of bacterial meningitis. A second lumbar puncture was performed. The CSF changes were consistent with those of bacterial meningitis. **Tab. 2.**

Blood and CSF cultures were positive for *N. meningitidis* serogroup C. The nasal microbial flora was positive for *N. meningitidis* as well.

On the fifth hospital day the patient was clinically improved. The temperature was sub-febrile. The asthenia presented, but the patient appeared rational, the blood pressure rose to quasinormal levels, the puls rate became normal, respirations – slower and deeper. On the following days her cardiovascular state remained stable, but well demarcated blue-black gangrenous areas on the lower extremities presented. **Fig 2, 3.** Later auto-amputation of the distal phalanges of the toes, feet and the knee of the right leg occurred.

Healing left large scars on her face, hands, arms and trunk.

Four weeks after admission the patient was discharged.

Her laboratorial findings were good. CSF and blood tests were negative for *N. meningitidis*. She was transferred to the plastic surgery unit where she had reconstructive surgical procedures.

Therapeutic interventions include:

- Antibacterial therapy on the basis of antibiogram – Medaxon and Penicillin in maximum doses
- Corticoids – Meteparin for the first 24 hours
- Dobutamin was given for the first 3 days
- Humman albumin
- Immunvenin
- Fresh frozen plasma
- Volume fluids

Six years later after 16 reconstructive surgical procedures she was in invalid wheel-chair and a mother of a 2-year-old son. **Fig. 4.**

C-reactive protein (mg/L0	0.0-6,0	246	320		45	11
Total protein (g/L)	58-80	57	61	72		
Albumin (g/L)	40-55	31	30	35		
Prothrombin time (sec)	11-14	55	41,9	15,2	11,4	12,8
Fibrinogen (g/L)	2,0-4,5	0,4	1,2	2,5	3,7	3,0

Tab. 2 Laboratorial findings in CSF in a patient with PF.

Variable (unit)	Reference range	Admittance	1-st day	5-th day	15-th day	28-th day
Glucose (mmol/L)	2,5-3,9	4,9	0,3	1,9	3,0	2,9
Protein (g/L)	0,15-0,45	0,36	6,36	1,30	0,75	0,54
White blood cells	0-6	0	2160	1572	480	20
Neutrophils(%)	/	/	82	56	26	28
Erythrocytes	/	208	130	433	109	16
Chlorides (mmol/L)	115-132	111	96	119	122	116
Pandy's	-	±	+++	++	+	-



Fig. 1. Image of hemorrhagic-necrotic rash.



Fig. 4 View of the patient's legs six years later.



Fig. 2. Formation of the demarcation areas.



Fig. 3 Severe defeat of the right step.

## DISCUSSION

PF is a rare syndrome and most commonly occurs in babies and small children, but it can also be a rare manifestation in young adults when it is associated with severe infections.

We have described a case of acute infectious PF associated with meningococcal sepsis in a 24-year old female. *N. meningitidis* serogroup C was confirmed as a causative agent. As it was noted 10 days before the onset of the disease her 1-year-old son has had an acute respiratory infection. The child has been hospitalized and his mother has nursed him. The suspicion arose that the child developed a mild form of meningococcal disease demonstrated with high fever, asthenia and sore throat, but the mother developed the most severe form of the same illness- an acute infectious PF associated with meningococcal sepsis. To confirm this suspicion the patient's household members had microbiological and serological tests for *N. meningitidis*. The child's nasal microbial flora was positive for *N. meningitidis* serogroup C and his serological test revealed IgG antibodies against *N. meningitidis* serogroup C.

The clinical course of the reported case is typical – an acute onset with the development of cutaneous hemorrhagic-necrotic rash in less than 24 hours.<sup>[1,10]</sup>

The appearance of skin lesions is characteristic – they began distally, has a proximal progression and in 48

hours spread to involve the whole body. Necrotic lesions progress to distal ischemia affected areas are painful and indurated, necrosis extends to muscle and bone.

Healing leads to scarring and auto-amputation of digits and extremities.

DIC and dermal vascular thrombosis causes hemorrhagic infarction of the skin. Septic shock manifests with hypothermia, tachycardia and hypotension.<sup>[5]</sup>

The first two days after admission clinical features of septic shock were predominant. There was no typical clinical and laboratorial presentation of a bacterial meningitis, but microbiological CSF tests were positive for *N. meningitidis* serogroup C.

On the third hospital day the CSF involvement became obvious – the patient developed the classic signs and symptoms of purulent meningitis. The CSF changes were consistent with those of a bacterial meningitis. As it is well known when meningococcal sepsis with obvious meningitis occurs the prognosis is better. On the fifth hospital day the patient was clinically improved. The clinical course from that time on was one of progressive improvement.

Typical hematological findings occurred and included prolonged prothrombin time, low concentration of fibrinogen, raised fibrinogen degradation products. Platelet count and concentration of protein C were reduced. Early administration of platelet concentrate minimizes purpura skin injury and reduces the inflammatory cascade before irreparable tissue injury occurs.<sup>[11]</sup>

Early surgical consultation is essential. Skin and soft tissue-releasing incisions should be considered early to reduce the incidence of extremity necrosis. Small necrotic areas usually separate spontaneously with secondary healing. Larger necrotic areas should be existed only after demarcation has been established.<sup>[6,12,13]</sup>

Early antibiotic administration and intensive care management according to the recommendations of severe sepsis and shock is crucial for patient's survival.<sup>[5]</sup>

In the reported case antibiotics on the basis of the antibiogram were given –Medaxon and Penicillin. Replacement of deficient blood component – fresh frozen plasma and clotting factors - is the main stay of therapy of PF with DIC. Intravenous immunoglobulin therapy should be implemented because these preparations contain significant antibodies against the causative endotoxins.<sup>[7]</sup>

Without treatment necrotic soft tissue may become gangrenous leading to loss of limbs. Once PF lesions

progress to full-thickness skin necrosis, healing takes between 4-8 weeks and leaves large scars.<sup>[5]</sup>

Meningococcal sepsis is the most common cause of PF and is associated with more than 50% mortality.<sup>[14]</sup>

The reported case illustrates the clinical presentation of meningococcal sepsis with obvious meningitis and PF. The clinical course includes an acute onset and hemorrhagic-necrotic skin lesions caused by DIC. The involvement of CSF indicates a better prognosis. The early and exact diagnose and prompt administration of appropriate antimicrobial therapy were important for a favorable outcome.

## REFERENCES

1. Chalmers E, Cooper P, Forman K, Grimley C, Khair K, Minford A, Morgan M, Mumford A D "Purpura fulminans: recognition, diagnosis and management". *Arch Dis Child*, 2011; 96(11): 1066–1071.
2. Betrosian AP1, Berlet T, Agarwal B. Purpura fulminans in sepsis. *Am J Med Sci.*, 2006 Dec; 332(6): 339-45.
3. Tuddenham, EG, Takase T, Thomas, AE, Awidi AS, Madanat FF, Abu Hajir MM, Kernoff PB Hoffbrand AV "Homozygous protein C deficiency with delayed onset of symptoms at 7 to 10 months". *Thromb Res*, 1989; 53(5): 475-84.
4. D'Cruz D, Cervera R, Olcay Aydintug A, Ahmed T, Font J, Hughes GR. Systemic lupus erythematosus evolving into systemic vasculitis: a report of five cases. *Br J Rheumatol.*, Feb 1993; 32(2): 154-7.
5. Nolan J, Sinclair R. Review of management of purpura fulminans and two case reports. *Br J Anaesth.*, 2001 Apr; 86(4): 581-6.
6. Numanoglu A, Bickler SW, Rode H, Bosenberg AT. Meningococcal septicaemia complications involving skin and underlying deeper tissues--management considerations and outcome. *S Afr J Surg.*, 2007 Nov; 45(4): 142-6.
7. Dries DJ, Peterson ML, Schlievert PM. Purpura fulminans due to *Staphylococcus aureus*. *Clin Infect Dis.*, 2005; 40(7): 941-7.
8. Wong VK, Hitchcock W, Mason WH. "Meningococcal infections in children: a review of 100 cases". *Pediatr Infect Dis J.*, 1989; 8(4): 224–227.
9. Manco-Johnson MJ, Abshire TC, Jacobson LJ, Marlar RA. Severe neonatal protein C deficiency: prevalence and thrombotic risk". *J Pediatr.*, 1991; 119(5): 793–798.
10. Ghosh SK, Bandyopadhyay D, Dutta A. Purpura fulminans: a cutaneous marker of disseminated intravascular coagulation". *West J Emerg Med*, 2009; 10(1): 41.
11. Smith OP, White B. Infectious purpura fulminans: caution needed in the use of protein C. *Br J Haematol.*, 1999; 106(1): 253-4.
12. Kaul R, McGeer A, Norrby-Teglund A, Kotb M, Schwartz B, O'Rourke K. Intravenous

immunoglobulin therapy for streptococcal toxic shock syndrome – a comparative observational study. The Canadian Streptococcal Study Group. *Clin Infect Dis.*, 1999; 28(4): 800-7.

13. Herrera R, Hobar PC, Ginsburg CM. Surgical intervention for the complications of meningococcal-induced purpura fulminans. *Pediatr Infect Dis J.*, 1994; 13: 734-7.
14. De la Maza LM, Pezzlo M. Purpura fulminans In *Neisseria meningitidis* sepsis. *N Engl J Med.*, 1996; 334: 1709.