

BACTEROIDES FRAGILIS MENINGITIS

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ABSTRACT

Bacteroides fragilis is an obligate anaerobic bacillus residing in the normal intestinal flora of the colon. Anaerobic bacterial meningitis due to this pathogen is rarely diagnosed and if present, a predisposing source of infection should be actively sought for. Anaerobic cultures of cerebrospinal fluids should be done for patients with meningitis, especially those with concomitant pathologies that predispose to anaerobic infections. Two cases of anaerobic meningitis due to *Bacteroides fragilis*, one associated with cholesteotoma and the other with nasopharyngeal carcinoma, are reported. Both were successfully treated with metronidazole.

Keywords: *Bacteroides fragilis*, anaerobic, meningitis, metronidazole

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INTRODUCTION

Bacteroides fragilis forms part of the normal flora of the colon and the female genital tract. The majority of infections caused by this pathogen occur when the normal mucosal barriers break down or when the normal immune defence is compromised. In general, the *Bacteroides fragilis* group predominantly causes infections occurring below the diaphragm such as intraabdominal sepsis and pelvic infections, but osteomyelitis, pleuropulmonary infections, brain abscesses and soft tissue abscesses are also some of the infections encountered^(1,2). However, bacterial meningitis in adults due to *Bacteroides fragilis* is rarely seen.

We report on two patients with anaerobic bacterial meningitis due to *Bacteroides fragilis*.

CASE REPORTS

Case One

A 42-year-old Chinese male presented with generalised, progressively severe headache for a week. Over the same period, he also had fever with chills and rigors, and vomiting. He did not have any significant medical history of note.

On examination, he was mildly dehydrated and febrile, with a pulse rate of 100/min. Mentally, he was rational and alert. His neck was very rigid and Kernig's sign was present. Cranial nerve examination was normal and there was no neurological deficit detected. Otoloscopic examination of the left ear revealed foul smelling discharge and infected cholesteatoma. The rest of the clinical examination was unremarkable.

Laboratory investigations were as follows: Total white cell count of $13.8 \times 10^9/l$, differential count of neutrophils 82%, lymphocytes 14% and monocytes 4%, haemoglobin 13.3 g/dl, cerebrospinal fluid (CSF) pressure of 6 cm water, CSF for microscopic analysis – cell count of 1,413 cells consisting of both polymorphs and lymphocytes (normal range [NR] 0 – 5), glucose 0.1 mmol/l (NR 2.5 – 5.5 mmol/L), chloride 113 mmol/l, total protein 1.6 g/l (NR 10 – 40 mg/l), globulin present, no acid-fast bacillus or cryptococcus seen, serum urea and electrolytes were normal, CSF and blood anaerobic cultures grew *Bacteroides*

fragilis, while aerobic cultures yielded no growth. Radiographs of the maxillary, sphenoid, ethmoid and mastoid sinus were normal. A swab specimen from his left ear requesting only for aerobic culture grew *Escherichia coli* sensitive to co-trimoxazole.

He was diagnosed to have bacterial meningitis and cholesteatoma of the left ear. He was treated with both intravenous chloramphenicol 1g 4-hourly and metronidazole 500 mg 8-hourly for 10 days. He also underwent radical mastoidectomy and labyrinthotomy 14 days after he was first admitted to hospital. At operation, a large cholesteatoma sac with squames eroding into the squamous and petrous bones, the furuncular canal and attic, associated with foul smelling pus was noted. Histological examination confirmed the presence of a cholesteatoma. His fever settled a week later with the above treatment and he was subsequently discharged with oral co-trimoxazole 2 tablets bid and oral metronidazole 400 mg tid for one week's duration. He did not come for outpatient follow-up review.

Case Two

A 51-year-old Chinese male complained of dysphonia and deafness for a week. He was also noticed to be lethargic with loss of appetite. There was no complaint of headache or photophobia. He had a past history of nasopharyngeal carcinoma treated with two courses of radiotherapy, in 1980 and in 1985.

He was ill and thin. He had a temperature of 37.5°C, pulse rate of 80 beats/min and blood pressure of 110/80 mmHg. He was conscious and could understand simple commands. His neck was stiff and Kernig's sign was present. Cranial nerve examination revealed bilateral sixth cranial nerve palsies, loss of the right corneal reflex and absent gag reflex. Fundoscopy showed no evidence of raised intracranial pressure. No lymph nodes were felt in the neck. Coarse crepitations were heard over the left lower chest and the rest of the clinical examination was normal.

Laboratory investigations were as follows: Total white cell count of $16.4 \times 10^9/l$, differential count of neutrophils 89%, lymphocytes 8%, monocytes 2% and eosinophils 1%, haemoglobin 14.4g/dl, CSF opening pressure of 12 cm water, CSF for microscopic analysis – cell count of 155 cells, predominantly polymorphs with a few lymphocytes, glucose 0.1 mmol/l, chloride 579 mmol/l, total protein 80 mg/l, globulin present, no acid-fast bacillus or cryptococcus seen, CSF anaerobic culture grew *Bacteroides fragilis* while the aerobic culture had no bacterial growth, sputum culture grew *Proteus mirabilis* and *Klebsiella* species, both susceptible to cephalothin, ceftriaxone, gentamicin and co-trimoxazole. Two blood cultures for aerobes grew no organisms. (No blood specimens were sent for anaerobic culture.) Chest radiograph showed a left basal pneumonia. Computer aided tomographic scan (CT scan) of the base of the skull showed a fairly large soft tissue mass on the right side of the posterior nasal space, but it did not involve the parapharyngeal

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space. The base of the skull was normal. The CT scan of the head showed only mild dilatation of the ventricular systems with no other gross abnormalities.

He was diagnosed to have bacterial meningitis, left basal pneumonia and recurrence of nasopharyngeal carcinoma. He was treated with intravenous ceftriaxone 1g 12-hourly and gentamicin 80 mg 8-hourly for 2 weeks for pneumonia, and oral metronidazole 400 mg tid for a week when the diagnosis of *Bacteroides fragilis* meningitis was made. With the above treatment both the bacterial meningitis and left basal pneumonia resolved and the patient returned to Hong Kong for continuation of treatment for the nasopharyngeal carcinoma.

DISCUSSION

Anaerobic infections can involve any region of the body, provided that the conditions in the tissues are suitable. The majority of anaerobic infections are caused by bacteria from endogenous sources^(1,2). Predisposing factors involved in the pathogenesis of anaerobic infections include surgical or other trauma, poor blood supply, tissue necrosis, malignancy and polymicrobial tissue infections with growth of aerobes or facultative anaerobes. All these factors tend to lower the oxidation-reduction potential, the oxygen tension or both, and hence, help provide a favourable environment for anaerobic growth.

Bacteroides fragilis is encountered frequently in a variety of sites as resident flora. It has a propensity for abscess cavities and mixed infections. The majority of infections such as brain abscesses⁽³⁾, osteomyelitis⁽⁴⁾ and pelvic infections⁽⁵⁾ occur when these sites are subjected to contamination by the resident *Bacteroides fragilis*.

Meningitis caused by *Bacteroides fragilis* is rare⁽⁶⁾. The disease usually occurs in the very young or elderly people. The initial focus of infection can be determined in about 60% of cases⁽⁷⁾ for example pilonidal sinus⁽⁸⁾, chronic otitis media⁽⁹⁾, ventriculoatrial shunt⁽¹⁰⁾, abdominal sepsis^(6,11,12), post-operative lumbosacral myelomeningocele⁽¹³⁾, and sacral decubitus sore⁽¹²⁾. Meningitis due to *Bacteroides fragilis* that is not secondary to a disease elsewhere in the body is uncommon⁽¹⁴⁾.

At our laboratory, CSF from patients with suspected meningitis is routinely cultured on both aerobic and anaerobic media. However, not all laboratories routinely culture CSF anaerobically, and anaerobic meningitis can therefore be missed. A complete clinical diagnosis or discussion with the laboratory is therefore necessary in order to avoid this problem. Since we started anaerobic culture of CSF 14 years ago, we have observed only 2 cases of *Bacteroides fragilis* meningitis, both of which are described here.

In both our patients, there were underlying head and neck pathologies which provided sources of infection and a breach of barriers into the sterile meningeal system. Patient One presented with symptoms and signs compatible with acute bacterial meningitis such as fever, headache, vomiting and neck rigidity. He did not volunteer any history indicative of ear infection, and it was only upon knowledge of the blood and cerebrospinal fluid culture results that a source of infection was actively looked for. The search then revealed an infected cholesteatoma of the left ear. Before his operation, he also developed a left ear discharge which grew *Escherichia coli*, for which he was treated with cotrimoxazole. It is interesting to note that although the cholesteatoma may be the underlying condition promoting the anaerobic meningitis, the organism recovered from the ear discharge was not the same organism responsible for the meningitis. This may be due to colonisation of the external auditory canal by *Escherichia coli*. Hence, the organism recovered from ear discharge need not reflect the true aetiological agent of meningitis⁽⁹⁾. It is unfortunate that the infected cholesteatoma

was not sent for culture, although recovery of the organism may have been compromised by prior antibiotic therapy. The importance of culturing operative specimens is emphasised. This will provide more accurate information and useful correlation with cultures from "superficial sites".

The second patient's presentation was less typical. The only clue to meningitis was nuchal rigidity, as his other symptoms and signs could be attributed to the chest infection. The source of his meningitis is probably the nasopharyngeal carcinoma, although a computer-aided tomographic scan did not show invasion of the posterior nasal space or the base of the skull.

Both patients were treated with metronidazole. The first patient was also treated with chloramphenicol for 10 days. The second patient was treated with one week of oral metronidazole. It is generally recommended that serious infections such as meningitis, should be treated with intravenous antibiotics to avoid any problems with absorption. However, metronidazole is absorbed rapidly and almost completely after oral administration. Its absorption is not affected by ingestion of food⁽¹⁵⁾. Metronidazole diffuses well into all tissues including the central nervous system. It is an excellent bactericidal antibiotic and the recommended duration of treatment of meningitis is for at least 7 days.

Most infections with the *Bacteroides* species involve collection of pus, as with the first patient. Hence, one of the mainstays of therapy is drainage of abscesses if present⁽²⁾. As for the second patient, there was no evidence of abscess formation.

Our laboratory does not perform susceptibility testing of anaerobic organism for individual patients, except in serious infections whereby there is failure of antibiotic therapy, as recommended by the National Committee for Clinical Laboratory Standards (NCCLS)⁽¹⁶⁾. There are a few classes of antibiotics that are effective against *Bacteroides fragilis*. Other than metronidazole and chloramphenicol, piperacillin, moxalactam, ceftioxin and clindamycin are also effective⁽¹⁷⁾. Resistance of *Bacteroides fragilis* to metronidazole is rare^(2,18,19). Although more than 95% of *Bacteroides fragilis* is sensitive to chloramphenicol^(8,20), treatment failures for meningitis due to *Bacteroides fragilis* have been reported^(9,11). This may be because of either resistance to chloramphenicol itself or due to the fact that it is a bacteriostatic drug. Clindamycin does not diffuse into the cerebrospinal fluid, even with inflammation of the meninges. *Bacteroides fragilis* is also sensitive to imipenem but because high serum levels of imipenem (especially in patients with renal failure and central nervous system disease) have been associated with seizures, the drug is not appropriate for meningitis⁽²¹⁾.

CONCLUSION

Although anaerobic bacterial meningitis is rare, this must be considered in patients with predisposing conditions such as head and neck, and gastrointestinal pathologies. Infection from these sites could give rise to anaerobic bacterial meningitis, as a result of direct or haematogenous spread. Management of the patient should include therapy for the meningitis, as well as the underlying condition. In the case of *Bacteroides fragilis* meningitis, metronidazole is the antibiotic of choice because of its excellent bactericidal activity, cerebrospinal fluid penetration and good clinical response.

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