Pneumocephalus associated with \textit{Bacteroides fragilis} meningitis

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ABSTRACT

Gas within the intracranial cavity (pneumocephalus) commonly results from trauma, \textsuperscript{1} after surgery, \textsuperscript{2} after lumbar drainage \textsuperscript{3} or as a result of post-radiation necrosis \textsuperscript{4} of skull appendages. Infection by gas-forming organisms \textsuperscript{5} is an extremely rare cause of pneumocephalus and often, is associated with \textit{Clostridium perfringens} meningitis \textsuperscript{5,6} and rarely with mixed aerobic-anaerobic meningitis. \textsuperscript{7} In adults \textit{Bacteroides fragilis} meningitis is very rare and often has a predisposing factor \textsuperscript{8} and pneumocephalus is not described in the literature with this organism. A case of pneumocephalus associated with \textit{Bacteroides fragilis} meningitis is being reported.

Case History

A 74-year-old woman with longstanding history of degenerative joint disease presented with worsening lower back pain of 2 weeks duration with fever and night sweats. She described pain across the lower back with radiation to posterior aspect of both thighs. She denied headache. There was no history of bladder or bowel incontinence. She denied leg weakness or paraesthesias. Her appetite was poor and she lost 15 pounds in the past 6 months. Her brother had tuberculosis 50 years ago. Her medications included aspirin, diclofenac and acetaminophen with codeine as needed. She had 45-pack years history of smoking. Physical examination revealed her to be in mild pain with temperature of 38°C and blood pressure of 160/80 mmHg. There was no lymphadenopathy. There was no neck stiffness and the Kernig sign was negative. The patient had pain with leg-raising in the lower back and thigh because of ongoing degenerative bone disease. Heart sounds were normal with 2/6 systolic murmur in the aortic area with transmission to the carotids. Lungs were clear. Abdominal examination was benign other than obese, soft abdomen. There was no renal angle fullness or tenderness. She was alert and oriented. Neurological examination was non-focal. The deep tendon reflexes were decreased but symmetrical. There was no focal tenderness of the spine. There was mild weakness of the lower extremities but symmetrical.

Laboratory data showed elevated white cell count of 21.5 (4.0-11.0 x10\textsuperscript{9}/L), elevated ESR of 115 (normal 0-20 mm/hr). Urinalysis was negative for blood and protein. Urine culture grew \textit{E. coli}. Renal and hepatic profile was unremarkable save for slightly low serum albumin of 31 g/L (35-50 g/L). Chest X-ray was unremarkable. A CT scan of the lumbar sacral spine showed severe facet hypertrophic osteoarthritis at L4-L5 and L5-S1 levels. There was no evidence of associated spinal stenosis. Extensive calcification was noted in the lower abdominal aorta and iliac arteries. Triple phase bone scan was unremarkable. Abdominal ultrasound showed benign cortical cyst in the left kidney and ectatic atherosclerotic aorta. Echocardiogram showed aortic sclerosis. There was no vegetation, specifically.

She was admitted to the hospital and treated with trimethoprim-sulphamethoxazole for urinary tract infection. She continued to have fever despite treatment of urinary tract infection. The possibilities of underlying vasculitis, neoplastic process and tuberculosis were entertained because of persistently elevated ESR and ongoing symptoms with fever and night sweats. This work-up remained negative. Work-up for collagen vascular disease was negative, including negative anti-nuclear antibody (ANA), normal complement levels (C3 and C4), and negative anti-neutrophilic cytoplasmic autoantibody (ANCA). Three sets of blood cultures remained negative. Repeat ESR was still elevated at 120. Six days later, she developed diffuse headache and became confused. A CT scan of the head showed multiple pockets of air in both cerebral hemispheres (Figure 1). Possibility of bacterial meningitis with gas-forming organisms, although rare, was considered and a lumbar puncture was performed. Opening pressure was 10 cm and cloudy fluid was obtained that showed low CSF glucose of <0.1 mmol/L (2.8-4.2 mmol/L), elevated CSF protein of 3.56 g/L (0.15-0.45 g/L), 0.7 x10\textsuperscript{9}/L of red blood cells and markedly elevated neutrophils. CSF grew anaerobic bacilli. She was started on intravenous clindamycin.
white cell count of 8.5 x10⁹/L (0-0.005). CSF gram stain showed moderate neutrophils and rare gram-negative bacilli. The CSF culture later revealed growth of *Bacteroides* species – *fragilis* group, Beta-lactamase producing organism. Tubercular culture was negative. She was treated with intravenous cefoxitin and metronidazole but her condition continued to deteriorate and she died ten days later. The family did not permit an autopsy.

**Discussion**

Many aerobes and anaerobes are known for their gas-producing property in tissues. These include *Escherichia coli*, *Klebsiella* species, *Peptostreptococcus* species, *Bacteroides* and *Fusobacterium* species, *Streptococcus pyogenes* (rare), and mixed facultative and anaerobic species, as seen in perianal phlegmon.

*Bacteroides* are thin, pleomorphic, non-motile, non-sporulating, gram-negative bacilli. All are obligate anaerobes, but the dominant pathogen, *B. fragilis*, produces enzymes superoxide dismutase and catalase that makes it relatively aerotolerant and is able to survive in the presence of oxygen up to 8 hours.

*Bacteroides* species are present as part of the normal human flora, principally in the oropharynx and colon. *B. fragilis* often causes intrabdominal abscesses, pelvic infections and peritonitis. It is the most common cause of anaerobic bacteremia, a life-threatening process that occurs commonly in debilitated patients who have intra-abdominal or pelvic disease. Meningitis with *Bacteroides fragilis* is rare and often occurs in premature infants and neonates. When it occurs in adults, there is often has an underlying cause such as cholesteotoma, nasopharyngeal carcinoma, chronic otitis media, para nasal sinus infection, and the source of infection should be actively sought.

All strains of *B. fragilis* produce beta-lactamases and are resistant to penicillin, but extended spectrum penicillins in combination with ß-lactamase inhibitors (ampicillin-sulbactam, ticarcillin-clavulanate, and pipracillin-tazobactam) are active against most strains. Other beta-lactam antibiotics that are active against most isolates are cefoxitin, cefotetan, cefotaxime, imipenem, and meropenem. Metronidazole, clindamycin, trovafloxacin (now withdrawn from the market), and chloramphenicol all have excellent activity. Metronidazole is the drug of choice for CNS infections. As *B. fragilis* is often associated with polymicrobial infections, it is important to eradicate other aerobic and facultative organisms simultaneously.

**References**