

Second Attacks of Meningococcal Meningitis

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IT IS STATED that second attacks of meningococcal infection are rare, and that an infection may even confer some immunity.¹ However, recent Navy experience in the San Diego, California, area suggests that individuals who have had meningococcal meningitis may have a high risk of recurrence, as illustrated by the following reports of two recent cases of proved second attacks of meningococcal meningitis in enlisted men.

Reports of Cases

CASE 1. An 18-year-old Caucasian male had completed his first month of recruit training at San Diego when he was put in hospital on November 15, 1961 because of frontal headache, lethargy and myalgia for one day.

On physical examination, temperature of 102°F, slight meningismus, pharyngeal injection, positive Brudzinski's sign and a generalized petechial rash with some ecchymotic areas were noted. Spinal fluid was obtained under normal pressure, and contained 44 mg of protein and 105 mg of sugar per 100 ml and 114 mEq of chlorides per liter. There were only 3 neutrophils and 4 lymphocytes per cu mm, but a Gram-stained specimen showed intracellular and extracellular Gram-negative diplococci. A chocolate agar plate culture of spinal fluid grew *N. meningitidis*; unfortunately, serological typing of the organism was not performed.

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From Research Project MR 005.09-1215, Bureau of Medicine and Surgery, Washington, D.C., 20390. The opinions and assertions contained herein are the private ones of the author and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

Submitted January 21, 1965.

Blood cultures were negative for pathogenic organisms.

The patient became comatose the day of admission despite intravenous administration of sulfadiazine and penicillin. He regained consciousness on the second hospital day and, although he complained of severe retrobulbar headache for the next six days, there was good response to continuous antibiotic treatment and he was discharged to full duty on December 6, 1961.

Between 1961 and 1964 he had excellent health. He served aboard a destroyer as an engine-man-fireman, made one cruise to the Orient, and was married in 1962. At 1800 on July 24, 1964, while aboard ship in San Diego harbor, he began to have chills and fever and was awakened twice during the night because of nausea, with a single episode of vomiting. The following morning, at sick call, he complained of pain on moving his legs.

He was immediately put in hospital, being admitted at 1000 on July 25, 1964. On admission he was alert and responsive but complained of generalized myalgia and "burning" in both legs. On physical examination petechiae were seen over the entire body, including the oral and conjunctival mucosae, and there were large patches of ecchymosis on the legs. Nuchal rigidity was not detected, and the blood pressure and temperature were normal.

Leukocytes numbered 33,400 per cu mm with over 90 per cent immature neutrophils. On lumbar puncture the opening pressure was 250 mm of water. There were only 12 cells per cu mm of spinal fluid, but it contained 118 mg of protein per 100 ml. A Gram-stained specimen of the spinal fluid showed Gram-negative diplococci, later proven to be group B meningococci resistant to 5 mg of sulfadiazine per 100 ml *in vitro*. Three cultures of blood taken on the day of admission also grew this organism.

Despite treatment, including intravenous fluids and antibiotics, use of hypothermia, vasopressors and, later, steroids, the condition of the patient worsened rapidly and he died July 31. Of particular interest was the development of fever of 108°F on the second day in hospital, accompanied by a fall in blood pressure despite the use of intravenous vasopressors.

On autopsy multiple hemorrhages in the internal organs were noted, including the adrenal cortex (Waterhouse-Friderichsen syndrome).

CASE 2. A 19-year-old Caucasian recruit had been in training at San Diego for one week when chills and fever developed the evening of December 14, 1960. The next morning he complained of severe frontal headache. Rectal temperature was 101°F.

When admitted to hospital at 1000 on December 15 the patient was lethargic and lying with the neck extended and heels drawn down. He answered questions slowly but accurately. On physical examination, pronounced nuchal rigidity, blurring of the right optic disc, and positive Kernig's and Brudzinski's signs were noted. On lumbar puncture the opening pressure was 420 mm of water. The spinal fluid contained 249 mg of protein and 50 mg of sugar per 100 ml and 2,000 cells per cu mm, of which 97 per cent were neutrophils. Gram-negative diplococci were seen on smears of the spinal fluid, and a culture grew *N. meningitidis*, type not determined. Blood cultures were negative for pathogenic organisms.

The patient responded well to treatment with intravenous penicillin, sulfadiazine and chloramphenicol and was discharged to full duty with no sequelae on January 26, 1961.

He completed recruit training and served aboard an aircraft carrier without incident until June 12, 1964, when he had sudden onset of fever, chills and generalized myalgia. Upon reporting to the ship's sick bay that afternoon he complained of pain and soreness of the upper back. Since obvious meningismus was noted on physical examination and the temperature was 104.8°F orally, he was immediately put in hospital.

On physical examination the pulse rate was 115 and the blood pressure 106/58 mm of mercury. Nuchal rigidity and multiple petechiae were noted. On spinal puncture the opening pressure was 190 mm of water. Clear spinal fluid was obtained. It contained 26 mg of protein and 58 mg of sugar per 100 ml, and no cells. However, cultures of the fluid later grew *N. meningitidis*, type B, resistant to over 10 mg of sulfadiazine per 100 ml *in vitro*. This organism was also grown on cultures of blood taken the day after admission. Serum protein electrophoresis was normal with 3.9 gm of albumin and 3.4 gm of globulin per 100 ml.

Despite vigorous intravenous administration of sulfadiazine, penicillin and chloramphenicol, and maintenance of the blood pressure with metaraminol, the patient remained in serious condition.

On the day after admission he became oliguric and large areas of ecchymosis appeared on both the upper and lower extremities. On the third hospital day, however, urine output increased and he became more responsive. On examination of the urine at that time, microscopic hematuria and abundant granular casts were noted. On the sixth hospital day it was possible to discontinue intravenous fluids and medications, but many of the peripheral ecchymotic areas had become gangrenous, necessitating subsequent amputation of two toes of the left foot, and leaving several large denuded areas on the lateral aspects of both legs. In October 1964, the patient was completely asymptomatic and was transferred to another hospital for completion of skin grafting procedures.

Discussion

The occurrence of fulminating second attacks of disease in these two men suggested an unusual lack of resistance to meningococcal infections, since the overall incidence of meningococcal infection in this area is low. Between June 1963 and October 1964, there were only eight other cases of meningococcal meningitis (exclusive of recruits) among approximately 70,000 active duty personnel in this naval district. Interestingly, one of the eight also had recurrent meningitis but that case is not included in the present report since only six months elapsed between attacks, and "chronic meningococcemia" could not be ruled out. In addition, one of 14 recruits who had meningococcal meningitis during this period also had a second attack four months after the first. Between December of 1960 and of 1961, when the two patients herein reported upon first had the disease as recruits, approximately 50,000 other men were processed through recruit camp with only nine other cases among them.

It was possible, of course, that the reported cases were caused by either overwhelming exposure or by contact with exceptionally virulent strains of meningococci. The former seems unlikely since neither of the men had been subjected to undue stress and since meningococcal carrier rates among their shipmates were well within normal limits. On the destroyer, positive cultures for meningococci were obtained from the nasopharynx in six of 57 men (10.6 per cent), while on the aircraft carrier there were eight positives in 146 cultures (5.5 per cent). The meningococci isolated from the two patients in the present cases

were not unusual: group B sulfadiazine resistant strains are at present the predominant meningococci in this area.² Since January 1, 1964 we have examined isolates from 19 cases of meningococcal meningitis in San Diego: all were group B and 16 were resistant to sulfadiazine *in vitro*. In addition, over 70 per cent of meningococci isolated from normal carriers in this area have proven to be group B and resistant to sulfadiazine.

Because of the difficulty in collecting data on other cases of meningococcal meningitis in adults outside this naval district, it is possible that recurrent disease is more common than was assumed previously. Since there was no evidence of debility or unusual stress in the two cases herein reported (or in two other cases in navy personnel in this area with shorter periods between attacks) it is possible that the patients lacked a "natural immunity" to meningococcal infection. At least in

Case 2, in which serum protein electrophoresis was performed, lack of resistance was not due to hypogammaglobinemia.

Summary

The occurrence of second attacks of meningococcal meningitis in two Navy enlisted men is described. It is suggested that the patients may have lacked natural resistance to meningococcal infection.

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REFERENCES

1. Bennet, I. L. Jr.: Meningococcal infections; From Principles of Internal Medicine, 4th ed., Vol. II., edited by Harrison, T. R., 1947 pp., N.Y.: McGraw-Hill, New York, 1958, pp. 924-927.
2. Millar, J. W., Siess, E. E., Feldman, H. A., Silverman, C., and Frank P.: In vivo and in vitro resistance to sulfadiazine in strains of *Neisseria meningitidis*, J.A.M.A., 186:139-141, Oct., 1963.

