Cryptococcal spinal arachnoiditis

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Infection of the central nervous system by *Cryptococcus neoformans* has been reported in the medical literature often enough to be now widely recognized as one of the causes of chronic meningitis. The symptoms and signs emphasized include headache, vomiting, papilloedema, progressive blindness, hemiplegia, and alterations of mental status. Cryptococcal meningitis is commonly associated with pre-existing diabetes mellitus, Hodgkin's disease, sarcoidosis, and corticosteroid therapy. Several reviews have described the clinical manifestations, laboratory data and therapy of the meningitis (Mosberg and Arnold, 1950; Rose, Grant, and Jeanes, 1958; Littman, 1959; Fitzpatrick and Poser, 1960; Butler, Alling, Spickard, and Utzh, 1964).

Although there have been many reports describing cryptococcal meningitis, mention of involvement of the spinal cord in these cases is quite rare. In 1951 Carton and Mount reported one case of a spinal-cord cryptococcal granulomatous mass and reviewed the literature, finding 10 cases with spinal cord involvement. Three of these cases demonstrated spinal cord symptoms clinically. In the remaining cases the spinal cord lesions were discovered coincidentally at necropsy. In the same year, Ley, Jacas, and Oliveras (1951) reported on their successful removal of a cervical spinal cord cryptococcal granulomatous mass, with excellent recovery of the patient.

Spinal arachnoiditis (Elkington, 1951) is a well-established syndrome, often difficult to diagnose clinically, with various and usually ill-defined aetiologies. Review of the literature in English does not reveal arachnoiditis as a specific clinical manifestation of cryptococcal infection of the central nervous system. This paper describes a patient with cryptococcal spinal arachnoiditis without intracranial symptoms or signs, diagnosed by biopsy, who was successfully treated with intravenous amphotericin-B. The purpose of this report is to present a probable previously undescribed complication of *Cryptococcus* infection of the central nervous system, and to emphasize the importance of fully investigating patients suspected of spinal

arachnoiditis or progressive myelopathies of undetermined aetiology.

CASE REPORT

R.V., a 26-year-old Caucasian male, was first examined in neurological consultation on 17 June, 1961. He complained of the sudden onset of urinary frequency, difficulty in starting urination, numbness, pins and needles, and heaviness of the left leg of about three days' duration. He had painful cramps and involuntary jerking of that leg.

His past history revealed good general health, with the usual childhood illnesses. He had an appendectomy and right inguinal herniorrhaphy without complications. He denied difficulty with his legs at any time in his early life and throughout his grade school and college athletic activities. In 1958, while serving in the United States Armed Forces in Germany, he fell from a truck and developed low back pain with some radiation into the back of both legs. He was hospitalized and received physical therapy and medication for these symptoms, which persisted up to the time of his discharge several months later. Mild back and leg pain persisted, so that he took aspirin daily, and occasional chiropractic treatments, but continued with his usual activities, including frequent golf and bowling.

The family history was non-contributory and neurological diseases were denied.

General physical examination revealed a slender, alert, well-developed young man with no abnormalities. There were healed surgical scars of an appendectomy and right inguinal herniorrhaphy.

Neurological examination revealed no abnormality of mental status or of the cranial nerves. The neck was supple. Strength, coordination, and muscle tone were normal in both upper extremities. There were no Hoffmann's signs. Finger-to-nose test and rapid alternating movements were normal in both arms. His gait was abnormal, with shuffling of both feet, characteristic of a moderately severe spastic paraparesis. The legs were paretic, more so on the left, with greatest weakness in the flexors of the hips and knees and the foot dorsiflexors. There was spasticity with sustained ankle clonus bilaterally, more on the left. Plantar responses were extensor bilaterally. Abdominal reflexes were absent bilaterally. Coordination tests were poorly performed in both legs, with a combination of marked weakness, clumsiness, and spasticity bilaterally. Vibration and position sense were intact in the legs. Light touch was

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FIG. 1.

FIG. 1. Myelogram performed by injecting Pantopaque, 6 ml. at the L3 level and 6 ml. at the cisternal level. There was subarachnoid block at the body of L1 with the patient in 85° tilt, head down. The appearance of dye caudal to the block is characteristic of arachnoiditis.

FIG. 2.

FIG. 2. Appearance of myelogram demonstrating the block at D7 to the caudal flow of Pantopaque injected at the cisternal level.

impaired in the left leg and over the trunk on the left to a dermatome level of about D10. Pin prick was absent in both legs up to the level of D10, with a hyperalgesia and dysaesthesia from about D6 to D10 bilaterally. Sensory examination of both upper extremities was normal.

The patient was hospitalized on the Neurological Service of the Department of Medicine in the Mercy Hospital, Springfield, Massachusetts. The admission urine analysis, complete blood count, fasting blood sugar, erythrocyte sedimentation rate, LE test, and blood urea nitrogen were all normal. Radiographs of the chest, thoracic, lumbar, and sacral spine revealed no abnormalities. On 23 June, a lumbar myelogram was performed at the L3-L4 level, revealing xanthochromic spinal fluid. A block to the cephalad flow of contrast material at the level of L1 was demonstrated (Fig. 1). Contrast medium was also injected with a cisternal puncture and caudal flow occurred down as far as D3, with irregular narrowing and a linear irregular distribution of the contrast material from D3 to about D7 (Fig. 2). The deformity of the contrast medium was interpreted as consistent with extensive meningeal involvement and arachnoiditis, with a sub-arachnoid block.

A laminectomy was performed from D3 through D7 on the same day. Epidural fat was present and did not have a granulomatous appearance. Surgical exposure revealed an opaque arachnoid, adherent along the right side for the length of the wound. The cord was seen to pulsate equally well throughout the laminectomy. The D6 root was involved in dense adhesions on the right. There was no abnormality encountered beneath the

spinal cord, and it was described as muddy in colour and shrunken in appearance. The dentate ligaments were sectioned bilaterally. The D6 root was divided. Wax-like material was removed from the surface of the spinal cord and specimens of this and the arachnoid and epidural fat were submitted for pathological examination. The dura was closed with continuous black silk sutures. The patient tolerated the procedure well and showed no new neurological signs post-operatively.

The culture of the exudate, arachnoid, and epidural fat obtained at laminectomy revealed no growth. The report of the biopsy was of a necrotic and suppurative meningeal exudate containing *Cryptococcus neoformans* (Fig. 3). Additional cerebrospinal fluid obtained by lumbar puncture 15 days post-operatively was xanthochromic, with low pressure. It contained 5 lymphocytes and 3 red blood cells per cu. mm; 89 mg sugar and 5 g total protein/100 ml. There were no organisms on smear, and no growth on culture for *Cryptococcus* after eight weeks. Amphotericin-B therapy was started intravenously after 18 days of observation had revealed no signs of recovery post-operatively. The initial dose was 0.25 mg/kg, gradually increased to 1 mg/kg. Therapy was given daily except on Sundays, and was omitted on three other days during the 38 days of amphotericin-B therapy because of severe anorexia, nausea, and vomiting. A total dose of 892 mg intravenously was administered. Side effects of the medication included severe headache, dizziness, depression, nausea, and vomiting. This was treated with antihistamines, sedatives, and analgesics.

During the patient's hospitalization the haemoglobin

FIG. 3. PAS ($\times 440$). Appearance of the biopsy of the necrotic and suppurative exudate from the spinal cord, demonstrating *Cryptococcus neoformans*. There are prominent, darkly staining nuclei with a lighter halo appearance surrounding them.

content of the blood fell from 14.2 g to 9.8 g/100 ml. The blood urea nitrogen increased to 20 mg/100 ml. The white blood count dropped from 6,700 to 3,400/cu. mm blood, with a fall in polymorphonuclear cells. He received colistin for several days for a urinary tract infection with mixed organisms. Erythromycin was administered post-operatively.

During amphotericin-B therapy the patient showed slow improvement in the sensory and motor function of the lower extremities. The low back and leg pains gradually subsided. At the time of discharge he had full return of sensory and motor function in the lower extremities, with hyperactive deep tendon jerks, sustained ankle clonus, and extensor plantar responses bilaterally. There was a mild tremor of heel to shin testing and slight unsteadiness on tandem walking in both legs. Bowel and bladder function were normal. The patient continued to show gradual improvement during the year following the therapy. Ankle clonus subsided and the plantar responses returned to normal. He has had rare mild low backaches, usually only after playing 18 holes of golf. He has married and has a child. He has carried on with his usual activities and has been asymptomatic during the years since his treatment.

DISCUSSION

While granulomata have been described in previous reviews of cryptococcal involvement of the spinal cord, the syndrome of spinal arachnoiditis, or clinically recognized myelopathy without intracranial symptoms or signs, has not been emphasized. In cases described as showing spinal cord symptoms, most are reported as space-occupying granulomata. The importance of *Cryptococcus neoformans* as one of the causes of spinal arachnoiditis has not been stressed.

The history of several years of low back and leg pain in this patient does occur with arachnoiditis, but may well have been overlooked or disregarded as insignificant in the absence of neurological symptoms or signs during the several years before the onset of his acute neurological illness. The rather acute onset and rapid progression might have been easily confused with a demyelinating disease or the syndrome of transverse myelitis, rather than with a chronic arachnoidal inflammation. Furthermore, there were no symptoms or signs of intracranial involvement, meningeal infection, or features of coexisting diseases to arouse particularly a suspicion of cryptococcal infection.

The cerebrospinal fluid revealed no evidence of the organism on smear or culture, and the aetiology was proven only after the biopsy was obtained at surgery. This illustrates the importance of performing a biopsy in some cases of spinal arachnoiditis or progressive myelopathies, when repeated cerebrospinal fluid examinations are abnormal but have

revealed no aetiology after repeated bacteriological studies (Castleman and McNeely, 1967). As in some cases of progressive cerebral disease, biopsy in spinal cord syndromes may produce the only demonstration of the aetiology. This more aggressive approach may provide the diagnosis in some patients with spinal arachnoiditis or the syndrome of transverse myelitis in whom the spinal fluid reveals xanthochromia, elevation of cells and protein, or the myelographic findings suggestive of arachnoiditis.

Although prolonged remissions with marked clinical improvement have been reported in proven cases of cryptococcal meningitis before effective therapy was available (Beeson, 1952), treatment in this case probably was responsible for the patient's recovery. Surgery may have played some part; however, clinical improvement did not begin until after the amphotericin-B was started more than 18 days post-operatively; and there was no evidence at surgery of spinal cord compression.

This presentation of cryptococcal spinal arachnoiditis probably represents a rare complication of infection of the central nervous system by this organism; however, it is particularly important because of the probable increasing frequency of infection with *Cryptococcus neoformans* (New England Journal of Medicine, 1964). The tendency for this infection to occur in patients with chronic diseases (sarcoidosis, lymphoma) which may also involve the spinal cord could produce confusion concerning the aetiology of myelopathies occurring in the course of these chronic illnesses. Cryptococcal infection may be responsible, rather than the progression of the pre-existing disease process. This case illustrates the necessity for investigating fully patients with spinal arachnoiditis or other disabling, progressive spinal cord syndromes of unknown aetiology, including biopsy of available tissue at laminectomy for stained sections and smear and culture for *Cryptococcus neoformans*.

SUMMARY

A patient with symptoms and signs of a spinal cord lesion of acute onset and rapid progression is described. There were no symptoms or signs of intracranial disease, or of meningeal irritation. The spinal fluid revealed xanthochromia, normal sugar, marked elevation of protein, with no organisms demonstrated on smear or culture. The myelogram showed the appearance of arachnoiditis with a subarachnoid block at D7 and L1. The biopsy of arachnoid and spinal cord exudate obtained at thoracic laminectomy revealed *Cryptococcus neoformans*. The patient gradually recovered during intravenous amphotericin-B therapy and has been

free of relapse, asymptomatic, without additional therapy up to the present time.

The author wishes to express his appreciation to Dr. Joseph Pendola, Department of Medicine, Mercy Hospital, for the opportunity of caring for this patient, and to Dr. Roger Cheney, Department of Neurosurgery, Mercy Hospital, for his valuable assistance with the treatment of this patient. Doctor Joseph Rini, Department of Pathology, supplied the photomicrographs. The Staff of the Record Room of Mercy Hospital provided valuable assistance in the preparation of the clinical data. Doctors Sheldon Wolf, John Wagner, Kaspar Fuchs, and Peter Dunne made helpful suggestions in the preparation of this manuscript.

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