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Case report

Fulminant Meningococcal Sepsis in a Young Child – A Case Report

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A B S T R A C T

We are presenting a case of isolated fulminant meningococcal sepsis with two and a half year old child. Initial symptoms were obscure and common to many medical conditions, but also previously described as symptoms of meningococcal sepsis. Unrecognizing the seriousness of the condition child died at home, within few hours after examination and discharge from the hospital. Autopsy and microbiological findings unquestionably proved that the child died from septic shock caused by fulminant meningococcal sepsis.

Key words: *sepsis, meningococcal infections, Waterhouse-Friderichsen syndrome,* Neisseria meningitidis

Introduction

Meningococcus (*Neisseria meningitidis*), a Gram-negative, oval, intracellular B proteobacterium, has been recognized as the cause of epidemic meningitis and sepsis, and it has inflicted rapid death and fear on disparate human populations for last for two hundred years[1]. Humans are the only hosts for the meningococcus, and the most common site of it's natural habit is epithelium of nasopharynx[1,2]. Other meningococcus habit sites in human body can be bucal mucosa, rectum, urethra, urogenital track, and dental plaque[1,2]. Virulence determinants of meningococcus include: polysaccharide capsule, outer membrane proteins and pili, the porins A and B, the adhesion molecule, iron sequestration mechanisms and endotoxin[1–3]. Meningococcal transmission among humans occurs trough respiratory secretions, and it has been found in pharynx in 8–25% human population (carriage), usually in adolescent age[1,3]. Acquisition of meningococcus in upper respiratory tract may pass without any symptoms, or may result in local inflammation, invasion of mucosal surfaces, access to the blood stream and fulminant sepsis of localized infections such as meningitis[1,3].

Meningococcal disease has the highest incidence in infants and young children less than 4 years old and adolescents[3,4]. The early stages are difficult to recognize because meningococcal disease is usually presented by general inflammatory symptoms which usually intimate viral infections[4–9]. Progression of disease can be rapid with development of life-threatening meningitis or septic shock syndrome within few hours after initial symptoms appear[4–9]. In infants and young children two basic forms of menongococcal disease are observed: firstly, meinigitis which is characterized by fever, usually above 39°C, nonspecific gastrointestinal signs such as refusal of feeding and vomiting, irritability, abnormal crying, bulging fontanel, unusual generalized seizures in infants before six months of age and lasting longer than 10 minutes; secondly, severe sepsis which is characterized by tachycardia, cold or molted limbs, or possible leg pain, and the

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late signs of disease progression: extensive hemorrhagic rash, development of limb ischemia and septic shock[4–9]. There are three forms of meningococcal sepsis: acute, fulminant (Waterhouse-Friderichsen syndrome), and recurrent, each can be accompanied with meningitis[4–9].

Thus, for clinicians it is crucial to recognize early signs of meningococcal disease, perform urgent tests, and threat disease with rapid fluid loading and antibiotic treatment before the septic cascade evolves to septic shock.

Case Report

A two and a half year old female child, who had varichella disease five months earlier, was examined at 4 hour p.m. by pediatrician because of high fever and body rash. Child was examined previously that day by primary health care pediatrician and sent to county hospital. Heteroanamnestic data obtained from mother by pediatrician showed presence of high fever and shivering (above 40°C) resistant to drugs given by mother, which lasted for one day, presence of maculous body rash for few hours before examination. Other anamnestics findings were normal. After obtaining anamnestics data pediatrician preformed clinical examination: rectal body temperature was 38.4°C, on skin there were three different sorts of rash: unspecified partially conflating white-pink maculous rash 1–2 mm in diameter on body hull, traces of mosquitoe bites, and scars of previously varichella disease. Vital functions were normal, neurological exam was within normal parameters: with negative meningeal sign, and without any signs of conscience disturbance. Lymph nodes were normal, nasal secretion was absent, and pharynx mucosa didn't show signs of inflammation. Pulmonary, cardiac, and abdominal statuses were within normal parameters.

Laboratory findings were: WBC 2.5 G/L, LYM 0.8 G/L (32.9%), MID 0.3 G/L (10.9%), GRAN 1.4 G/L (56.2%), UNSEG. GRAN 2%, RBC 4.82 T/L, HGB 103 g/L, HCT 0.320 L/L, MCV 66.4 fL, MCH 21.4 pg, MCHC 322 g/L, RDW 17%, PLT 207 G/L, MPV 8.0 fL.

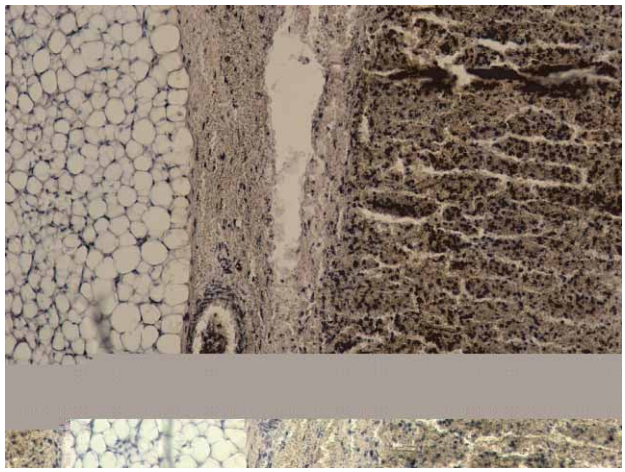

Fig. 2. Patohistological findings of bleeding in suprarenal gland hemalaun-eosin staining.

Upon completed examination and laboratory findings pediatrician concluded that the child suffered from exanthemal viral infection based on weakened immunity caused by previous varichella disease, and recommended house care, fluid intake, usage of antipyretic drugs if needed, and control examination by primary health care pediatrician.

On following day in early morning hours parents discovered dead child body. Child corpse was transported to department of pathology at county hospital were experienced pathologist preformed an autopsy.

Major autopsy findings were: female child body, 87 cm long, on entire body skin were areas of point-like (purpura) bleeding mixed with areas of conflating irregularly shaped livid spots several centimeters in diameter with necrosis in center. The rest of external findings were normal, without sings of violence. Macroscopic organ exami-

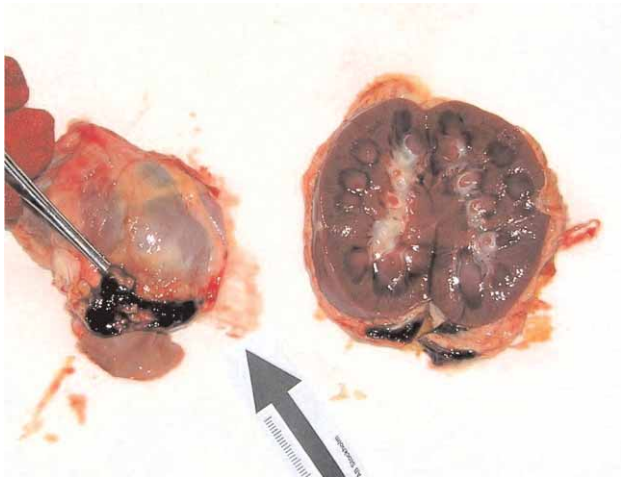

Fig. 1. Autopsy finding of bleeding in suprarenal gland (Waterhouse-Friderichsen syndrome).

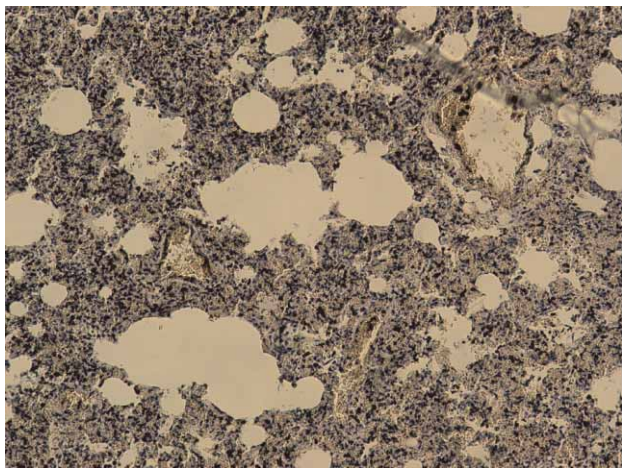

Fig. 3. Patohistological findings of acute respiratory distress syndrome in lungs hemalaun-eosin staining.

nation shoved: brain edema, on left lung wing were areas of partial emphysema, and on both lung wings edema and bleeding was present, significant bleeding was present in both suprarenal glands (Figure 1). The rest of macroscopic organ findings were within normal parameters. Tissue samples, blood and urine samples, as well as mucosa samples for microbiological cultivation were obtained from all organs.

Major microscopic findings were: skin finding: vascular and perivascular infiltrates of polymorphonuclear cells, vascular thrombosis, minor necrotic areas in dermal connective tissue; brain findings were: dilatation of perivascular and periglial spaces with proliferation of neighbouring capillars; findings of multiple microthrombosis in capillars and artheriolas with extravasations of blood cells in kidney, suprarenal glands (Figure 2), brain, heart, lungs, liver, an gastrointestinal system; and lungs findings were: hyalin membranes in alveolar tissue, sites of necrosis and extravasations of blood cells (Figure 3).

Microbiological samples taken from pharynx were positive for Neisseria meningitidis.

The pathologist conclusion was that child died from natural death caused by fulminant meningococcal sepsis.

Discussion

Fulminant meningococcal sepsis (Waterhouse-Friderichsen syndrome) is the most severe form of meningococcal disease with sudden onset and rapid progression leading to death within few hours in more than 90% of cases[4,8,9,10]. Initial symptoms are common to many infectious and non infectious diseases, and they include high fever usually higher than 39°C, nausea, vomiting and loss of appetite, and sometimes with symptoms of mild nasopharyngitis[4,5,8]. Those symptoms are quickly followed by symptoms of serious toxemia with rapid progression to septic shock and multiorganic failure, what unavoidably leads to death in about 95% cases, even with adequate and properly timed therapy[4,5,8]. The most often internal organs affected by meningococcal sepsis are suprarenal glands, heart, brain, and lungs, and clinical picture depends on severity of affection and loss of functions of those organs[4,5,8,11]. Leading symptoms in our patient at pediatrician exam were high fever resistant to home administrated antipyretic drugs and diffuse hemorrhagic rash. Vital functions were normal, and laboratory findings showed leucopenia with mild microcytic anaemia. Although, presented symptoms were obscure, and they intimated benign viral infection, differential diagnosis of high fever and hemorrhagic rash is very wide (Table 1 and 2), and decision to discharge child with diagnosis of exanthemal viral infection based on weakened immunity caused by previous varichella infection without further investigation proved to be fatal.

After meningococcus enter blood stream, the most often entry point is nasopharyngs but other entry points were described, the main pathophysiological disorders are caused by meningococcal endotoxine[1–3]. Event cascade leads to vasculitis and blood vessel wall damage, development of disseminated intravascular coagulation syndrome, which causes skin and internal organ bleeding,

TABLE 1
OFTEN MEDICAL CONDITIONS RELATED TO HIGH FEVER

Adrenal hemorrhage, neonatal	Lysteria monocytoigeneses meningitis	SARS
Amebic dysentery	Malaria	Scarlet fever
Babesiosis	Mastitis	Septicemia
Bacterial toxic-shock syndrome	Mastoiditis	Staphylococcal toxic shock syndrome
Bortonneuse fever	Measles	Still's Disease, Adult-Onset
Chagas disease	Melioidosis	Systemic Juvenile Rheumatoid Arthritis
Common cold	Meningitis	Tetanus
Dehydration	Meningococcal disease	Thrombotic thrombocytopenic purpura, congenital
Dengue fever	Miscarriage	Toxic Shock Syndrome – High fever
Diphtheria	Neuroleptic Malignant Syndrome	Trichinosis
Ebola	Neutrophilic dermatosis, acute febrile	Trypanosomiasis, east-African
Endocarditis	Peritonitis	Typhoid fever
Epidemic typhus	Plague	Typhus
Epiglotitis	Pneumococcal meningitis	Ulcerative colitis
Francisella tularenis infection	Pneumococcal pneumonia	
Herpes stomatitis	Pneumonia, Bacterial	Viral Hemorrhagic Fevers
Japanese encephalitis	Q fever	Viral meningitis
Juvenile Rheumatoid Arthritis	Quinsy	Weil's syndrome
Legionnaires' disease	Reye's syndrome	Yellow fever
Leptospirosis	Rubella	

TABLE 2
CAUSES OF HEMORRAGIC RASH

Subacute bacterial endocarditis
Epidemic typhus
Hemorrhagic fevers
Meningococcal disease
Waterhouse-Friederichsen syndrome

TABLE 3
DIFFERENTIAL DIAGNOSIS OF MENINGOCOCCAL DISEASE

Meningitis – various other types possible.
Pneumococcal meningitis
Hib meningitis (type of Bacterial meningitis)
TB meningitis
Viral meningitis
Bacterial meningitis
Encephalitis
Group A Streptococcus (GAS)
Invasive Group A Streptococcus
Flu – because meningitis has early flu-like symptoms
Viral infections – another cause of flu-like symptoms.
Subarachnoid haemorrhage
Migraine
Influenza
Brain abscess
Brain tumor
Delirium tremens
Pediatric febrile seizures
Subdural empyema
Other causes of increased intracranial pressure
Other causes of altered mental status

necrosis and organ failure[1,11]. Extensive hemorrhagic rash, tachycardia, cold or molted limbs, etc. are signs and consequence of organ damage and function failure caused by endotoxin and immunological reaction to bacteriemia[3,11]. Direct cause of death like in our case, is combination of several factors: circulatory collapse with development of intravascular disseminated coagulation syndrome, suprarenal gland insufficiency, and acute respiratory distress syndrome[11].

Autopsy findings, pathohystological tissue examinations and microbiological tests clearly proved cause of death to be meningococcal infection which led to septic shock and multiple organ failure. Macroscopic and tissue findings of affected organs were in conformity with previously described results of meningococcal sepsis[11]. Hallmark of meningococcal sepsis (Waterhouse-Friderichsen syndrome) is bleeding to suprarenal glands[11] that was confirmed in our case. Lungs were edematous and tissue exam showed presence of hyaline membranes and necrosis with bleeding in alveolar tissue, signs of acute respiratory distress syndrome which often accompanies severe sepsis[11]. Presence of microthrombotic masses in blood vessels of skin and internal organs points to development of disseminated intravascular coagulation syndrome[11], and same finding was present in skin and all internal organs with our patient.

Microbiological cultivation showed presence of *Neisseria meningitidis* in sample taken from nasopharyngeal mucosa. Other samples taken from possible entry points were negative. Cultivation test clearly pointed nasopharyngs as infection entry point of infection and also excluded other possible microorganisms, such as pneumococcus, staphylococcus and influenza type B virus, as cause of sepsis[3,8,9].

The source of meningococcal infection has remained unclear. Humans are the only carriers of meningococcus[1], but no evidences of meningococcal disease or carriage related to people from child surrounding were found. Possible underlying cause of child susceptibility for meningococcal infection was partially investigated. Macroscopic and microscopic findings of spleen were normal, with exception of previously described signs of disseminated intravascular coagulation syndrome, and there were no evidences of any organ damage caused by possible autoimmune disease. Kidney and liver findings didn't show any signs of previous disease. Because no immunological tests were preformed possible hidden complement, properdin or other disturbance can't be excluded. But, based on child anamnestic data and autopsy findings it is less like that existence of hidden immunological disorder was underlying cause of susceptibility for meningococcal infection.

Thus, because of obscure initial symptoms which are common to many medical conditions (Table 3), especially viral infections, fulminant meningococcal sepsis is difficult but crucial to recognize before development of fatal septic shock. Do to rapid onset, progression, and often fatal end any clinical symptom of possible meningococcal sepsis, especially in children younger than 4, must be investigated and patient should be considered as it has meningococcal sepsis until proved otherwise.

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FULMINANTNA MENINGOKOKNA SEPSA KOD MLAĐEG DJETETA – PRIKAZ SLUČAJA

S A Ž E T A K

Prikazujemo izolirani slučaj fulminantne meningokokne sepse kod dvoipogodišnjeg ženskog djeteta. Početni simptomi bili su oskudni i zajednički mnogim bolestima, ali također ranije opisani kod meningokokne sepse. Neprepoznavanje ozbiljnosti djetetovog stanja dovelo je do smrti djeteta kod kuće nekoliko sati nakon pregleda u bolnici. Obdukcija i mikrobiološko testiranje uzoraka obrisa grla djetetovog leša sa sigurnošću su pokazali da je dijete umrlo zbog septičkog šoka uzrokovanog fulminantnom meningokoknom sepsom.