

Recurrent Bacterial Meningitis Due to a Cerebrospinal Fluid Fistula and Its Prophylaxis

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ABSTRACT. A cerebrospinal fluid fistula after trauma was observed by ^{111}In -DTPA cisternography and $^{99\text{m}}\text{Tc}$ -MDP bone scintigraphy in a patient who had had three occurrences of bacterial meningitis. We studied the efficacy of sulfamethoxazole-trimethoprim by measurement of their concentrations in cerebrospinal fluid. The patient was followed for more than two years to observe the effect of low-dose SMX-TMP on the closing fistula.

Key words : Recurrent bacterial meningitis — SMX-TMP —
Cerebrospinal fluid fistula

Cerebrospinal fluid fistulas are very rare in pediatric practice, but we have found them to be a cause of recurrent meningitis. As prophylactic administration of antibiotics for meningitis is not effective, some fistulas are operated upon for the correction of leakage with risk. However, since most CSF fistulas will close spontaneously, we followed the course of one patient for about two years with prevention of meningitis by low-dose sulfamethoxazole-trimethoprim therapy.

CASE REPORT

An eleven-year-old boy was admitted to our hospital because of fever, vomiting and headache on 22nd Jan., 1983. Positive findings were neck stiffness and Kernig's sign. The patient was stuporous, when he arrived, and generalized tonic and clonic seizure occurred for about ten minutes. The laboratory findings for CSF were cells 17000/3, protein 400 mg/dl, and glucose 5 mg/dl. Cultures of CSF and blood were negative due to the use of antibiotics by a previous doctor, but latex particles (Bio Mérieux) were aggregated for streptococcus pneumoniae. Before this admission, the patient had experienced bacterial meningitis twice, 22nd May, 1979 and 28th July, 1981. On the first occasion, the lumbar tap for CSF showed cells 13300/3, protein 210 mg/dl, glucose 29 mg/dl, and streptococcus pneumoniae was cultured. On the second occasion findings were cells 16700/3, protein 196 mg/dl, glucose 31 mg/dl, and nothing was cultured.

About two months before the first occurrence of meningitis the patient had fallen from approximately two meter high jungle gym and hit his right forehead. At that time his parents noticed bluish skin around the right eye.

寺田喜平, 三浦 洋, 守田哲朗

However, the fall did not appear to have had any serious effect on him and he was healthy up until the time of his first admission. There was no special family history nor was there any past history of bacterial infections other than meningitis. Laboratory investigations showed T cells and B cells, immunoglobulins and an NBT test that was normal. A CT scan showed no abscess in his brain. The first thing noticed was a positive change in the Testape® of his nasal discharge. To confirm the CSF fistula, we packed cotton into his nose during ^{111}In -DTPA cisternography (Fig. 1). The results showed the RI count of the cotton to be 115 times that of the background, clearly indicating the existence of a CSF fistula. $^{99\text{m}}\text{Tc}$ -MDP bone scintigraphy was then done and suggested a right basal bone fracture. Localization of the fracture, however, was not shown by CT metrizamide cisternography. Finally, after discussion

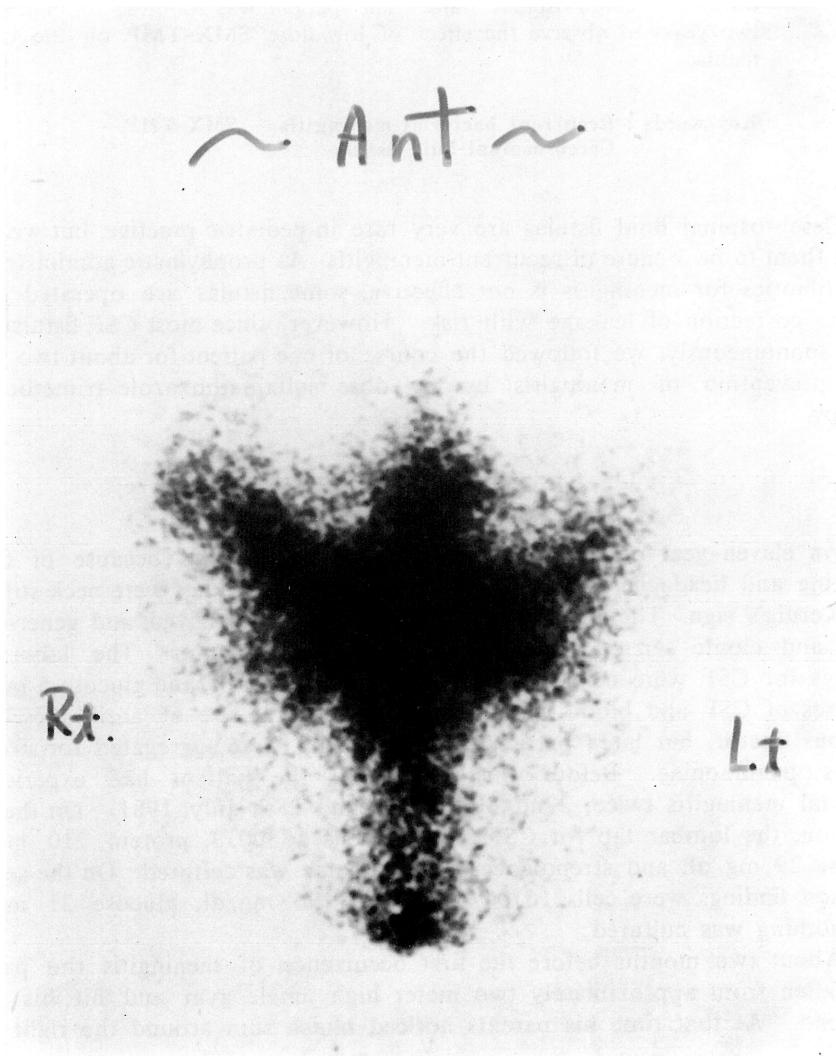


Fig. 1. ^{111}In -DTPA cisternography

with neurosurgeons, we decided to follow him up without surgery.

Based on the data from a trial usage, sulfamethoxazole (SMX) 120 mg - trimethoprim (TMP) 24 mg b.i.d. was prescribed for prophylaxis of the bacterial meningitis. Twelve hours after its administration, we drew serum and CSF to measure their concentrations. The results (Table 1) showed the concentration of SMX in CSF to be 1.6 and 2.5 times as high as the MIC of streptococcus pneumoniae. The MIC of various standard bacteria for SMX was streptococcus pneumoniae DPT 1.4 $\mu\text{g/ml}$, staphylococcus aureus 209-P JC-2 0.74 $\mu\text{g/ml}$, haemophilus influenzae 0.05 $\mu\text{g/ml}$. The initial dosage has since been doubled to SMX 240 mg - TMP 48 mg because we concerned about the efficacy of the drug.

TABLE 1. The concentration of SMX and TMP in serum and CSF by SMX 4 mg-TMP 0.8 mg/kg body weight/day b.i.d. (Both were drawn twelve hours after SMX-TMP was given).

	First			Second		
	Serum	CSF	CSF/Serum(%)	Serum	CSF	CSF/Serum(%)
SMX($\mu\text{g/ml}$)	11.4	3.76	32.9	15.3	2.39	15.6
TMP($\mu\text{g/ml}$)	0.016*	0.016	—	0.09	0.016*	—

* means less than the figure

We have seen the patient regularly for the last two years and checked his nasal discharge by Testape®. There has been no recurrence of meningitis even though he experienced tonsillitis. Since no change was shown by Testape® in his nasal discharge during one and half years after the making of the initial diagnosis, we investigated the closing fistula by ¹¹¹In-DTPA cisternography and found the RI count of the packed cotton to be only 5 times as high as the background.

DISCUSSION

The positive change in the patient's nasal discharge shown by Testape® suggested CSF rhinorrhea, and this was confirmed by ¹¹¹In-DTPA cisternography. A detailed interview and bone scintigraphy suggested a traumatic fracture of the basal bone. Ray¹⁾ reported that 27% of CSF fistula result from skull fracture, 10% are congenital, 37% are associated with intracranial tumors and 47% follow neurological or otolaryngological surgery. Patients with CSF fistula have a 25²⁾-37³⁾% risk of meningitis. The incidence of meningitis is higher in CSF otorrhea than in rhinorrhea.⁴⁾ The possible onset of meningitis is about 50% within two weeks, whereas it is only 25% after one year.⁵⁾ Approximately two months passed between trauma and the onset of meningitis in this patient. Mincy³⁾ reported that the chance of spontaneous cessation is 85% within seven days. As it might be easier in children than in adults for a fistula to close as the result of bone growth, we expected a spontaneous closure if low-dose SMX-TMP was used without surgery. Although prophylactic antibiotics have generally been used before, MacGee⁶⁾ reported that the effectiveness of

antibiotics had not been statistically significant for CSF fistulas. Although the penetration of antibiotics into CSF is poor due to the blood-brain barrier, it is good in meningitis. Even so, resistant bacteria must be taken into account.

Long term usage of SMX-TMP for prophylaxis of urinary tract infections in patients of vesico-uretero reflux and bacterial infections in chronic granulomatous disease has been successful. Weening⁷⁾ showed that there were no SMX-TMP resistant microorganisms in chronic granulomatous disease patients who had received SMX-TMP for a long period of time. Both SMX and TMP penetrate easily into CSF, Lafaix⁸⁾ showed that the CSF/serum penetration ratio of SMX and TMP is 45% and 67%, respectively. Our data showed that the penetration to be less than Lafaix's data because of CSF leakage. As their bioavailability is 100%, the reason for the low concentration of TMP may be that it is metabolized.

The most common causative bacteria for meningitis due to fistulas is streptococcus pneumoniae, and we have found it to be causative bacteria in two of the three occurrences of meningitis in this patient. Since the concentration of SMX-TMP in CSF is now at least 3.2 times as high as the MIC of streptococcus pneumoniae with an 8 mg - 1.6 mg/kg body weight/day dose of SMX-TMP (this being about half the dose for chronic granulomatous disease), we think therapy with this drug can be considered effective, useful, and safe, since we have found no side effects during the two years it has been administered.

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