Cerebral tuberculosis with expansion into brainstem tuberculoma

Report of two cases

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There are only scattered case reports of intracranial tuberculosis in industrialized nations; brainstem tuberculoma is even more unusual, accounting for 2.5% to 8% of all intracranial tuberculoma. In developing nations, however, central nervous system tuberculosis (CNS-TB) is not rare and intracranial tuberculoma may account for 5% to 30% of all intracranial masses. The authors present two cases of CNS-TB with expansion to brainstem tuberculoma in patients who were undergoing treatment and had no known prior exposure to Mycobacterium tuberculosis.

KEY WORDS • tuberculosis • tuberculoma • central nervous system

Intracranial tuberculoma is a common entity in developing nations. Researchers have implicated Mycobacterium tuberculosis in 5% to 30% of all space-occupying central nervous system (CNS) lesions.4,10,17,18 Rare case reports9,33 of CNS tuberculosis (TB), either tuberculosis meningitis or tuberculoma, have appeared in western literature, and a recent rise in incidence has been reported in Great Britain.4,24 It is believed that this increase in the number of cases is due to the recent immigration of people from areas in which tuberculosis is endemic.

A recent review reports the incidence of tuberculous infection at 11.1 per 100,000 population in the United States.19 Of the 1.7 billion infected individuals worldwide, 8 million cases of tuberculosis meningitis have been identified. Five percent of these cases have been reported in the United States,23 and attention has been focused on the increasing number of patients infected with human immunodeficiency virus (HIV).28 It is these individuals, as well as others who reside in proximity to infected individuals (for example, in correctional institutions and in homeless shelters), in whom an increased incidence of tuberculous infections has been identified. The incidence of tuberculosis in these individuals is up to 3000 times the rate seen in the general population.4,11,12,15,19,20,27 Few cases of M. tuberculosis CNS infection have been reported in the United States; it is estimated that 15% of these 4000 yearly cases of extrapulmonary tuberculosis involve the brain or spinal cord.25 Most of these are cases of meningoencephalitis or a spinal column disease; however, a rare case of intracranial tuberculosis may be seen during treatment of tuberculous meningitis.14,24,26,32 These cases are usually seen in association with immune system suppression and are often found in patients with miliary tuberculosis. It is quite unusual to identify a case of symptomatic intracranial tuberculoma in an otherwise healthy host.

We report two cases of symptomatic brainstem tuberculoma that developed during treatment of CNS-TB. These patients have no history of contact with infected individuals, and they have no infection from any known retroviruses.

Case Reports

Case 1

This 28-year-old right-handed man grew up in Spain and immigrated to the United States several years ago. The patient initially presented to another hospital with signs and symptoms of increased intracranial pressure (ICP). He suffered a rapid deterioration in his neurological status and was comatose
on the third hospital day. A computerized tomography (CT) scan of the head revealed acute hydrocephalus with transependymal absorption of cerebrospinal fluid (CSF). He underwent an emergency right frontal ventriculostomy, with resolution of his symptoms over a 1-week period. Initial CSF results obtained at the time of the ventriculostomy revealed a glucose level of 8 mg/dl, a protein level of 60 mg/dl, and a white-cell count of two per high-powered field (hpf). The rest of the CSF results could not be located and no cultures were obtained. He was discharged home after removal of the ventriculostomy and instructed to continue a three-drug (isoniazid (INH), rifampin, and ethambutol) regimen for the treatment of presumed M. tuberculosis infection.

Examination. The patient presented at our institution with clear, colorless CSF leaking from a loosely sutured stab wound on the right side of his forehead. Initial neurological examination revealed a mild right pronator drift, truncal ataxia, gait apraxia, brisk (+3) reflexes, and bilateral Babinski signs. Visual examination revealed a left superior oblique muscle palsy and bilateral papilledema. His medical history was otherwise unremarkable, and the patient denied any exposure to infected individuals, travel to areas where tuberculosis is endemic, or any history of substance abuse. He was unmarried and reported only rare heterosexual encounters. He was living with his family, none of whom had tuberculosis. Serological examination for HIV was negative. Initial magnetic resonance (MR) imaging demonstrated basilar enhancement and hydrocephalus. There was no evidence of space-occupying lesions (Fig. 1A).

Operation and Postoperative Course. The patient underwent a ventriculoperitoneal shunt, and repeat examination was consistent with results reported by the other hospital. Acid-fast bacillus stains were negative. He was discharged home on a course of rifampin, INH, ethambutol, pyrazinamide (PZA), and folic acid. A follow-up examination 2 weeks later revealed marked improvement in his gait and other neurological deficits. The patient was followed by the neurosurgical, ophthalmological, pulmonary, and infectious disease services on an outpatient basis.

After 6 weeks of incubation, CSF cultures obtained at surgery grew M. tuberculosis, which was sensitive to INH. The infectious disease service stopped the other medications. He then underwent a neuroophthalmological examination and was found to have a complete right third nerve palsy. The patient was immediately referred to our neurosurgical service, but he delayed examination for 3 weeks. At the time of examination, he had a left hemiparesis as well as the third nerve palsy. He was also noted to have severe truncal and limb ataxia, swallowing dysfunction, and hoarseness. The patient reported compliance with his medication course and underwent CT and MR scans with and without contrast enhancement. These studies revealed multiple solid enhancing masses in and around the pons and a worsening of his hydrocephalus (Fig. 1B). Screening for HIV and for human T-cell lymphotropic virus types 1 and 2 was negative; his chest x-ray film was normal.

An elective stereotactic biopsy of the largest lesion was performed because the lesion had expanded despite a presumably adequate medical regimen. The biopsy was nondiagnostic, and an open biopsy was performed through a right suboccipital approach. The cerebellopontine angle was traversed; however, no pathological process was identified in the subarachnoid space. A pontine biopsy yielded only areas of nonspecific granulation. The patient’s previous four drug regimen was resumed, and his shunt was revised. His neurological deficits have slowly improved; the third nerve palsy and hoarseness, and his left hemiparesis have resolved; he is ambulatory with mild...
ataxia. After undergoing 11 months of treatment, the patient’s follow-up CT and MR images reveal shrinkage of the lesions (Fig. 1C).

Case 2

This 25-year-old, right-handed African-American man presented with a lesion in the vermis that was causing signs and symptoms of increased ICP. The patient was HIV-negative and purified protein derivative-positive; as in the first case, he had no known exposure to M. tuberculosis. Various regimens of antituberculosis and antitoxoplasmosis medications were given including INH, rifampin, PZA, ethambutol, ciprofloxacin, capreomycin, pyramethamine, and sulfasalazine. A neurological examination revealed that the patient had diplopia, a right sixth nerve palsy, and severe ataxia. A CT scan of the head showed obstructive hydrocephalus as well, and an excisional biopsy was performed (Fig. 2A and B). The pathological examination was consistent with infection with M. tuberculosis, revealing caseating necrosis and Langerhans-type giant cells, but no acid-fast bacilli. The patient’s antitoxoplasmosis medication was discontinued, and a ventriculoperitoneal shunt was placed because hydrocephalus persisted.

Outcome. The patient was discharged in good condition and was followed as an outpatient by the infectious disease, neurosurgical, and pulmonary services. The number of his medications was tapered to three: INH, rifampin, and ciprofloxacin. After 3 months, he was readmitted with complaints of headache, stiff neck, fever, blurred vision, nausea, and vomiting. A neurological examination revealed severe truncal and limb tremor with left-sided dysmetria, and the patient could not ambulate without falling to the right. A CT scan revealed a uniformly enhancing lesion in the prepontine cistern with extension to the optic chiasm (Fig. 2C and D). A nonreactive right pupil was noted, and his vision was markedly impaired. Reflexes were pathologically brisk with sustained clonus in both lower extremities. To rule out bacterial infection, his shunt was tapped and CSF was obtained. The CSF evaluation was consistent with that found on initial admission (glucose 66 mg/dl; protein 37 mg/dl; lactate 2.7; eight red blood cells/hpf; 56 white blood cells/hpf; segmented cells 11%; lymphocytes 75%; monocytes 9%; bacterial cultures were negative). His drug regimen was then broadened to include ethambutol and PZA.

At follow-up examination, the patient was ambulating independently with mild ataxia. His vision had improved; however, his right pupil remained nonreactive. He reported compliance with his medication course.

Discussion

Recent epidemiological studies have documented a rise in the number of reported cases of systemic tuberculosis. Approximately 1.7 billion individuals worldwide are infected with M. tuberculosis. Infection with HIV is thought to represent the most important risk factor for subsequent infection by M. tuberculosis; it is estimated that 3.1 million individuals are coinfected. In the United States, mandatory reporting of tuberculous infections began in 1953 at approximately the time that effective medical therapies for the treatment of tuberculosis became available. A significant decline in the incidence of tuberculosis followed, with an annual incidence of 9.4 cases per 100,000 population reported in 1979. In recent years, however, there has been a resurgence of tuberculosis in the United States. The groups most at risk for infection include poor minorities, those infected with HIV, the homeless, prison inmates, foreigners from areas in which tuberculosis is endemic, and those without ready access to health care. Not only has the national annual incidence of tuberculosis risen to 11.1 cases

Fig. 2. Contrast-enhanced computerized tomography scans in Case 2. A: Initial scan revealing vermian tuberculoma and hydrocephalus. B: Scan after craniectomy and an excisional biopsy that revealed infection with Mycobacterium tuberculosis. C and D: Three months postbiopsy, scans revealing tuberculoma originating in the prepontine cistern and a mass extending to diencephalon; note ventricular dilatation.
per 100,000 but the incidence in the New York state prison system has reached 134 cases per 100,000 population. The incidence in African-American migrant workers is nearly 3000 times that of the national average.

In industrialized countries, cases of tuberculosis are not uncommon; however, isolated M. tuberculosis infection of the CNS is rare, since cases of CNS-TB are most commonly found in association with an infection in another organ system or with miliary tuberculosis. In 1979, there were 4000 reported cases of extrapulmonary tuberculosis in the United States, of which approximately 600 were cases of meningitis, which is a dramatic rise in the number of reported cases of CNS-TB. Of the 1.7 billion infected individuals worldwide, approximately 8 million new cases of CNS-TB were reported in 1991; approximately 400,000 of these cases were found in developed nations, representing 5% of the total.

Intracranial tuberculomas, both supratentorial and infratentorial, continue to be of major concern around the world. In developing countries, masses of the CNS are due to tuberculosis in 5% to 30% of cases. Brainstem tuberculoma, on the other hand, remains an uncommon entity even in India and Africa and accounts for only 2.5% to 8% of all intracranial tuberculomas.

Treatment of CNS-TB remains conservative. First-line drugs include INH, rifampin, PZA, and ethambutol. Second-line drugs include streptomycin, kanamycin, capreomycin, ciprofloxacin, ofloxacin, ethionamide, and cycloserine. Drug regimens vary depending on the age of the patient, degree of systemic involvement, and evidence of drug-resistant strains or coinfection with HIV. With the use of INH, which penetrates the blood-brain barrier, resolution of CNS-TB may be expected within 6 to 8 weeks. Standard treatment includes PZA, which also crosses the blood-brain barrier, and rifampin for nonresistant strains. With certain exceptions (meningitis, military TB, and bone and joint disease), three-drug therapy for CNS-TB is continued for 2 months, followed by a 4-month course of INH and rifampin as suppressive therapy. Suppression should be continued for 7 months in HIV-infected patients.

For cases of bone and joint disease, 1- and 2-year regimens have been suggested. For CNS-TB in children, the American Academy of Pediatrics recommends a 2-month course of INH, PZA, rifampin, and ethambutol or streptomycin, followed by a 10-month course of INH and rifampin. Recent studies that include PZA throughout the course of treatment have demonstrated a similar outcome with 6 months of three-drug therapy. Many reports include consideration of corticosteroids as adjuvant therapy. For multiple-drug-resistant tuberculosis, a combination of INH, PZA, rifampin, ethambutol, or streptomycin may be used for 18 months in HIV-infected patients, or 12 months in non-HIV-infected patients.

Although drug regimens are the mainstay of therapy, surgical intervention has its role in the management of intracranial tuberculosis. Shunting procedures are necessary for the treatment of obstructive hydrocephalus due to either basilar meningitis or the selectively occurring tuberculoma. Performing a biopsy on a suspected tuberculoma continues to be debated recently.

Expansion of CNS-TB has been previously reported. Implicate an immunological response as the cause of a “paradoxical” expansion of the tuberculoma. In these cases expansion was generally seen in immunocompromised patients. Our two cases document tuberculous infection of the CNS with secondary brainstem involvement in otherwise immunocompetent patients, who had no known exposure to infected individuals.

Conclusions

Our experience suggests that 1) patients with CNS-TB should receive a prolonged course (up to 18 months) of at least INH, rifampin, ethambutol, and PZA; 2) monitoring of their compliance and neurological status is critical due to the risk of expansion of lesions; and 3) a biopsy of persisting lesions may be necessary if the patient has been completely compliant with an adequate drug regimen.

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