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Bacteroides Meningitis Successfully Treated with Metronidazole

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Bacteroides meningitis without associated cerebral abscess occurred in an elderly man who had a long history of chronic otitis media. Anaerobic cultures of the cerebrospinal fluid revealed bacteroides organisms. Sensitivity testing showed them to be resistant to penicillin and chloramphenicol but sensitive to metronidazole. Appropriate therapy with this agent eradicated the causative organisms and produced rapid clinical improvement.

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Therapy with metronidazole may be lifesaving in some cases of meningitis due to anaerobic organisms that are resistant to usual antibiotic therapy. In the following case, early anaerobic cultures and sensitivity testing led to successful treatment.

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A 77-year-old white man at the age of 22 had developed a left mastoiditis treated by mastoidectomy. The patient had continued to have a nearly continuous foul-smelling discharge from his left ear for the next fifty-five years. In May, 1974, he developed impairment of equilibrium. When admitted to the hospital, he was free of headache and fever but manifested a wide-based gait, loss of hearing in the left ear, and mild nystagmus on right lateral gaze. Reflexes were normal.

Five days after admission the patient had a temperature of 39.5°C, complained of headache, and had a stiff neck. Lumbar puncture showed an opening pressure of 80 mm H_2O; the cerebrospinal fluid contained 70 neutrophils and 600 monocytes per cubic millimeter with 126 mg of protein and 50 mg of glucose per deciliter. Gram stains, routine blood and chocolate agar cultures, and cultures for fungi and acid-fast organisms revealed no growth, but anaerobic cultures grew out bacteroides. Later, subspeciation revealed the organisms to be *B. ruminacola* and *B. nodosa*. Since brain abscess was initially suspected, the patient was started on chloramphenicol and ampicillin therapy. A radioisotope brain scan and cerebral angiogram were normal, so chloramphenicol was discontinued after two days; ampicillin was continued.

During the next two weeks the patient became more obtunded, temperature remained elevated, and he had nuchal rigidity. During this period, several lumbar punctures were done that showed glucose dropping to 10 mg per deciliter, protein going up to 534 mg per deciliter, and white cells ranging up to 3,800. Nine days after ampicillin was started it was discontinued, and penicillin G, 5 million units every 6 hours, and chloramphenicol, 1 gm every 6 hours, were initiated. No surgical condition of the ear or mastoid was found, but a culture of the fluid draining from the left ear grew out *B. nodosa* and several other organisms.

Eight days after penicillin and cloramphenicol were started there had been no improvement. Sensitivity testing revealed that the organisms were sensitive to metronidazole, so penicillin was discontinued and treatment with this agent was begun. Metronidazole was given for four weeks at a dosage of 250 mg three times daily by mouth. Chloramphenicol was continued during the first two weeks of metronidazole therapy. Four days after metronidazole was started the patient became alert, and he continued to improve thereafter. At the end of the course of metronidazole the spinal fluid was acellular. In the four years since treatment there has been no recurrence of either central nervous system symptoms or drainage from the ear.

Discussion

In this patient with bacteroides meningitis, sensitivity testing demonstrated that the causative organism was resistant to chloramphenicol and penicillin but sensitive to metronidazole. His poor response to chloramphenicol but excellent clinical response to metronidazole, plus demonstration on sensitivity testing that the organisms were resistant to chloramphenicol but sensitive to metronidazole, shows the

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effectiveness of the drug in this case of bacteroides meningitis. Appropriate anaerobic cultures and sensitivity testing made successful treatment possible.

Anaerobic intracranial infections are often associated with brain abscesses, but meningitis due to anaerobic organisms unassociated with brain abscess is uncommon. When it occurs, it is usually secondary to chronic otitis media or surgery of the mastoid or middle ear. Ballenger et al [1] stated that only 11 cases of bacteroides meningitis had been reported prior to 1940. More recently, several cases have been reported [5, 8, 9, 11] and occasional cases have been treated in several centers, but the illness remains an uncommon type of meningitis. Possibly more cases would be identified if anaerobic cultures were obtained routinely in patients with meningitis.

A strain of bacteroides may be susceptible to any one of numerous antibiotics, including penicillin, clindamycin, chloramphenicol, erythromycin, tetracyclines, or metronidazole. Penicillin is the drug of choice against most anaerobes, but bacteroides organisms are often resistant to it. For these, chloramphenicol and clindamycin are usually the drugs of choice, but metronidazole is often effective. Minimal inhibitory concentrations of metronidazole against most susceptible organisms are less than 16 μg per milliliter [3, 10, 12]. Pharmacokinetic studies show that metronidazole is readily absorbed from the gastrointestinal tract. Its mean peak serum level occurs between 1 and 2 hours after administration [9]. Protein binding is minimal and the agent readily penetrates into the central nervous system [7, 9, 12, 13], so its CSF concentration is similar to its serum concentration. The serum half-life is 8 to 10 hours [9, 14]. Metronidazole in doses of 1 gm four times per day gave serum values that varied from 15 to 72 μg per milliliter over 24 hours [4].

Although not approved for routine treatment of anaerobic infections, metronidazole has been shown to be effective against bacteroides in vitro and in vivo. Several reports describe the successful use of this drug for systemic infections due to anaerobic organisms that were resistant to commonly used agents such as penicillin, chloramphenicol, and clindamycin [2, 13, 15]. Metronidazole has also been used to treat brain abscesses that contain anaerobic organisms [6]. Feldman [5] and Ralph et al [9] have reported cases of bacteroides meningitis successfully treated with this drug.

In cases of anaerobic infection, including those due to bacteroides, which are resistant to usual therapy, appropriate identification of the organisms and sensitivity testing may lead to successful treatment with metronidazole.

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