Chronic Coccidioidal Meningitis

Report of Two Cases

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SINCE Posadas’ cases \(^{16,17,23}\) of coccidioidal granuloma reported from Argentina in 1892, interesting and valuable information has accumulated from studies made of infections occurring largely in the San Joaquin Valley of California. \(^{2,6,8,9,11-14,16,18-20,22}\)

The central nervous system has been affected in some 25% of the fatalities of the disseminated granulomatous variety.

Instances of so-called primary coccidioidal meningitis happen infrequently, seldom are diagnosed prior to autopsy, and often such patients are operated upon for suspected intracranial tumors. \(^{1,5,17,21,24,25}\)

Since the introduction of the antifungal antibiotic, amphotericin B, the importance of establishing an early diagnosis in instances of this elusive disease is readily apparent. \(^{7,9,25-27}\)

The differential diagnostic problems involved in cases of chronic coccidioidal meningitis are again apparent in the following two cases.

Case Reports

Case 1. A 38-year-old woman was seen in consultation August 14, 1952, at the Foster Memorial Hospital in Ventura. Severe right-sided headaches associated with vomiting and blurred vision were noted about June 20.

She found the onset much like influenza with generalized aching and some stiffness of the neck. Her family and past history was not remarkable. She was admitted to the hospital on July 19.

Examination. The patient appeared ill and kept the right eye closed because of blurred vision. Both optic disks were blurred. There was no neck stiffness. There was a non-purulent inflammatory swelling of the mucus membranes of the frontal sinuses. A radiograph of the chest on July 20 disclosed an inflammatory process in the right upper lobe. The white blood cells count was 11,000, 96% of which were lymphocytes.

It was believed the patient was suffering from a virus type of encephalomyelitis. The possibility of chronic coccidioidal meningitis was considered, but a negative skin test was believed to have eliminated this possibility. A spinal fluid culture was sterile, and virus studies of the blood were non-contributory. No yeast cells were found in the spinal fluid.

Ventriculography on September 30 showed that both ventricles were about twice normal size; the lateral films outlined the fourth ventricle. It was felt these findings eliminated the possibility of an expanding lesion and were consistent with a virus encephalomyelitis. Radiographs of the chest on July 28 demonstrated incomplete resolution of the inflammatory process of the right upper lobe.

Gradually the patient became afebrile, the headaches diminished, and she was discharged on October 8. Her husband reported that she lost consciousness on one occasion 3 weeks after discharge but otherwise continued to improve until 5 weeks after discharge when the right leg became so weak that she was unable to stand.

The patient was admitted to the Ventura General Hospital November 21, 1952, where she died May 3, 1953.

Autopsy. An autopsy disclosed coccidioidomycosis of the brain, spinal cord, and meninges with communicating hydrocephalus, chronic suppurative pyelocystitis, and pulmonary atelectasis.

Comment. The negative coccidioidin skin test led to erroneous exclusion of the diagnosis ultimately established by necropsy. Quite often patients with disseminated coccidioidomycosis do not react to the skin test,\(^{29}\) while the complement fixation test is invariably positive, its titer generally reflecting the severity of the infection. Blood sent for virus studies was not diagnostic. As is often the case in chronic coccidioidal meningitis, the spinal fluid culture was negative. Since the introduction of amphotericin B, the significance of the complement fixation test has new importance. At the time this patient was
seen, there was no therapeutic agent which would have altered her prognosis.

Case 2. This 15-year-old boy had an illness diagnosed as measles in September, 1956. After apparent recovery, he became lethargic, with occasional frontal headaches, vomiting, and a low-grade fever.

Examination. Examination on June 18, 1957, disclosed an ill, gaunt boy who nonetheless was mentally clear and cheerful. The general physical and neurological examination failed to reveal anything noteworthy. The referring record included a normal urinalysis, a moderate leucocytosis with an elevated sedimentation rate, a negative radiograph of the chest, a negative coccidioidin skin test, a negative purified protein derivative (PPD) test, and a normal electrocardiogram. Febrile antigens in January and again in May, 1957, were negative as was the serology. The spinal fluid cell count was 13 lymphocytes, the protein 236 mg%, and the colloidal gold and serology were negative. Large, irregular, slow waves with a phase reversal in the left frontal region were described in the electroencephalographic report. It was believed this was a case of measles encephalitis and not an expanding lesion, and that the elevated protein in the spinal fluid was consistent with that seen in a Guillian Barré syndrome from an infectious neuritis due to virus encephalitis.

When seen in July, 1957, the patient felt much better; there had been no change in the general physical or neurological examination. Radiographs of the chest were still normal. However, in December, 1957, although the patient was able to remain up longer, his hands were becoming weak, and he was bothered with blurred vision. At this time there was papilledema bilaterally, Hoffmann and Babinski signs were present on the left side, and there was ataxia of the upper and lower extremities. The dynometric reading was minimal in the right hand and unattainable in the left.

Because of this change, he was admitted to the Santa Barbara Cottage Hospital on December 16, 1957. An arteriogram and ventriculogram were completed on December 18. Although the anterior cerebral artery was in its normal midline position, the vascular pattern suggested symmetrical ventricular en- largement. This was verified by a ventriculogram, and was felt to be consistent with an expanding lesion in the posterior fossa.

Operation. Exposure of the cerebellum through a suboccipital craniotomy disclosed whitish granulomas over both cerebellar hemispheres and along the spinal cord visualized beneath the cerebellar hemispheres. Although similar to tubercular granulomas, because of the long period of survival, it was believed this was a manifestation of chronic coccidioidal meningitis. Arachnoid strips, obtained for pathological examination, revealed active and inactive lesions containing numerous characteristic spores of *Coccidioides immitis*.

Postoperative Course. In view of the patient's debilitation, his postoperative course was gratifying. The admission coccidioidin skin test had again been negative. During a period of 2 months, he received a total of 1500 mg of amphotericin B intravenously. Complement fixation tests sent to the California State Laboratory confirmed the diagnosis of disseminated coccidioidal infection. The patient improved and was returned home for further convalescence. He gained weight, but was again troubled with headache, nausea, and vomiting.

The patient was readmitted July 29, 1958, and received a total of 150 mg of amphotericin B intravenously in injections of 25 mg each. At this time the spinal fluid protein was 7.6 gm, and the sugar 12 mg%; there were 64 lymphocytes and the gold curve was paretic. Again the complement fixation tests were strongly positive. After being discharged August 5, he was readmitted for additional treatment five times, the last being from October 26 to December 17, 1959. During these admissions, he received a total of 1525 mg of amphotericin B intravenously and 4 mg intrathecally. The high titer of complement fixation of serum and spinal fluid remained unimproved. While there was some variation in his condition, he failed to show any significant improvement.

The patient was last seen at home February 27, 1960. At this time he was quite ill and had the appearance of a severe case of progressive muscular atrophy. He was unable to move his arms and legs. There seemed no indication for further medication, not only because of his intolerance to the drug, but because any