TITLE OF CASE
Meningococcemia: A Pediatric Emergency

AUTHORS OF CASE Please indicate corresponding author by *
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SUMMARY Up to 150 words summarising the case presentation and outcome
The patient is a 21-month-old female who presents to the Emergency Department with mother for complaint of fever, rash, and altered mental status. Patient was diagnosed with an upper respiratory infection in the ED the night before, received Tylenol for fever, improved, and was discharged. The patient arrives unresponsive, displays a diffuse non-blanching macular rash, and fever. Oxygen, IV access, fluids, and monitoring were quickly established. One gram of Rocephin and 125mg of Solumedrol were given empirically for an assumed diagnosis of meningococcemia. A lumbar puncture was done and cerebrospinal fluid (CSF) was sent to the lab for analysis.

DeVos Children’s Hospital was consulted and transfer arrangements were made. Accepting pediatrician ordered an additional dose of Rocephin (600mg) and 240mg of Vancomycin. The patient was in stable condition at the time of transfer. After arriving at DeVos the patient’s petechiae progressed to purpura but no other complications arose. The patient made a full recovery.

BACKGROUND Why you think this case is important – why you decided to write it up
Meningococcemia is a true emergency. Patients who present with symptoms suspicious of this disease process must be managed accurately and efficiently to avoid morbidity and mortality. The practitioner must have a high index of suspicion for this diagnosis. The triad of fever, petechial rash, and altered mental status should be an indication for aggressive management. Emperic antibiotic and supportive treatments should be initiated quickly to avoid adverse effects of the disease process which can be very serious: gangrenous extremities, myocarditis, purpura fulminans, disseminated intravascular coagulation, and death. It is important for every practitioner to suspect meningococcemia and manage appropriately.

CASE PRESENTATION Presenting features, medical/social/family history
HPI
• M.G. is a 21 month old female who present to the emergency department on 5/18/09 with fever, rash, and altered mental status.
• Diagnosed on 5/17/09 with upper respiratory infection at a different local ED. Was given Tylenol which decreased her fever, symptoms improved, and was sent home.
• Twelve hours after her initial ED visit, the patient was unresponsive and febrile in the Hackley ED.

PMH
• URI diagnosed the day before
• Up to date with vaccinations
• No other major medical problems

PSH
• None
Family History
• No ill contacts and otherwise non-contributory

Social history
• Exposed to second hand smoke

Medications
• Tylenol and Motrin prn for fever. Last doses were at 6:45 am and 7:15 am respectively.

Allergies
• No known drug allergies

Review of Systems
General: fever, unresponsive
Skin: rash
Lungs: mild upper respiratory symptoms recently. Mother denies cough.
GI: + for vomiting today
Otherwise unremarkable

Physical exam
Vitals:
• Temperature: 102.7° rectal
• Pulse: 152
• Respirations: 26
• Blood pressure: 114/55
• Oxygen saturation: 99% on room air
General: well-developed, well-nourished, 21 month old female, with decreased arousal
Skin: non-blanching, pink, macular rash located predominantly on trunk and lower extremities
Head: normal cephalic, atraumatic
Eyes: Pupils equal, round, reactive to light
Cardiac: regular rate and rhythm, without murmur
Respiratory: diffuse ronchi noted
Abdomen: soft, nondistended

INVESTIGATIONS If relevant

Laboratory studies
Complete blood count
• WBC 6.4
• RBC 4.51
• Hgb 12.1
• Hct 35.9
• Platelets 359

Basic Metabolic Profile
• BUN 13.0
• Cr 0.40
• Sodium 131 (L)
• Potassium 3.4 (L)
• Chloride 103
• CO2 17 (L)
• Glucose 145
• Calcium 8.5 (L)

CSF analysis
• WBC 5100 (H)
• RBC 0
• Polys 95 (H)
• Lymphs 5 (L)
• Mono/Macro 5 (L)
• Appearance Hazy
• Protein 161 (H)
• Glucose 63

CSF culture
• Positive for gram-negative diplococci. Neisseria meningitidis grown.

Urinalysis
• WBC esterase Neg
• Nitrite Neg
• pH 6.5
• Protein 30 (H)
• Glucose 30 (H)
• Ketones 2+ (H)
• Urobilinogen Neg
• Blood Neg

Radiologic studies
Chest x-ray showed no infiltrates or cardiomegaly

DIFFERENTIAL DIAGNOSIS If relevant

Meningococcemia was always highly suspected. However, a differential of meningococcemia includes: Rocky Mountain Spotted Fever, Typhus, endocarditis, HSP, TSS, ITP, TTP, and drug reaction. These were all either ruled out by history and physical exam or lab tests.

TREATMENT If relevant

The patient was immediately given PR Tylenol for fever and started on an empirical dose of one gram of Rocephin IV. Supportive fluids (0.9%NS) were started and a bolus of 20cc/kg was given. Solumedrol 125mg given IVP. After consulting DeVos Children’s Hospital an additional dose of Rocephin 600 mg was given IVP along with 240mg of vancomycin and a second fluid bolus.

OUTCOME AND FOLLOW-UP

The patient was starting to improve by the time AeroMed arrived to transport her to DeVos Children’s Hospital. Her level of arousal increased to the point that she would occasionally wake up and call for her mother and eventually was playing with toys and smiling. A report from DeVos obtained later stated that the patient’s petechiae turned to purpura later that same day. However, she made great improvements over night, made a full recovery, and was discharged to home.

DISCUSSION including very brief review of similar published cases (how many similar cases have been published?)

1. What is meningococcemia?
2. What are potential complications of meningococcemia?
3. What is the treatment of choice for meningococcemia?
4. Are there any new treatments that improve outcomes and prevent complications?

1. Meningococcemia is a potentially fatal condition in which Neisseria Meningitidis seeds the bloodstream and produces characteristic signs, symptoms, and complications. It most commonly affects children from 6 months to 5 years and young adults. Risk factors are ill contacts, crowding, tobacco smoke, and a recent URI. Symptoms include fever, headache, nausea, vomiting, and mental status changes. The characteristic sign is a non-blanching rash called petechiae and first appears on the extremities. Palpable purpura may also appear as the disease progresses. The pathogenesis of meningococcemia begins in the upper respiratory tract with initial colonization of the nasopharynx. Transmission is via respiratory secretions followed by upper respiratory colonization and the production of mild symptoms including irritability, myalgia, emesis, diarrhea, cough, and rhinorrhea7. The bacteria then seed the bloodstream and take one of two paths.
Either they multiply slowly and the patient experiences signs of local infections such as meningitis, joint infections, and pericarditis or they multiply quickly and the patient experiences the petechial rash, altered mental status, and possibly more serious complications such as purpura fulminans and DIC which occur in 10-20% of cases but carry a mortality rate of 50-60%.

2. Complications of meningococcemia include loss of extremities, gangrene, myocarditis with congestive heart failure (CHF) or conduction abnormalities, joint infections, purpura fulminans, and DIC. The loss of extremities is secondary to the fibrin deposition intravascularly. Decreased blood supply leads to ischemia and tissue death and sets up an environment that supports the development of gangrene. Amputation is often the treatment of choice for this complication. Myocarditis is the most common complication. Joints are seeded with bacteria from the bloodstream and may result in septic joints. Purpura fulminans affects 15-20% of patients with meningococcemia and is found most commonly in infants and small children. The condition is associated with sepsis and infection and manifests as cutaneous hemorrhage, skin and soft tissue necrosis, hypotension, fever, and multi-organ failure. DIC is a potentially deadly complication that follows the development of purpura fulminans. The coagulation problems that cause the initial petechia and purpura progress to systemic activation of the coagulation system leading to abnormal formulation of thrombin and abnormal fibrinolysis. The treatment of choice is addressing the underlying cause, which in this case requires prompt administration of antibiotics.

Prognosis can be determined by looking at signs and symptoms. One study suggested that poorer prognosis is associated with hypotension, rash, decreased or normal white blood cell count, decreased or normal ESR, cyanosis, coma, oliguria, metabolic acidosis, increased PT, and age greater than 60 years. These factors predispose the patient to the formation of sepsis, shock, organ failure, and progression towards DIC. These patients should be monitored closely and every appropriate treatment must be made.

3. The treatment of choice for meningococcemia is broad-spectrum antibiotics. Several sources recommend the use of third generation cephalosporins others suggest high dose penicillin. The duration of therapy should be based on the patient’s progress and demonstration of negative blood and CSF cultures. Recommended minimum length of treatment is seven days. Supportive care includes fluids, antipyretics, monitoring and urinary catheterization. Steroids may be considered to reduce systemic inflammation. There is some discussion about the benefits of adding protein C and antithrombin 3 to treatment protocols to prevent fibrin deposits and therefore purpua fulminans and DIC. Close contacts with the patient may receive a single prophylactic dose of 500mg Cipro orally. Teens should be vaccinated before leaving for college as the close quarters of dorm life increases the risk for developing illnesses associated with Neisseria meningitidis.

4. Ultimately, prevention is the best treatment. Knowing the risk factors and working to reduce them is the most effective means of managing the disease. In addition to the already proven treatments of broad-spectrum antibiotics there has recently been research concerning the potential benefits of using Protein C and Antithrombin III (AT3) for the treatment of meningococcemia. The pathophysiology of the disease leads to the depletion of protein C and antithrombin 3 through the activation of coagulation via inflammatory mediators. In one small study the administration of protein C decreased D dimmer levels, reversed organ dysfunction, and no major side effects were noted. Although the initial results are promising further studies are needed to determine whether these results can be replicated in larger patient groups.

LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points
- Know the signs of meningococcemia: fever, altered mental status, and petechiae. This makes the diagnosis efficient and improves the patient’s chance for survival.
- Empirically treat with broad-spectrum antibiotics as soon as possible. Do not delay this important treatment for any studies. A lumbar puncture is necessary for diagnosis but
should be done after starting antibiotics.
• Get the patient to the appropriate care facility.

REFERENCES
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