

Acute meningococcemia in childhood. Case report and review.

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Abstract

Acute meningococcemia is a disseminated infection caused by *Neisseria meningitidis*, a gram-negative diplococcus, with high mortality rates in those with fulminant disease. The disease is acquired through asymptomatic carrier(s) due to nasopharyngeal colonization or invasive disease. It affects only humans. The clinical septicaemic features can present themselves either with or without meningitis and it is considered an invasive meningococcal disease. Fever and skin involvement such as purpuric rash can be the most dramatic aspect of the disease and is often the first sign that leads to the clinical consideration of meningococcemia. Early recognition is critical to implement prompt antibiotic therapy and supportive care.

We report a case of acute meningococcemia without meningitis of a four year-old male child with clinical history of one week onset of upper respiratory infection that progressed to lower respiratory infection accompanied by fever and purpuric rash. The cerebrospinal fluid analysis revealed bacteria, gram negative diplococci suggestive of *Neisseria meningitidis* infection. He received prompt antibiotic therapy and fluid resuscitation reflected in the survival of this patient with no apparent sequelae.

Key words

Meningococcemia, *Neisseria meningitidis*, purpura fulminans, fever.

■ INTRODUCTION

Meningococcemia is defined as dissemination of meningococci into the bloodstream. It is caused by *Neisseria meningitidis*, an encapsulated, gram-negative diplococcus that infects only humans; there is no animal reservoir [1]. Acquisition of these bacteria can result in asymptomatic pharyngeal colonization or invasive disease. There are at least 13 serogroups of the bacterium, with the most important being serogroups A, B, C, and W-135. Patients with acute infection can present clinically with (1) meningitis, (2) meningitis with meningococcemia, or (3) meningococcemia without obvious meningitis. Of invasive meningococcal disease cases, 30-50% present with meningitis alone, 40% have meningitis with septicaemia, and 7-10% have septicaemic features [2]. Meningococcemia can kill more rapidly than any other infectious disease. *N. meningitidis* is a major infectious cause of childhood death in developed countries. The mortality rate remains around 10%, although in some specialized centres, it has decreased to less than 5%.

The clinical syndrome results from the activation and continued stimulation of the immune system by proinflammatory cytokines producing four basic processes (i.e. capillary leak, coagulopathy, metabolic derangement, myocardial failure) and when combined, multiorgan failure that usually ends in cardio-respiratory depression and possibly renal, neurologic and gastrointestinal failure [2,3].

The clinical difference between septicaemia and meningitis is important because patients who present with shock or rapid circulatory collapse are treated differently than patients who present primarily with increased intracranial pressure. Early recognition is critical to implement prompt antibiotic therapy and supportive care. Treatment must be instituted rapidly, because irreversible shock and death may occur within hours of the onset of symptoms. Cutaneous manifestations in meningococcemia may be important clues to the diagnosis. Skin involvement can be the most dramatic aspect of the disease and is often the first sign that leads to the clinical consideration of meningococcemia.

In relation to prognosis, meningococcal disease may progress very quickly and can result in loss of life. In survivors, the outcomes can be considerable, including neurologic sequelae such as sensorineural deafness, cognitive impairments and amputations.

In view of the significance of early recognition and detection of this fatal but rare disease, the following case of acute meningococcemia in childhood is reported in Belize.

■ CASE REPORT

A 4 year-old child with unremarkable clinical history, presented with onset of upper respiratory infection one week before admission, characterized by fever, cough, runny nose and nasal congestion. He was treated symptomatically with acetaminophen and diphenhydramine without relief. Five days later, the patient presents with a purpuric rash to face,

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scalp, trunk, lower back, upper and lower extremities accompanied by hyperthermia and cough. Patient denied emesis or seizures. Due to the aforementioned, parents seek further medical attention.

At the time of admission, neurologically the patient was irritable, lethargic, but conscious and alert with a Glasgow score of 15, no signs of focalized symptoms, motor deficits, cranial nerve impairments or meningeal physical signs. His vital signs revealed temperature of 38°C, heart rate 150/min, and respiratory rate 26/min with blood pressure of 72/49 mmHg. On physical examination the patient showed moderate dehydration of the oral mucosa, hyperaemic oropharynx, without exudates. The patient presented with hypoventilated bilateral lungs, with crackles and moderate expiratory wheezing. Cardiovascular examination revealed tachycardia, with no murmurs or gallop. Abdomen was soft depressible with hepatosplenomegaly 3cm below bilateral costal borders, mild tenderness on palpation. A non-pruritic, coalesced, non-blanching palpable purpuric rash to face, scalp (Fig. 1), chest, lumbar region, upper and lower extremities (Fig. 2 and 3) was detected, and a peripheral capillary refill of 3/sec. All of these geared up to an acute systemic inflammatory response syndrome (SRIS), severe sepsis and shock.



Figure 1 Purpura fulminans distribution to face



Figures 2 and 3: Purpura fulminans distribution to chest, upper and lower extremities

Complementary haematological tests reported the following:

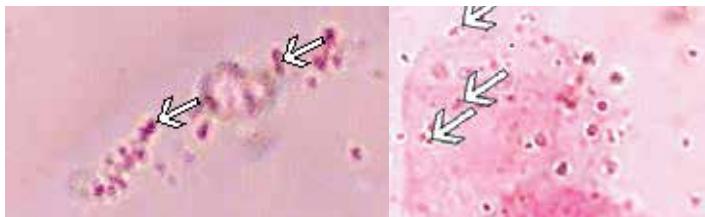
Table 1: Laboratory data on admission

WBC	43,400 μ l	Uric Acid	6.75mg/dl
Neutrophils	35%	T. Prot	6.51g/dl
Lymphocytes	58%	Albumin	5.40g/dl
Monocytes	1%	T. Bilir	0.60mg/dl
Eosinophils	6%	AST	445 IU/L
Hb	15.7g/dl	ALT	258.90 IU/L
Hto	42%	Alk Phosp	745 IU/L
Plt	112,000 μ l	LDH	2625 IU/L
Blood film	Megakaryocytic WBC, Normocytic normocromic RBC, thrombocytopenia	Trig	160.4mg/dl
Glucose	96.7mg/dl	Na	131.9meq/l
Bun	13.93mg/dl	K	5.14meq/l
Creatinine	0.60mg/dl	Cl	103.4meq/l
India ink prep	Negative	PT	14(14)secs
CSF culture	Mixed growth	PTT	36(33)secs

WBC: white blood cells, Hb Hemoglobin, Hto Hematocrit Plt: Platelets, BUN: Blood urea nitrogen CSF cerebrospinal fluid T. Prot: Total proteins T. Bilir: Total Bilirubin AST: aspartate aminotransaminase ALT: alanine aminotransaminase Alk Phosp: alkaline phosphatase LDH: lactic acid dehydrogenase Trig: Triglycerides Na: sodium K: potassium Cl: Chloride PT: Prothrombin time PTT partial thromboplastin time

Based on the clinical presentation and tests, a lumbar puncture was done. Cerebrospinal fluid (CSF) analysis showed the presence of Gram negative diplococci (Figure 4.0 and 4.1); glucose, 76.9mg/dl; cell count >10% polymorphonuclear (PMN) granulocytes. After 4 days on treatment, CSF analysis was repeated and reported negative to diplococci. CSF culture and sensitivity test were sent to confirm diagnosis, but due to a delay of 3 days to process it, mixed growth was reported. For the same reasons, the blood culture results were unreliable due to 4-day delay to process it. India ink preparation was negative on two occasions. Chest radiograph was performed considering the respiratory physical findings, reporting presence of bilateral pulmonary radio opacities consistent with bronchopneumonia, as primary site of infection (Figure 5).

Based on the clinical presenta-



Figures 4.0 and 4.1: Photomicrograph showing gram stain of CSF with gram negative intracellular diplococcus, characteristic of *Neisseria meningitidis* bacteria (arrows). Courtesy of Salome Huitz laboratory technician, Corozal Community Hospital.



Figure 5: Patient recovered with disappearance of emboli foci.

days follow up was unremarkable and uneventful.

■ DISCUSSION

Although *N. meningitidis* is divided into 13 serogroups based on capsular polysaccharide structure, only six serogroups (A, B, C, W-135, X, and Y) cause life-threatening diseases [4]. Analysis of serogroup typing was not done in our patient due to lack of resources and is something not commonly practiced in our setting. The patient has not visited any foreign countries and had not had direct contact with patients with meningococcal infection. Consequently, we thought that he was infected with *N. meningitidis* from asymptomatic carrier(s) due to nasopharyngeal colonization. A mortality rate of 40-80% in patients with meningococcmia is associated with the acute onset of petechiae less than 12 hours before admission, shock, coma, high fever, low peripheral leukocyte count, thrombocytopenia, and high serum antigen titer, absence of meningitis, metabolic acidosis, and disseminated intravascular coagulation (DIC). Half of all patients with shock who die do so within the first 12 hours of hospitalization. Meningococcmia associated with DIC has a mortality rate higher than 90% [2].

In our setting, leucocytosis prevailed as part of the metabolic response to trauma seen in the cascade of systemic inflammatory response syndrome (SRIS) [5] and is considered to be a better prognostic factor as portrayed in the remarkable response to treatment. On the other hand, leucopenia is reported and considered a poor prognostic factor in patients with severe pneumococcal pneumonia as portrayed

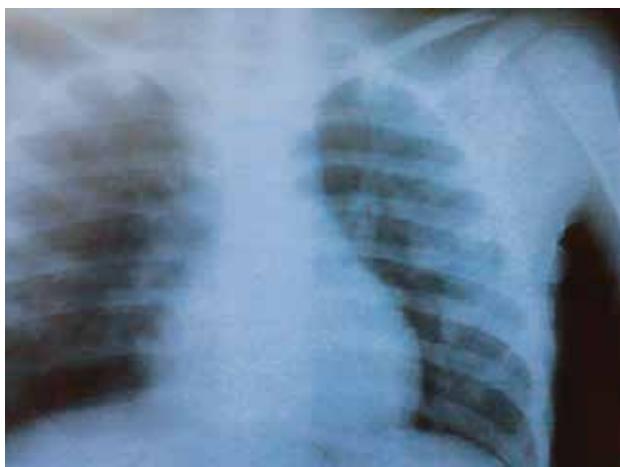


Figure 5: Chest X-ray with bilateral radio opacities consistent with bronchopneumonia, courtesy of X-ray technician Wendy Manzanilla, Corozal Community Hospital

tion, physical, haematological, biochemical and CSF analysis, the diagnosis of acute meningococcmia (sepsis) without obvious clinical meningitis, bronchopneumonia and secondary acute hepatocellular injury was integrated. All close contacts of the patient and medical personnel were administered rifampicin as secondary prophylaxis against *N. meningitidis* infection.

The treatment of this patient in our setting involved the use of fluid and electrolyte resuscitation, intravascular steroids (metilprednisolone) and double antibiotic therapy with 3rd generation cephalosporin (ceftriaxone at meningeal dosages) and macrolids (erythromycin) for 10 days; the patient responded favorably, with practical disappearance of emboli foci (Figure 5) The patient was discharged and the seven

Aine Bon

Potassium diclofenac

FAST RELIEF FOR INFLAMMATION, PAIN AND FEVER

- Short-lasting treatment for inflammatory, painful and febrile conditions
- Easy dosage according to child weight
- Rapidly reaches therapeutic concentrations in plasma



by Georges and coworkers. [6]. Other laboratory indicators of sepsis that were present were low platelet count (thrombocytopenia) seen in overt DIC and elevation of liver enzymes as indication of acute hepatocellular injury caused by hypoperfusion, also mentioned in other literature by LaRosa [5]. Coagulopathy with partial thromboplastin time (PTT) of greater than 50 seconds or a fibrinogen concentration of less than 150 µg/dL indicates poor prognosis, as referred by Mahmud [2]. On the contrary our patient had PTT of 36 seconds, which favoured better prognosis.

The patient started with an upper respiratory infection, which progressed to bronchopneumonia, consequently thought to be the primary focus of infection. Meningococcal pneumonia has been described and probably results from aspiration of *N. meningitidis* [2] and accounts for 5-15% of the cases with meningococcal invasive disease, particularly with serogroups Y, and W-135 [9]. The most common infective cause of purpura fulminans is meningococcemia, followed by pneumococcal sepsis [7]. Because most cases are due to *N. meningitidis*, a third generation cephalosporin that is also effective against streptococcus is recommended as the empiric antibiotic treatment for purpura fulminans. In this case report, we used ceftriaxone at meningeal doses, because of its good CSF penetration as reported by Shrestha [8]. We also used a macrolid (erythromycin) considering atypical presentations in community acquired pneumonias [4]. Early management algorithms of meningococcal disease in children are available from the Meningitis Research Foundation and can be accessed at <http://www.meningitis.org>.

Culture of CSF on admission yielded mixed growth, probably due to contamination secondary to the delay in processing it; but it could be positive even in patients who do not have clinical evidence of meningitis, and should always be examined when meningococcemia is suspected [4]. The blood culture taken on admission followed the same fate due to the delay and was reported as negative after processing it. One important aspect to consider was that our patient had received ambulatory treatment prior to admission with one stat dose of ceftriaxone. It has been reported by Almeida-Gonzalez and others that blood cultures can be positive in approximately 75% of patients with meningococcal meningitis and could be higher in patients with meningococcemia, but sensitivity and specificity diminishes when antibiotics have been used prior to this antibiotic treatment, even after a single dose has been used [9].

According to the Belize Health Information System (BHIS), from 2009 – 2012, the statistics showed that three paediatric persons below 15 yrs of age presented meningococcal disease: 2 acute meningococcemia (<1 year and the 4 year-old of the present case report) with no mortality reported and 1 meningococcal meningitis (1 year-old) whose death was attributed to neurological sequelae since childbirth [10].

■ CONCLUSION

In our particular case, meningococcemia without meningitis, which occurs in only 7-10% of patients with meningococ-

cal disease, was characterized by abrupt onset of fever and purpuric rash which progressed to purpura fulminans. This was early diagnosed and prompt antibiotic therapy and supportive care implemented. This was reflected in the survival outcome of our patient with no apparent sequelae.

■ ACKNOWLEDGEMENTS

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