Topic:

Meningococcal disease: A trail of fatalities and incapacitations.

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Abstract:

Meningococcus is an obligatory aerobic bacterium that poses a global health challenge in the form of serious, often fatal, sporadic epidemic meningitis and septicemia. Children and young adults are more susceptible to this infection. *N. meningitidis* is responsible for this illness which involves infection of the meninges and the blood stream. Different strains of this microorganism exist worldwide. *N. meningitidis* usually colonizes the nasopharynx, which facilitates the spread of the organism as salivary droplets or secretions of the upper respiratory system and throat. Risk factors that aid spread of the disease include social, economic and environmental dispositions. The morbidity and mortality rates associated with meningitis is high, so early detection and rigorous treatment with antibiotics are very important. Meningococcal vaccines that use different serogroups of *N. meningitidis* are now available to prevent infection.

Introduction:

Meningitis can be caused by bacterial and nonbacterial organisms. Meningitis from bacterial infection are more severe and poses a greater danger to life than viral meningitis. Essentially, most cases of meningitis are as a result of infections from three bacteria, namely, *Neisseria meningitidis*, *Streptococcus pneumonia* and *Haemophilus influenza* type b, that cause meningococcal meningitis, pneumococcal meningitis and influenza, respectively. Most of the bacterial meningitis in newborns, such as those caused by Group B Streptococcus spp, are from their mothers. The occurrence of meningitis is highest in infants less than one month. Children that are older are more often infected by *H. influenza*, *N. meningitidis*, and *S. pneumoniae*. Either *N. meningitidis* or *Streptococcus pneumonia* can cause meningitis in adults, but they are mainly due to Strep pneumoniae infections. These bacterial spread mostly through the blood, some use the nerve as a pathway to enter the brain (such as viral meningitis from rabies and herpes simplex virus). Factors that predispose people to meningitis include inadequate treatment of infections of the sinus or ear, infection include diabetes, low innate immunity, cancer, treatment with steroids, HIV, advanced age, traveling to endemic areas for an extended period of time, active and passive smoking, kissing, over-crowded places, patronizing pub and bars and low economic status [1,2,3]. *Neisseria meningitidis*, which belongs to the kingdom Bacteria, phylum Proteobacteria and genus *Neisseria*, is responsible for causing most of the illnesses that are
collectively referred to as meningococcal disease and it is the only microorganism that is capable of causing epidemic outbreaks of meningitis.

Infections from various forms of *N. meningitidis* occur world-wide with highly fatal outcome [1]. The occurrence of *N. meningitidis* in different populations of the world is highly unpredictable because of the differences in distribution, frequency of the disease and serological groupings [1]. Globally, about 1.2 million cases of meningococcal infection occur annually, with about 135,000 deaths [1]. Most of the morbidity effects and mortality of meningococcal disease occur in children less than 1 year old, with lesser risks in adolescent and young adults of 15-25 years. The carriage pattern of *N. meningitidis* tends to be higher in adolescents and younger adults than in children and new-born [1]. Epidemics of the disease occur seasonally, with the tendency to start in the dry season and end at the commencement of the rainy season [2]. Out of the 13 meningococcal strains identified so far: A, B, C, E-29, H, I, K, L, W-135, X, Y, Z, AND Z’ (29E), six serogroups - A, B, C, W (formerly W-135), X and Y - cause almost all invasive disease cases [2]. Serogrouping is the usual method of classifying meningococcus spp using biochemical properties that are targeted against their polysaccharide capsule. The capsule is one of the determinants of virulence and it is a focus of interest in the development of meningococcal vaccines [2]. Other classification methods include the use of monoclonal antibodies, PorinA, PorinB, lipooligosaccharide LOS structures and multilocus sequence typing (MLST) of their DNA genes or a combination of these methods [1]. If these DNA genes are closely related, they are called clonal complex (3). Presently, MLST is the present gold standard for classifying *N. meningitides*. Demographically, serogroups A and W ST-11 can be found in Africa, Taiwan, South America, Argentina, South Africa and United Kingdom, serogroups B and C in Latin America and all five serogroups have been reported in Asia. Serogroups B, C, Y and W-135 have been found in North America [1,4].

**History:**

Identification of Meningococcus dates back to the 19th century when Weichselbaum first discovered it in a patient’s CSF [2]. However, Albert Neisser, who jointly discovered *Mycobacterium leprae*, also discovered the first human pathogenic example of meningococcus, *N. gonorrhea*, in 1879. The earliest description of the epidemic form of meningococcus meningitis was by Vieusseux in 1805, Daniel and Mann in 1806 and in Africa in the 1900s by
Greenwood [2]. Previously, serogroup W was scarcely associated with meningococcal pathogenicity until the year 2000 when meningococcal epidemic illness caused by this strain occurred in Mecca, Saudi Arabia at the annual pilgrimage. This strain was called Hajj clone [3]. Recently, genotyping has become valuable in differentiating various strains of Neisseria and strains that are capable of causing epidemics and in monitoring efficacies of vaccines against the organism [3].

**Morphology/stains/culture media:**

*N. meningitidis* is cultured for 18-24 hours and grows best in a capnophilic environment that requires 35-37°C incubation with 5% CO2 [2]. It grows on blood agar media (BAP), trypticase soy agar (TSA) and supplemented chocolate agar plate (CAP). It is a fastidious, encapsulated, aerobic, gram-negative diplococcus and kidney/coffee/bean shaped bacteria that appears on media as gray in color, round, moist, glistening, convex and smooth with an edge that is clearly defined [1, 2]. This organism is non-hemolytic and tests positive both for catalase and Kovac’s oxidase reactions. Carbohydrate utilization test on blood agar plate helps to validate the positive result obtained with Kovac’s test. Serological testing using slide agglutination serogrouping (SASG) further identifies the organism.

**Pathogenicity:**

Bacterial meningitis presents with identifiable symptoms that include skin rash that appear purple or reddish, vomiting, photophobia, fever, irritability, headache, painful and stiff neck and general malaise [1]. A vital diagnostic procedure for meningitis is lumbar puncture in order to obtain the CSF. The CSF can be examined microscopically for the presence of microorganisms and white blood cells – an indication of meningitis. Most people with meningitis find it difficult to lower/bend their head and chin forward to their chest. This manipulations can be an additional confirmatory test that a patient has meningitis. Many factors combine to enhance the virulence of *N. meningitidis*. Factors such as minor and major surface adhesive proteins (pili), lipoooligosaccharide (LOS), capsule, cell envelope and other molecules like iron binding proteins [1, 2]. The endotoxin LOS is vital both in the adhesion and stimulation of innate immunity, and it has been found that a direct link exists between the levels of LPS, seriousness of meningococcal disease and resistance to host defense mechanisms [5]. *N. meningitidis* may reside in the nasopharyngeal region with no obvious health implications. Alternatively, meningitis and
bacteremia can occur 1-14 days after colonization in about 50% of the cases. Development of innate immunity controls *N. meningitidis* infection, but in naïve immune individuals, an infection can lead to pneumonia, myocarditis, conjunctivitis, arthritis, pharyngitis, urethritis [1]. Severe infections may precipitate fulminant meningococcemia (hemorrhagic adrenalitis) that may result in fatalities [2].

**Treatment:**

Serum therapy by Flexner in 1913, and thereafter the sulfonamides, have been deployed in the treatment of meningococcal disease [4]. Due to this organism's resistance to sulfonamides, penicillin and ampicillin are the recommended drugs of choice. Cephalosporins may also be used in resistant cases or in presumptive management of the disease [4]. In the US, ceftriaxone, rifampicin, and azithromycin are used to eliminate *N. meningitidis* carriage due to the emergence of resistant strains to fluoroquinolone. Ceftriaxone can safely be administered to children and pregnant women when treating *N. meningitidis* that has colonized the nasopharynx [4]. Presently, there are vaccines that are effective in protection against all five serogroups of the disease, including the three serogroups that occur in the US. Available vaccines in the US are:

Meningococcal polysaccharide vaccine (MPV) which is a bivalent vaccine that protect against serogroups A and C (bivalent), the trivalent vaccine protects against serogroups A, C and W-135, while the tetravalent component protects against serogroups A, C, W-135 and Y. Meningococcal conjugate vaccines (MCVs) include MenACWY that protect against serogroups A, C, W-135 and Y. Hib-MenCY-TT is a bivalent vaccine against serogroups C and Y or as monovalent against serogroups A or C, and vaccines against serogroup B use outer membrane vesicles (OMV) preparations [4].

As mentioned earlier, infections caused by bacteria *N. meningitidis* could be fatal if it is not treated urgently. The case-study which is presented below helps to buttress this fact.

**Case study [6]:**

**Summary:** A 68-year old male had facial cellulitis caused by *N. meningitidis* without any other infection outside his facial soft tissue. He was successfully treated with intravenous ceftriaxone followed by amoxicillin orally. Although *N. meningitidis* is known to mainly cause bacterial
meningitis and septicemia, it is important to include \textit{N. meningitidis} in the differential diagnosis of cases involving infections of tissues of the head and neck regions.

**Case presentation:** A 68-year old male was seen in an emergency room (ER) with a swollen face that started at the upper part of his lip. He was diagnosed with allergic reaction caused by food, treated with diphenhydramine, methylprednisolone, and discharged. Two days later, he returned to the ER with a temperature of 38.2°C (febrile) and increased swelling of the right cheek, jaw and upper part of the neck. When questioned, he said he had a little laceration recently while shaving at a barber shop.

**Lab report:** The patient had a WBC count of 16,000, accompanied by a left shift. The CT scan was negative for fluid collection in the jaw and facial areas but showed stranding of tissues in the submandibular region and the right cheek. Initial treatment was with IV clindamycin but the swelling worsened. Thus, vancomycin and piperacillin-tazobactam were used instead. He was admitted to the hospital.

**Investigations:** A 2-day blood culture revealed a Gram-negative diplococci. Further tests identified the causative organism as \textit{N. meningitidis}. Cerebrospinal fluid (CSF) obtained by lumbar puncture showed no infection.

**Differential diagnosis:** Acute infection of facial tissue cells include \textit{Staphylococcus aureus}, \textit{Streptococcus pneumonia}, \textit{Streptococcus pyogenes}, \textit{Haemophilus influenza} type B (but now an uncommon cause of this condition due to vaccinations).

**Treatment after laboratory results:** While on admission at the hospital, the patient received intravenously administered ceftriaxone. There was an improvement in erythema and swelling, the WBC also decreased to 6,000. So the patient was discharged and placed on oral amoxicillin to be taken for 14 days. He was advised to follow up with his primary Healthcare Provider for further medical examinations and treatments, if required.

This case study illustrates that in the differential diagnosis of immunocompetent patients presenting with infections of the skin and soft tissues of the face, head and neck regions, \textit{N. meningitidis} needs to be considered as one of the possible causative organisms. Because \textit{N. meningitidis} is associated mostly with epidemic meningitis rather than facial cellulitis, this
patient would have been misdiagnosed and the infection would have progressed with fatal outcome.

**Interesting information about *N. meningitidis***:

*N. meningitidis* colonizes the upper respiratory tract of people without any obvious signs or symptoms. These people become sources of infection to other people who may become sick and die within 24 hours post-infection. Therefore, carriers are naïve sources of spread of this disease in their environments, and the ‘symptomless’ characteristic of this organism in some carriers, mostly young adults, makes it difficult to detect and treat. Conversely, people that are infected with *N. gonorrhoea*, causes gonorrhea disease, cannot remain “silent carriers” for too long without the manifestations of some the uncomfortable signs and symptoms that are associated with the disease including burning sensations when urinating and pelvic inflammatory disease (PID). This often prompts “carriers” of *N. gonorrhoea* to seek for medical treatment which helps to reduce the spread of the disease in the communities.

**Conclusion:**

The devastating effects of epidemic meningococcal disease to human health persists around the world. These adverse effects often result in the loss of many lives. Survivors of these infections have trails of sequelae that include blindness, deafness, and interruption of the normal flow of CSF which are the consequences of compressed or damaged meninges and/or permanent damage to nerves and specific areas of the brain. Bacterial meningitis are more severe than viral meningitis, and low levels of immunity make infants to be highly susceptible to these infections. Presently, *N. meningitidis* is solely responsible for causing epidemics of meningococcal meningitis in humans. Prophylaxis by vaccinations and treatment with antibiotics are the available options for the control and management of this disease. Vaccines targeted against the different serotypes of bacteria that cause meningococcal disease have been developed. Immunizations with these vaccines have reduced the incidence of severe epidemic meningitis in the more vulnerable population, such as infants and children. The emergence and spread of resistant strains of these organisms have limited the choice of antibacterial agents that are available for combating meningococcal disease.
References:


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