

Fulminant Meningococcaemia With Purpura Fulminans and Multiple Organ Failure In An Immunocompetent Adult Patient

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ABSTRACT

Fulminant meningococcaemia (FM) is a rare severe life threatening illness caused by *Neisseria (N.) meningitidis*. FM can cause different complications such as septic shock and purpura fulminans. Early aggressive treatment like fluid infusion and antibiotic therapy can improve the survival rate. A 41 year old previously healthy woman was admitted to the intensive care unit (ICU) from the emergency department due to septic shock and purpura fulminans. On admission to ICU, the patient presented with features of septic shock. Due to respiratory failure the patient was intubated. Within hours as well as acute renal failure, disseminated intravascular coagulation (DIC) occurred. Aggressive fluid therapy, broad spectrum antibiotics and vasopressors were given. In addition, hemodialysis and plasma exchange was initiated. On 5th day, *N. meningitidis* was isolated from the patient's blood culture, which was drawn at the emergency room. On 14th day the patient was extubated. The patient's neurological examination was completely normal. On 32nd day the patient was transferred to the Plastic Surgery Department, where she underwent right food amputation from the metatarsopharengal joint. Then she was discharged from the Plastic Surgery Department. Meningococcal infection should be considered in the differential diagnosis of any patient with sudden onset of a febrile illness, with petechiae and/or meningeal signs. A person who has any risk factor should be vaccinated for meningococcal disease. Anyone who had close contact with the index patient should take antimicrobial chemoprophylaxis immediately.

Key words: Meningococcaemia, Purpura Fulminans, Multiple Organ Failure, intensive care unit

Introduction

Fulminant meningococcaemia (FM) is a rare severe life threatening illness caused by *Neisseria meningitidis (N. meningitidis)*. Mortality rate of FM is very high and varies from 20% to 80% [1]. FM can cause different complications such as shock, disseminated intravascular coagulation (DIC), purpura fulminans, sepsis and multiple organ dysfunction syndrome (MODS) [2]. Early aggressive treatment like fluid infusion, specific antibiotic therapy, respiratory and inotropic support, can improve the survival [3-5].

In this manuscript we present a case of FM characterized by purpura fulminans, sepsis syndrome and respiratory failure followed by acute renal failure.

Case Presentation

A 41-year-old previously healthy woman was transferred to the intensive care unit (ICU) from the

emergency department due to septic shock and purpura fulminans. The patient's complaints started on the same day and manifested with myalgia, fever up to 40°C, nausea and vomiting. During her stay in the emergency department (05.00 am–2.00 pm), the patient was conscious and had hypotension, tachypnea and hemorrhagic skin lesions. Meningeal symptoms (headache and neck stiffness) were not observed. The laboratory parameters are presented in Table 1. Meningococcaemia and viral hemorrhagic fever were considered. The blood was sampled for microbiological testing (60 minutes after hospital admission) and the patient received 1 gr intravenous ceftriaxone in the emergency department. The patient was then transferred to the ICU for further treatment.

On admission to the ICU, the patient presented with features of septic shock. Tachycardia was

Table 1. Assessment of patient's clinical status at Emergency admission, ICU admission and discharge

Parameters	Emergency admission	ICU admission	6 hour	12 hour	24 hour	ICU discharge
White blood cells $\times 10^3 / \mu\text{L}$ (3.83–5.06)	6.5	15.2	24.0	30.1	38.2	34.6
Hemoglobin g/dL (11.7–15.5)	12.6	11	9.7	9.5	8.5	9.4
Platelets $\times 10^3 / \mu\text{L}$ (159–388)	152	75	49	41	26	238
Creatinin mg/dL (0.5–0.9)	0.96	1.72	2.62	3.43	4.28	2.0
D-Dimer (0–0.55)	–	>40	>40	>40	>40	4.6
Fibrinogen (219–403)	–	181	140	305	–	399
INR* (0.86–1.20)	1.34	2.9	1.58	–	1.95	1.09
Lactate mmol/L (0.9–1.7)	–	10.5	7.5	7.8	9.1	1.2
Procalcitonin $\mu\text{g/L}$ (0–2)	–	17.7	–	–	44	0.2
C-reactive protein	–	10.9	–	–	13.6	2.6

* International normalized ratio

observed — 120 min⁻¹; mean arterial pressure was 50 mmHg and noradrenalin infusion was initiated with the dose of 0.05mcg/kg/min. Due to respiratory failure (respiratory rate 35 min⁻¹, Oxygen saturation of arterial blood (SaO₂) 81%, oxygen pressure of arterial blood and fractioned inspired oxygen ratio (PaO₂/FiO₂) 75), the patient was intubated and mechanical ventilation was started. Hemorrhagic lesions spread to all limbs. Within hours as well as acute renal failure, which required intermittent hemodialysis, disseminated intravascular coagulation (DIC) occurred. Aggressive fluid therapy, broad-spectrum antibiotics (meropenem and teicoplanin) and high dose noradrenalin (0.5mcg/kg/min) and dopamin (30mcg/kg/min) were administered for severe septic shock. In addition, hemodialysis and plasma exchange was initiated. Crimean-Congo hemorrhagic fever and hantavirus tests were negative.

On the 2nd day of ICU admission, cardiac arrest occurred five times. Cardiac resuscitation was performed for approximately ten minutes after each cardiac arrest. Therapeutic hypothermia was performed for 24 hours.

Invasive cardiac monitoring with pulse contour cardiac output was used. Fluid and vasopressor treatment were continued according to measurement of cardiac output, stroke volume variation and other parameters.

On 5th day, *N. meningitidis* was isolated from patient's blood culture, which was drawn in the emergency room. The patient's vasopressor requirement decreased, then vasopressors were discontinued. Hematological parameters improved and plasma exchange treatment was discontinued.

On 14th day, sedation was discontinued and patient was awakened. After extubation, patient's neurological examination was completely normal.

Hemorrhagic lesions turned into necrotic lesions as a complication of purpura fulminans (figure 1, 2). On 30th day, the patient began to urinate and urinary output increased within days.

The patient was transferred to the Plastic Surgery Department for amputation of her foot on 32nd day. Her right foot was amputated from the metatarsophalangeal joint and other necrotic lesions were debrided. She was then discharged from the Plastic Surgery Department.



Figure 1. Necrotic lesions caused by purpura fulminans

Patient's consent was obtained for the publication of this case report.

Discussion

N. meningitidis is a gram-negative diplococcus which causes different clinical manifestations ranging from transient fever to fulminant disease with death ensuing within hours of the onset of clinical symptoms. Mortality rate can be very high in patients with meningococcal disease if the infection is not treated appropriately and long-term sequelae can be severe even in successfully managed cases [6].

Incidence of invasive meningococcal disease in United States varies from 0.5 to 1.5 cases per 100000 population [6]. We don't know the prevalence of invasive meningococcal disease in our country.

Meningococcal disease occurs in all age groups however burden of disease is highest among infants aged <1 years, young adults aged 16 through 21 years and persons aged ≥ 65 years. There are a lot of risk factors for meningococcal disease. Risk factors for meningococcal disease can be grouped according to organism, host and environmental factors. Firstly, more virulent strains of *N. meningitidis* can circulate in a population and cause increased incidence of disease or increased mortality. Secondly, patients who have persistent deficiencies in the common complement pathway (e.g., C3, properdin, Factor D, Factor H, or C5-C9) have up to a 10,000-fold increased risk for meningococcal disease and can experience recurrent disease. In addition, patient with anatomic or functional asplenia also appear to be at increased risk for meningococcal disease. Thirdly, environmental risk factors for meningococcal disease demonstrated that race, low socioeconomic status and occupational exposure such as healthcare workers, ambulance



Figure 2. Necrosis of the right foot

workers, police officers and laboratory workers also increase risk [6,7]. In our case there were no host related risk factors such as anatomic or functional asplenia or complement deficiency.

Acute systemic meningococcal disease most frequently presents by three syndromes: meningitis alone, meningitis with accompanying meningococemia, and meningococemia without meningitis. In our patient fulminant meningococemia occurred without meningitis. FM is the predominant presentation in 20–30% of cases of acute systemic meningococcal disease [8]. FM may progress rapidly to shock and MODS. Early and appropriate antibiotic treatment improves the outcome of meningococcal infections and sepsis [3-5]. If meningococcal infection is seriously considered, ideally appropriate antibiotic should be given in the first thirty minutes [9]. In our case, antibiotic was administered in the first hour.

Purpura fulminans is a severe complication of FM [10], occurring in approximately 15 to 25 percent of those with FM. It is characterized by the acute onset of cutaneous hemorrhage and necrosis due to vascular thrombosis and DIC. Early and aggressive treatment with antimicrobials and support of vascular perfusion are necessary for prevention of purpura fulminans. Surgical intervention is often required.

DIC is another serious complication of FM [11,12]. The pathogenesis may be related in part to high levels of circulating microparticles that originate from platelets or granulocytes and have procoagulant activity. Primary treatment of DIC is treatment of the underlying cause. Hemodynamic support is essential.

Chemoprophylaxis is indicated in close contacts of patients with meningococcal infection, and should be given as early as possible following the ex-

posure [6]. Close contacts may include; Household members, contacts at a child-care center, young adults exposed in dormitories, military recruits exposed in training centers or individuals who have been exposed to oral secretions (eg, intimate kissing, mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management). In addition, prophylaxis is not recommended for healthcare workers who have not had direct exposure to respiratory secretions. Regimens for antimicrobial prophylaxis have been defined by the Centers for Disease Control and Prevention (CDC), and include ceftriaxone, ciprofloxacin and rifampisin [6]. Antimicrobial chemoprophylaxis should be administered as early as possible (ideally <24 hours after identification of the index patient). In our case, we recommended prophylaxis to anyone who had had close contact with the patient. We used ciprofloxacin for prophylaxis. There were no secondary cases.

The Advisory Committee on Immunization Practices (ACIP) recommends meningococcal vaccination for the following groups of adults; military recruits, microbiologists exposed to *N. meningiti-*

tis, individuals with functional or surgical asplenia, individuals with complement component (properdin, Factor D, Factor H, and late complement components [C5 through C9]) deficiencies and travelers or persons living in areas of the world where meningococcal infection is hyperendemic or epidemic (eg, the meningitis belt of sub-Saharan Africa during the dry season, particularly if contact with local populations will be prolonged; vaccination is required within the past three years for all travelers to Mecca, Saudi Arabia, during the annual Hajj [6,13].

In summary; FM is a rare severely life threatening illness. Early diagnosis is critical in the treatment of patients with meningococcal disease. Meningococcal infection should be considered in the differential diagnosis of any patient with the sudden onset of a febrile illness, with petechiae and/or meningeal signs. A person who has any risk factor should be vaccinated for meningococcal disease. Anyone who had close contacts with the index patient should take antimicrobial chemoprophylaxis immediately.

Conflict of interest: No conflict of interest to declare.,

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