BACTERIAL CAPSULAR POLYSACCHARIDES IN THE CEREBROSPINAL FLUID OF PATIENTS WITH PURULENT MENINGITIS [1]

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With increasing use of antibiotics, the recovery of specific causative organisms in bacterial infections is made less frequently. Failure to demonstrate the specific bacteriological agent involved is commonly encountered in patients hospitalized after the administration of varying amounts of antibiotics. During the course of infections due to the pneumococcus, type-specific capsular polysaccharides have been detected in blood, urine, sputum and pleural exudate (1–6). There is no record of the demonstration of type-specific capsular polysaccharides in the cerebrospinal fluid of patients with pneumococcic meningitis, although the occurrence of capsular polysaccharides in the cerebrospinal fluid of patients with meningococcic meningitis is well established (7–10). The purpose of this communication is to report the detection of capsular polysaccharides in the cerebrospinal fluid of five patients with pneumococcic meningitis and one patient with meningitis due to Klebsiella pneumoniae.

MATERIALS AND METHODS

Group and type-specific rabbit anti-pneumococcal sera, types 1 to 33, were obtained from the New York City Department of Health. Group-specific rabbit anti-Klebsiella pneumoniae sera, groups A and B, were provided by Dr. Michael Heidelberger.

As has been previously shown, the presence of C-polysaccharide and C-antibody may interfere with the interpretation of positive precipitin reactions (7, 8). In the present studies, the cerebrospinal fluid of two patients with pneumococcic meningitis showed the presence of C-polysaccharide when tested with horse-serum containing a high titre of C-antibody. For that reason, all typing and grouping sera used were first absorbed with 5 micrograms of C-polysaccharide per milliliter of serum to remove the C-antibody present. The C-polysaccharide used in the absorption was derived from a type VII pneumococcus.

In attempting to demonstrate the presence of a pneumococcus polysaccharide, a preliminary test was done using polyvalent sera, types 1 to 33, each containing precipitins to four types of pneumococci. Five-tenth milliliter portions of C-absorbed group-specific antisera were placed in small sterile test tubes. Five-tenth milliliter portions of cerebrospinal fluid, which had been cleared by centrifugation, were added to each of the tubes containing group-specific antisera. Saline was added to the serum and cerebrospinal fluid control specimens. The contents of the tubes were mixed and allowed to stand for one hour at room temperature. The tubes were then centrifuged and examined for the presence of a precipitate; if none was visible, the tubes were placed at 4° C. and reexamined at the end of 24 and 48 hours. If one of the tubes contained a precipitate, the cerebrospinal fluid was then set up in a similar manner against each of the four type-specific antisera in that group.

When attempting to demonstrate the presence of capsular polysaccharide of Klebsiella pneumoniae, in addition to tests with specific antisera, one spinal fluid sample was set up against type II pneumococcus antiserum. It has been demonstrated that the capsular polysaccharide of Klebsiella pneumoniae group B organisms cross-reacts with antiserum to type II pneumococcus (11).

RESULTS

Seventeen specimens of cerebrospinal fluid from 10 patients with purulent meningitis were tested. All of the patients received penicillin in large dosage by parenteral and intrathecal routes immediately after the initial cultures of the cerebrospinal fluid were obtained. Results of cultures and the precipitin tests are shown in Table I. All control tests were negative. Specimens from two patients showing no growth on culture were negative for pneumococcal polysaccharide. One patient with Actinomyces bovis and one patient with Cryptococcus hominis on spinal fluid culture showed no pneumococcus polysaccharide. One patient from whom an untypable Friedlander's bacillus was cultured, was shown to have capsular polysaccharide of Klebsiella pneumoniae group A in his spinal fluid. The corresponding type-specific capsular polysaccharide was demonstrated in the spinal fluid of each patient with proven pneumococcic meningitis. One patient in whom a pneumococcus infection was suspected but with a negative spinal fluid culture showed type I capsular polysaccharide.

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TABLE I

Patient	Culture of CSF	Test for polysaccharide in CSF	Persistence of polysaccharide
			(*days*)
1	Negative	Negative	—
2	Negative	Negative	—
3	Actinomyces	Negative	—
4	Cryptococcus hominus	Negative	—
5	Kleb. pneum. ? type	Kleb. pneum. Group A	3
6	Pn. VIII	Pn. VIII	3
7	Pn. VI	Pn. VI	6
8	Pn. XIX	Pn. XIX	2
9	Pn. VI	Pn. VI	8
10	Negative	Pn. I	—

The polysaccharides, when detected, were shown to persist in specimens obtained at least two days after the cerebrospinal fluid cultures were negative. In one patient, the polysaccharide was still demonstrable eight days after the cultures had become negative (see Table I).

COMMENT

The test described is quite sensitive since as little as 2 or 3 micrograms of capsular polysaccharide, in the presence of a potent specific antiserum, will give an easily visible precipitate. A positive test is probably specific if preliminary removal of C-antibody from the typing sera is carried out. A negative test does not necessarily rule out the possibility of a pneumococcal meningitis because, under the conditions of the test, there is no information on the absolute amount of antigen added. Cerebrospinal fluid containing capsular polysaccharide in low concentration may have to be added in large amounts to produce a visible precipitin reaction. In the presence of unusually high concentrations of capsular polysaccharide, the precipitin reaction may possibly be inhibited by virtue of entering the zone of large antigen excess (12).

Identification of the specific causative organism in bacterial meningitis has been made much more difficult because of the liberal use of antibiotics. The detection of bacterial polysaccharides in the cerebrospinal fluid may be of assistance in making the specific bacteriological diagnosis in patients with meningitis who have received previous antibiotic therapy.

SUMMARY

1. Capsular polysaccharides have been demonstrated in the cerebrospinal fluid of five patients with pneumococcic meningitis and one patient with meningitis due to Klebsiella pneumoniae.

2. The capsular polysaccharide was still demonstrable in cerebrospinal fluid specimens taken from two to eight days after the cerebrospinal fluid cultures showed no growth.

3. The demonstration of specific capsular polysaccharide in the spinal fluid may be of diagnostic value in establishing the nature of the pathogen involved in patients in whom the organism cannot be recovered because of previous antibiotic treatment.

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