Case 42

This 19-year-old student was in his usual state of health until the evening prior to admission, when he went to bed with a headache. He told his mother that he felt feverish, and on the following morning his mother found him in bed, moaning and lethargic. He was brought to the emergency room, where he appeared toxic and drowsy but oriented. His temperature was 40°C, his heart rate was 126/min, and his blood pressure was 100/60 mm Hg. His neck was supple. He had an impressive purpuric rash (Fig. 1), not blanching, most prominent on the trunk, legs, and wrists. A Gram stain of material taken from one of the patient's skin lesions is shown in Fig. 2. His white blood cell count was 26,000/μl with 25% band forms. The platelet count was 80,000/μl.

Blood cultures were obtained, a lumbar puncture was performed, and the patient was begun on intravenous ceftriaxone. Cerebrospinal fluid (CSF) glucose, protein, and white blood cell count were normal, and CSF bacterial culture was negative. Blood cultures grew the organism seen in Fig. 2.

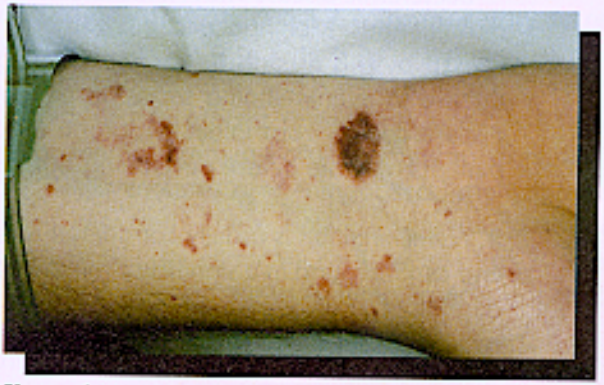

Figure 1

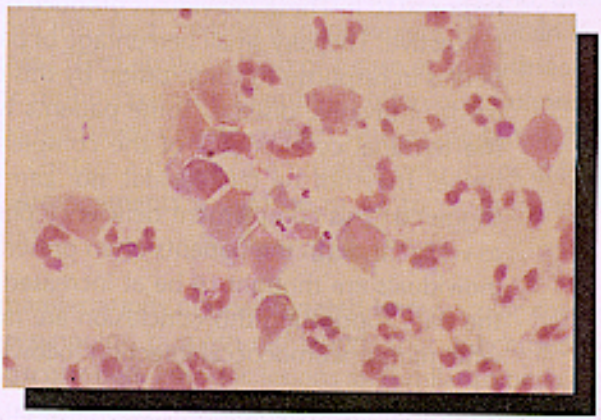

Figure 2

1. What bacterium was causing this patient's illness? Is the finding of a normal CSF profile, without evidence of meningitis, commonly observed in infection with this organism? Explain your answer.

2. Is this organism ever part of the normal oropharyngeal flora? Explain your answer.

3. Which immunologic abnormalities predispose individuals to infection with this organism?

4. Which serogroup(s) causes illness? The serogroup is based on antigen from which part of the bacterium?

5. Which prophylactic strategies are useful for large populations?

6. Which prophylactic strategies can be used for exposed individuals?

7. What is a purpuric rash, and which virulence factor plays a central role responsible for its appearance?

42

Case Discussion

1. The clinical presentation and the presence of gram-negative diplococci growing in the blood and seen on the Gram stain of a skin lesion strongly indicated that the etiologic agent of this infection was *Neisseria meningitidis*. *N. gonorrhoeae* is also a gram-negative diplococcus, but the patient's clinical picture is more suggestive of infection with *N. meningitidis* than with *N. gonorrhoeae*. The two organisms can be differentiated in the clinical laboratory by biochemical means; *N. gonorrhoeae* oxidizes glucose, while *N. meningitidis* oxidizes both glucose and maltose.

Bacteremic disease with *N. meningitidis* does not always result in the development of meningitis. Meningococcemia without meningitis is a well-recognized syndrome caused by this organism. Cases of meningococcemia can vary clinically from mild disease to overwhelming sepsis. In patients with fulminant meningococcemia the disease course from initial symptoms to death can be measured in hours. These patients may die before developing signs and symptoms of meningitis.

2. *N. meningitidis* is usually considered to be part of the normal oropharyngeal flora and can be found in a significant minority (2 to 10%) of healthy people. During epidemics of meningococcal disease in institutionalized populations such as new recruits to the military, colonization rates may increase dramatically.

3. Most people who are colonized with this organism mount a humoral immune response to it. These individuals produce bactericidal antibodies, which appear to be protective. The very small percentage of patients who do not make bactericidal antibodies in response to colonization by this organism are at high risk for the development of invasive disease. Some patients who make antibodies have deficiencies in the terminal components of the complement pathway, and therefore these antibodies may not be bactericidal, nor can the alternative complement pathway be triggered. This complement deficiency places them at risk for disseminated disease as well, although the patients often present with less severe disease. Finally, asplenic individuals are thought to be at increased risk for infection with this organism, but the data supporting this conclusion are not as convincing as are the data for overwhelming pneumococcal infection following splenectomy.

4. The *N. meningitidis* serogroups most commonly associated with meningitis in the United States are types A, B, C, Y, and W135. The two most frequently isolated serogroups are B (50%) and C (20%). Typically, groups A and C are thought of as epidemic strains because of their association with epidemics, whereas group B isolates are most likely to cause sporadic cases. Cases due to group B are most frequent because of the rarity of epidemics of *N. meningitidis* groups A and C in the United States. The serogroups are based on the biochemical structure of the capsular polysaccharide that surrounds the organism. Nonencapsulated organisms rarely cause invasive disease, indicating that encapsulation is critical to the pathogenicity of the organism. This patient's blood isolate was identified as belonging to group C.

5. Vaccination is the mainstay of prophylactic strategies for large, at-risk populations. Vaccines derived from capsular polysaccharide are highly protective against groups A and C in adults and children over 2 years of age. The duration of group A immunity does not exceed 3 years; it is longer for group C. A quadrivalent vaccine for groups A, C, Y, and W135 has been developed and is used in at-risk populations. Currently no vaccine is available for group B meningococci because of the poor immunogenicity of this capsular polysaccharide.

6. Both vaccination and chemoprophylaxis may be in order for exposed individuals, especially health care workers who come into close contact with respiratory secretions of infected individuals. Rifampin is the drug of choice for antimicrobial prophylaxis. It penetrates well into respiratory secretions and is well tolerated. The purpose of chemoprophylaxis is twofold, first to protect the individual receiving the drug, and then to eliminate nasopharyngeal carriage of the organism to limit its spread in the general population. However, cases of meningococcal meningitis in patients given rifampin have been reported. These isolates were found to be rifampin resistant. In addition, rifampin will not eliminate carriage in 10 to 20% of colonized individuals. It is worth noting that treatment with penicillin does not eradicate nasopharyngeal carriage of the organism.

There are three practical points concerning rifampin prophylaxis. First, patients should be informed that it causes secretions to turn orange. Urine, breast milk, and tears will be affected, and contact lenses can be permanently stained. Second, pharmacies in rural areas may not stock this drug, making it inconvenient to obtain and thus adversely affecting compliance. Third, in the setting of a case or an outbreak of meningococcal disease, antibiotic prophylaxis with rifampin is often given unnecessarily to many individuals who did not have intimate contact with a case but, due to the panic surrounding the event, contact a health care provider who is not able to properly evaluate the situation. Arrangements should be made to ensure that all close contacts can obtain this drug.

7. Purpuric skin lesions can be manifestations of disseminated intravascular coagulation (DIC). Petechial lesions are pinpoint, purplish-red lesions that are caused by hemorrhage in the intradermal vascular bed. Purpuric lesions are similar to petechial lesions but are larger, probably representing coalescence of a number of petechial lesions. Although many different events can initiate DIC, the endotoxin found in the outer membrane of *N. meningitidis* is a well-recognized mediator of DIC.

Reference

1. **Moore, P. S., and C. V. Broome.** 1994. Cerebrospinal meningitis epidemics. *Sci. Am.* **November:**38–45.