CASE REPORT

SALMONELLA AS A CAUSE OF BACTEREMIA AND SUBDURAL EMPYEMA IN A PATIENT WITH HIV INFECTION

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With the increased incidence and knowledge of the acquired immunodeficiency syndrome (AIDS), it has become evidence that *Salmonella* is an important opportunistic infection in patients with AIDS (Sperber and Schleupner, 1987; Celum *et al*, 1987; Levine *et al*, 1991). *Salmonella*-infected patients with AIDS often present with bacteremia, and *Salmonella* infection can relapse in spite of appropriate antibiotic treatment and may be an early manifestation of AIDS (Jacob *et al*, 1985; Glaser *et al*, 1985; Profeta *et al*, 1985; Nadelman *et al*, 1985; Fischl *et al*, 1986). Since an infection due to *Salmonella* may respond to therapy more predictably than many of the other infections occurring in persons with AIDS, its recognition is particularly important. Although *Salmonella* bacteremia is common in patients with human immunodeficiency virus (HIV) infection, the occurrence of subdural empyema is an unusual and rare manifestation of salmonellosis (Rodriguez *et al*, 1986). We report such a case of *Salmonella* bacteremia and subdural empyema in a patient with HIV infection.

A 63-year-old Thai man was admitted to his local hospital with a two-week history of fever and headache. On examination he was febrile and confused. Lumbar puncture disclosed clear CSF containing 56 WBC, 40 neutrophils and 16 lymphocytes, with a glucose level of 29 mg/dl (serum glucose was 91 mg/dl). Gram stain was negative for bacteria. Antibiotic treatment was begun with intravenous penicillin (24×10^6 U/day) and intravenous chloramphenicol (4g/day). Two days later, he was transferred to Chon Buri Hospital. Physical examination revealed a temperature of 37°C, pulse rate 98/minute, respiratory rate 20/minute and blood pressure 110/80 mmHg. The patient was conscious, not pale or icteric. The cardiovascular and respiratory systems were unremarkable. Neurologic examination revealed mild left hemiparesis without papilledema. Laboratory data revealed a WBC count of 12,100/mm^3 with 90% neutrophils and 10% lymphocytes. Antibodies to HIV were detected by ELISA. Chest and skull roentgenograms were unremarkable. Computed tomography (CT) of the head revealed subdural fluid collection at right frontotemporoparietal region with right-to-left shift of midline structures (Fig 1). At operation, a greenish-yellow purulent collection of fluid was found and drained. Treatment was begun with intravenous cefotaxime (12g/day) and intravenous metronidazole (1,500 mg/day) pending cultures. One week later, pus and blood cultures grew *Salmonella* group D. Antibiotic therapy was changed to intravenous ceftriaxone (2g/day) for ten days. The patient's overall condition gradually improved. Studies performed after the acute illness revealed a severely depressed helper-to-suppressor ratio (0.1) among T cells. He was discharged on the 22nd hospital day and was given ciprofloxacin, zidovudine and trimethoprim-sulfamethoxazole. He remained well at the time of follow-up visits.

Salmonella infections in humans present a spectrum of clinical syndromes that include gastroenteritis, enteric fever, bacteremia, localized infections and the chronic enteric or urinary carrier state (Saphra and Winter, 1957; Miller *et al*, 1995). Any *Salmonella* species is capable of producing every one of these clinical syndromes. The clinical syndrome of *Salmonella* bacteremia is characterized by a hectic febrile course lasting for days or weeks. The organism is isolated from blood, but stool cultures are often negative. Localized infection may occur at any site after *Salmonella* bacteremia irrespective of the associated clinical syndrome. Localized infection occur relatively frequently in patients with the *Salmonella* bacteremia syndrome but may also occur with enteric fever to gastroenteritis. Localized infection has been reported in the heart, lungs, brain, bones, joints, thyroid, liver, spleen, pancreas, adrenals, urogenital tract, soft tissues, aneurysm, hematoma, benign or malignant tumors, and cyst (Saphra and Winter, 1957; Black *et al*, 1960; Cohen *et al*, 1987; Miller *et al*, 1995).

Patients with impaired cellular and humoral

immune mechanisms are at increased risk for development of salmonellosis. Impairment of host defenses caused by malnutrition, malignancy, infection with HIV or therapeutic measures such as corticosteroid and immunosuppressive therapy also predispose to infection and disease. *Salmonella* play a prominent role among the several systemic infections encountered in patients with AIDS. As the number of persons infected with HIV increases and as physicians in practice see increasing numbers of patients with AIDS, awareness of the incidence of salmonellosis in this population should be heightened (Sperber and Schleupner, 1987; Celum *et al*, 1987; Levine *et al*, 1991). *Salmonella* bacteremia occurs at a much higher frequency in AIDS than in the general population, and may be the initial manifestation of AIDS. The possibility of HIV infection should be considered in patients who present with *Salmonella* bacteremia, especially if the bacteremia is recurrent (Jacob *et al*, 1985; Glaser *et al*, 1985; Profeta *et al*, 1985; Nadelman *et al*, 1985; Fischl *et al*, 1986).

Several factors contribute to the pathogenesis of salmonellosis: the inoculum size of *Salmonella*, the virulence of the strain, the host's immune response, and the local protective factors. *Salmonella* is a facultative intracellular organism, and a cell-mediated immune response depends on macrophage function, however antibody production may account for some degree of protection. Increased susceptibility to *Salmonella* infection is thought to be due to several factors : prolonged exposure to the organism, impairment of the cell-mediated immune response, impairment of phagocytosis, alteration of local protective factors, and presence of diseased tissue (Keusch, 1994; Miller *et al*, 1995).

Subdural empyema is a localized collection of purulent material between the arachnoid and dura mater. Subdural empyema is most often a complication of otorhinologic infection, with paranasal sinusitis predominates as the cause in most recent series. Subdural empyema may also occur as a result of meningitis, head trauma, cranial surgery, or bacteremic spread from a distant focus of infection (Helfgott *et al*, 1991; Greenlee, 1995).

The most common symptoms and signs are headache, fever, neurologic deficit, and stiff neck. Vomiting and malaise are often reported as well. Seizures, papilledema, and altered level of consciousness, ranging from drowsiness and disorientation to coma also occur frequently. These neurologic changes may be presenting signs or, as is often the case, may develop during the course of the illness. Diffuse neurologic signs such as altered level of consciousness, papilledema, and generalized seizures are a result of increased intracranial pressure. Focal neurologic abnormalities such as hemiparesis, Jacksonian seizures, dysphasia, and cranial neuropathies may be secondary to local pressure on the underlying cortex by the subdural process and may be precipitated by cortical venous thrombosis with accompanying brain inflammation and infarction. Such focal neurologic signs may help to localize the empyema (Helfgott *et al*, 1991). Symptoms may be fulminant in onset or may develop over a period of several weeks. Development of symptoms in case arising after craniotomy may be extremely insidious. Prior antibiotic therapy may minimize systemic symptoms and may mask sinusitis or otitis, to make the clinical presentation that of brain abscess. Infections metastatic to the subdural space or to a preexisting subdural hematoma may fail to produce sinus tenderness or systemic symptoms. In such cases, particularly in the alcoholic with an infected subdural hematoma, the patient often is seen late in the illness, and mortality is higher (Greenlee, 1995).

The cardinal features of headache, fever, stiff-neck, and neurologic signs are not specific for subdural empyema. The differential diagnosis also includes brain abscess, epidural abscess, meningitis, meningoencephalitis, subdural hematoma, and intracranial thrombophlebitis (Helfgott *et al*, 1991). Clinical grounds alone do not allow the exclusion of most of these possibilities. Therefore, more specific testing should be undertaken as soon as the diagnosis of subdural empyema is suspected.

Routine studies such as blood tests and plain roentgenograms are of little value in patients with suspected subdural empyema. Aerobic and anaerobic cultures of blood should be obtained. Plain films of the skull are not useful except to demonstrate a sinusitis or mastoiditis. CT and magnetic resonance imaging (MRI) are the diagnostic procedure of choice. Spinal fluid changes are nonspecific, and the danger of transtentorial herniation represents an absolute contraindication to lumbar puncture (Helfgott *et al*, 1991; Greenlee, 1995).

The typical CT appearance is of a crescentic or elliptically shaped area of hypodensity below the cranial vault or adjacent to the falx cerebri. Loculations may be seen, and associated mass ef-

fect with displacement of midline structures is common. After the administration of contrast material, a fine intense line of enhancement is seen between the subdural collection and the cerebral cortex. However, false negative CT scans have been reported (Luken and Whelan, 1980; Dunker and Khakoo, 1981). MRI provides greater clarity for morphologic detail and may detect empyema not seen clearly on CT. MRI is of particular value in identifying a subdural empyema located at the base of the brain, along the falx cerebri, or in the posterior fossa. Cerebral angiography should be employed on an emergent basis when MRI is unavailable and subdural empyema is strongly suspected despite a normal CT scan.

The organisms cultured most often from subdural infections are aerobic and anaerobic streptococci. *Staphylococci* are cultured less frequently, followed by aerobic gram-negative bacilli and non-streptococcal anaerobes. In the majority of cases a single organism is responsible for subdural empyema. However, polymicrobial infections are also common (Helfgott *et al*, 1991; Greenlee, 1995).

Generally the causative organism is predictable based upon the anatomic focus from which the infection originated. Otorhinogenic subdural empyemas are most often due to aerobic and anaerobic streptococci and are less often due to coagulase-positive staphylococci and other anaerobes. Infections secondary to head trauma, surgery, or an indwelling foreign device are caused by coagulase-positive and coagulase-negative staphylococci and gram-negative bacilli. Subdural empyemas originating from distant foci of infection are caused by a variety of organisms. In infants with meningitis, subdural empyema is caused by the same organism responsible for the meningitis, usually *Steptococcus pneumoniae* or *Hemophilus influenzae*. Other less frequently reported organisms include *Salmonella* species (Rodriguez *et al*, 1986), *Campylobacter fetus, Serratia marcescens, Neisseria meningitidis, Pasteurella multocida, Actinomyces israelii,* and *Actinobacillus actinomycetemcomitans* (Helfgott *et al*, 1991).

Subdural empyema is unusual and rare manifestation of salmonellosis. In several extensive reviews of subdural empyema, *Salmonella* was not mentioned as an etiologic agent (Hitchcock and Andreadis, 1964; Bhandari and Sarkari, 1970; Coonrod and Dans, 1972). *Salmonella* is rarely the cause of subdural empyema and is an infrequent clinical consideration. In a review of salmonellosis of the central nervous system (CNS), Cohen *et al* (1987) identified 158 cases of *Salmonella* CNS infection. Meningitis was the most common CNS manifestation, occurring in 91% of the cases. Other *Salmonella* CNS infections in their review included brain abscesses (9 cases), infected subdural hematomas (3 cases), and epidural abscesses (2 cases). In another review of *Salmonella* focal intracranial infections, Rodriguez *et al* (1986) identified only 20 well-documented cases of *Salmonella* subdural empyema reported in world medical literature from 1884 to 1984.

Subdural empyema is a surgical emergency. While awaiting operative intervention, antibiotics should be chosen based on the suspected source of infection, the known organisms associated with that focus of infection, and the host immune status. A combined medical-surgical approach is optimal for the management of these patients. The comparative efficacy of multiple burr holes versus an open craniotomy has not been subjected to rigorous clinical trial. Craniotomy is believed to have a lower rate of complications than use of burr holes and may be essential in posterior fossa subdural empyema (Bannister *et al*, 1981; Feuerman *et al*, 1989). Use of burr holes and irrigation of the subdural space may be possible in early cases (Miller *et al*, 1987).

In our patient, *Salmonella* bacteremia and subdural empyema developed in association with HIV infection. He was treated with appropriate antibiotics combined with surgical drainage. Third-generation cephalosporins and quinolones have been considered for the treatment of systemic salmonelloses because of emerging resistance among *Salmonella* species to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (Bryan *et al*, 1986; Soe and Overturf, 1987). Because of the high incidence of bacteremic relapse, a prolonged course of antibiotic therapy may be necessary. Oral quinolone therapy may be the reasonable drug of choice for long-term suppression (Jacobson *et al*, 1989). Quinolones have a synergistic antibacterial effect with zidovudine that may favor organism irradication if the patient is taking both medications. If the organism is susceptible and the patient can tolerate trimethoprim-sulfamethoxazole, this agent may be preferred for long-term suppression because it can also be administered for *Pneumocystis* prophylaxis (Miller *et al*, 1995).

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