BRAIN ABSCESS CAUSED BY NOCARDIA ASTEROIDES

Oscar A. Turner, M.D.

Department of Neurological Surgery, Youngstown Hospital Association, Youngstown, Ohio

(Received for publication November 5, 1953)

Although as late as 1945 infections of the central nervous system with Nocardia asteroids were considered rare, an increasing number of cases both of metastatic involvement from pulmonary disease and occasionally of primary infections are being reported. This is of interest to the neurosurgeon since brain abscess is said to be a complication in from one-third to one-half of the cases in which the primary infection is in the lung. As in Actinomyces bovis almost any part of the body may be involved, but Stevens in the most recent review of the subject pointed out that Nocardia, while rare, is more virulent, spreads by the hematogenous route, and is more likely to involve the central nervous system.

Only occasional cures of brain abscess have been reported. The organism is a Gram positive aerobic fungus which is generally considered to have some sensitivity to the sulfonamides, but a considerable variability exists in individual cases in the response both to the sulfonamides and antibiotics. With the use of chemotherapy and antibiotics as an adjunct to surgery, it seems worthwhile to record additional experiences.

CASE REPORTS

Case 1. A 15-year-old boy was first admitted on Oct. 6, 1950. Two weeks previously, his left arm and leg had suddenly become numb and his left leg would not support his weight. These symptoms lasted only a few hours, but were followed by frontal headache, more severe on the right. The headaches became increasingly severe and 4 days after onset he had episodes of vomiting, lethargy, and drowsiness. Intermittent diplopia developed, and 2 days before admission he had his first generalized convulsive seizure.

Past history was not remarkable; he had been in good health with no history of ear infection or pulmonary disease. He was right-handed.

Examination. Temperature was 97.6, respiratory rate 18 per min., pulse 64 per min., and B.P. 108/70. He was well nourished but so drowsy that at times it was difficult to obtain any verbal response. He had bilateral papilledema of the optic disc of 3 D. on the right and about 1 D. on the left. There were fine nystagmoid movements on lateral gaze, and definite weakness of the right internal rectus muscle with difficulty in fixing the eyes in full adduction. He had a mild left hemiparesis, greater in the lower extremity. Movements of the left upper extremity were extremely awkward and in the finger-to-nose test he had considerable dysmetria. There was unsustained ankle clonus on the left and a marked Babinski sign. Severe nuchal rigidity was present. The sensory disturbance was that of a hypesthesia which involved the entire left side of the body including the face.

X-rays of the skull revealed no significant abnormality. X-rays of the chest disclosed a few minute calcifications in the upper third of the right lung with no evidence of active disease. Urinalysis was normal. He had a mild leukocytosis and the blood serology was negative.

Operation. On the day after admission ventriculography was done and a large abscess cavity in the right parietal region was entered at a depth of 4 cm. Twenty cc. of greenish-yellow pus were removed and 3 cc. of pantopaque introduced before withdrawal of the needle. A small bone flap was reflected in the right superior parietal region. The exposed brain had some pallor but was not otherwise unusual. A thick-walled abscess was easily enucleated through an incision in the cortex, the adjacent brain being relatively avascular (Fig. 1).

Course. The drains were removed in 34 hours, and the wound healed well without evidence of infection. He continued to have increased intracranial pressure and on Oct. 21, 1950, 2
weeks after operation, the spinal fluid pressure was still between 300 and 400 mm. of water. At the time of discharge from the hospital on Nov. 8, 1950, there was still mild papilledema and the bone flap was slightly elevated.

**Bacteriological Studies.** A stain of the pus obtained at operation disclosed a very occasional Gram positive small bacillus but no other organism. The culture was sterile for bacterial growth but a fungus grew out on incubation at room temperature. An acid-fast stain of the pus disclosed no tubercle organism. The fungus isolated from the culture was sent to Dr. David T. Smith at Duke University and was reported as Nocardia asteroides. At the suggestion of Dr. Smith, sulfamerazine therapy was started with blood levels maintained between 14 and 18 mg. per cent.

**Pathological Report.** The abscess measured 4.5 cm. in diameter and had a thick, well formed capsule (Fig. 1). The wall of the abscess was composed mainly of mature fibrous tissue with areas showing various stages of organization of fibroblasts and capillaries. There were numerous foci of acute inflammation outside of the wall, these being composed of neutrophilic leukocytes, and some lymphocytes and plasma cells (Fig. 2).

**Course.** The patient continued to show evidence of infection, with progressive papilledema, episodes of numbness and tingling of the entire right side of the body, and finally spontaneous vomiting.

2nd Admission, Nov. 18, 1950. Pneumoencephalography was done with the introduction of 60 cc. of filtered helium. The right ventricle was quite small, with the gas confined to the posterior portion of the body and temporal horn. The left ventricle showed good filling with no significant distortion of the midline structures. At this time the spinal fluid pressure was 385 mm. of water, and the fluid was quite clear and colorless.

3rd Admission, Dec. 20, 1950. There was papilledema of from 4 to 5 D. with numerous retinal hemorrhages in both fundi. He had slight facial weakness on the right, a fanning response on plantar stimulation on the right, and the bone flap was elevated more than it had been.

Aspiration through one of the previously placed trephine openings yielded 4–5 cc. of pus and on Dec. 23, 1950, the bone flap was removed. The dura mater was opened, with exposure of a large abscess which had formed in the cavity from which the previously encapsulated abscess had been removed. There was no definite capsule, and drainage was established through a stab-wound in the scalp.

Up to this time the patient had been receiving sulfamerazine, maintaining a blood level of from 10–11 mg. per cent. Because of lack of response, the medication was changed to sulfa-diazine in large amounts, with a blood level which reached 20 mg. per cent on one occasion.

On Jan. 2, 1951, there was seen the first evidence of spread of the infection with the development of progressive lymphadenopathy in the cervical region. The wound, which had been healing well, began to break down and multiple sinuses appeared along the suture line. The dissolution of the suture line was progressive with the development of a large cerebral fungus. Mycelia could be identified in smears from the surface of the protruding granulomatous mass. Aspiration of the cerebral fungus again localized an abscess.

4th Admission, Jan. 20, 1951. The granulation tissue over the abscess was incised with the
electrosurgical unit and the abscess cavity was again drained and packed with sulfathiazole powder. He was now receiving sulfathiazole as well as potassium iodide. Nocardia asteroides was again grown from the pus and tests showed a possible sensitivity to aureomycin and terramycin. He was discharged from the hospital receiving terramycin, 500 mg. 4 times a day.

Course. The patient was seen at frequent intervals. Several lumbar punctures were done, with intraspinal pressures recorded as high as 500 mm. of water. The fluid was yellow and on occasions the pleocytosis reached between 2,000 and 3,000 cells, of which approximately 70 per cent were polymorphonuclear leukocytes.

5th Admission, Mar. 26, 1951. At this time he had nuchal rigidity, headache and elevation of temperature. It seemed likely that most of the hemisphere was the site of a chronic granulomatous infection. The patient expired on Apr. 9, 1951.

Autopsy. Gross findings. The significant findings were chronic granulomatous meningoencephalitis with abscess formation in the right parieto-occipital area. There was no evidence of specific inflammatory disease in the lungs, and the other organs were essentially normal. There was marked herniation of brain through the operative site with adhesions between the fungating cerebral tissue, the scalp, and the edge of the bone defect. The base of the brain was covered with an abundant translucent greenish-yellow gelatinous exudate and a marked pressure cone involved the tonsils of the cerebellum and the brain stem. There was a purulent ependymitis which had extended to involve the right temporal lobe, where an area of inflammatory softening and cystic degeneration communicated with the inferior portion of the right temporal horn. Sections through the site of the fungus disclosed hemorrhagic tissue which was in places bright yellow and in other areas brown and somewhat glassy in appearance. The area of inflammation extended medially to compress the posterior portion of the body of the ventricle and measured about 7 cm. X 5 cm. (Fig. 3).

Microscopic examination disclosed a diffuse meningitis which was most severe at the base

Fig. 2. Case 1. Photomicrograph showing details of inflammatory process in outer layers of abscess wall and adherent tissues.
Fig. 3. Case 1. Cut section of brain showing character and extent of the inflammatory process. Note involvement of the structures about the 4th ventricle.

of the brain and over the area of cerebral fungus. The infiltrate was composed of lymphocytic cells, particularly plasma cells and monocytes, many of which were distended and some of which contained punctate basophilic masses. In some areas polymorphonuclear leukocytes were present.

While the most severe reaction was in the area of abscess formation and about the base of the brain, the suppurative process had extended to involve the ependymal lining of the ventricles, the subependymal tissues and the choroid plexus. There were compact masses of inflammatory cells forming foci closely resembling tubercles. These foci contained a core of distended histiocytes and monocytic cells with a surrounding area of lymphocytes and plasma cells. The perivascular infiltration was particularly evident in the subependymal tissues. Areas of necrosis, hemorrhages and inflammation were evident in the subcortical tissues.

The lungs showed some evidence of a nonspecific inflammatory process while the remaining organs were normal.

Comment. In this case therapy with antibiotics and sulfonamides proved to be totally ineffective. Penicillin, terramycin, sulfamerazine, sulfadiazine, and sulfadiazole were used with adequate blood levels.

It is of interest that spinal fluid smears and cultures taken as late as 4 days prior to the patient’s death were sterile and failed to reveal any filamentous structure.
Blood cultures on three separate occasions were sterile and throat cultures grew out only a hemolytic Staphylococcus albus. On almost every occasion smear of the pus showed mycelia and at no time did the cultures give rise to any bacterial growth.

Autopsy failed to disclose a primary source for the infection other than the nervous system, although there was local lymphatic spread terminally from involvement of the scalp. The removal of a well encapsulated abscess at the first operation had suggested a good prognosis but the course of the illness thereafter was indicative of progressive involvement by the organism, a course that was never influenced by chemotherapy or antibiotics.

**Case 2.** A 31-year-old man was admitted on Dec. 16, 1952, with occipital headache of 2 weeks' duration. There had been some soreness about the right eye, but no visual disturbance and examination by an optometrist was said to have disclosed no abnormality. Three to four days before admission he began to suffer drowsiness, increasingly severe headache, and vomiting. At this time a mild upper respiratory infection with slight elevation of temperature had been treated with aureomycin. There was a vague history of convulsive movements of one side of the body but no history of muscular weakness, sensory disturbance, or speech disorder. The patient was right-handed.

The only past history was that of chest pain associated with a pleural effusion 1 year previously but no details concerning this illness were available. He also had had a furuncle of the neck.

**Examination.** The patient was extremely lethargic, but able to cooperate to a fair degree. B.P. in the right arm was 120/80, pulse rate 52 per min., and respirations 20 per min. There was 1 D. of papilledema of the right optic disc, and the disc margin on the left was blurred. There was minimal weakness of the facial musculature on the left. Babinski response was positive bilaterally. He had slight tenderness on percussion in the right frontal area. The neck was supple and there was no muscular weakness or sensory disturbance. During examination the patient vomited several times and had occasional hiccoughs. Laboratory studies revealed only a mild leukocytosis while x-rays of the skull and chest were normal in appearance.

Lumbar puncture revealed clear, colorless fluid, with an initial pressure of 400 mm. of water. The fluid contained 1 cell and gave a 1+ Pandy reaction, insufficient fluid having been removed for quantitative protein determination.

**Course.** Within a few hours after examination the patient's condition began to deteriorate rapidly. He became totally unresponsive and respiratory irregularity developed. Ventricular puncture was attempted through occipital trephines, but the right ventricle could not be entered. A small amount of air in the left ventricle showed the system to be shifted to the left. During the operative procedure respiratory arrest developed and he expired within a short time.

**Autopsy. Gross findings.** The cerebral convolutions were flattened and there was evident softening of the right frontal region. Upon removal of the brain the right frontal cortex ruptured, exuding considerable yellow creamy pus. There was no gross reaction in the leptomeninges over this abscess.

Section of the brain revealed multiple abscesses in the right frontal lobe. The largest measured 3 cm. in diameter; it seemed to have a moderately well developed capsule. Surrounding it were three smaller abscesses, the largest of which measured 0.7 cm. in diameter. The total area involved by the inflammatory process measured approximately 4.5–5 cm. in diameter. There was hemorrhage in the right internal capsule, midbrain, and lower pons, with punctate hemorrhages in the cerebellar peduncles.

Examination of the lungs disclosed a relatively small fibrotic area which involved the pleura and parenchyma of the right apex. There was slight enlargement of the peribronchial and mediastinal lymph nodes. The remaining organs appeared normal except for some passive hyperemia.

**Microscopic findings.** The largest brain abscess had a poorly formed, almost nonexistent capsule, the wall of which was formed by a narrow band of moderately compressed cerebral
tissues sparsely infiltrated by polymorphonuclear leukocytes and lymphocytic cells. In this area capillaries were numerous and the appearance was that of a granulomatous type of inflammation with plasma cells predominating.

At some distance from the abscess there were scattered discrete foci of exudate and infiltration suggesting multiple abscesses in various stages of formation. The pia arachnoid over the abscess showed acute inflammatory response with some thickening and infiltration. There were scattered areas of encephalomalacia and edema but no evidence of a diffuse inflammatory process throughout the brain. Special stains failed to reveal any tubercle bacilli and no mycelia could be identified.

Sections through the lung tissue in the right apex showed thickening of the pleural surface with dense fibrous tissue containing foci of lymphocytic accumulations. Beneath the pleural surface were large clusters of lymphocytic cells, may of these containing a central area of epithelioid cells surrounded by fibrillar material. These tubercle-like formations were widespread beneath the fibrotic pleura and present in the parenchyma at some distance from the pleural surface itself. No giant cells were seen and acid-fast stains failed to reveal tubercle organisms or fungi. The histologic changes in the lungs were those of a granulomatous inflammation of the right apex associated with hyperplasia of the bronchial epithelium and unresolved pneumonitis. Proliferative arteritis and focal fibrosis were also present.

Histologic examination of the remaining organs of the body disclosed no significant abnormality.

Material taken from the abscess at the time of autopsy and cultured for tubercle bacilli revealed within 1 week a pure growth of Nocardia asteroides.

Comment. Although the patient expired before any therapy could be established, this case represents the most frequent complication of pulmonary involvement. It is of interest in that the local pulmonary lesion was relatively silent other than one episode of pleural effusion 1 year before the cerebral manifestations occurred.

DISCUSSION

At the present time infections with Nocardia asteroides cannot be considered as rare and are being recognized as an entity somewhat apart from the more frequently encountered actinomycosis caused by Actinomyces bovis. Adequate therapeutic measures for infection of the nervous system have not yet been established, and Stevens' lists only 3 cases from the literature and 1 of his own as cures, 2 of these having had follow-up studies for only 7 months.

There has been considerable individual variability in the response of the organism to chemotherapy and antibiotics, and though the sulfonamides seem to have the best effect, this is neither constant nor adequate.

While results of treatment in cases of infection with Actinomyces bovis seem to be improving to some degree, particularly when the infection is outside of the nervous system, the prognosis for nocardiosis still remains poor. This despite the fact that histologically the tissue response to invasion by the two organisms is practically identical. It is of interest that in Case 1 the inflammatory process could be identified in the outer wall of the abscess and in the adherent tissue, despite the well-organized character and thickness of the capsule. Thus, while extension of the infection probably occurred from spillage, it might well have been the result of direct extension.

SUMMARY

Two cases of brain abscess caused by Nocardia asteroides are reported, one of apparently primary origin, and the other secondary to pulmonary disease.

In the first case surgical removal of the abscess in combination with the use of
sulfonamides and antibiotics failed to halt the spread of the infection, and death resulted from recurrent abscess formation and meningitis. In the second case death occurred before any definitive therapy could be instituted, and the abscess, which at autopsy was poorly localized and poorly encapsulated, proved to be of pulmonary origin. In this case both the pulmonary disease and the cerebral extension were quite insidious.

I wish to acknowledge the kindness of Dr. David T. Smith, and Dr. Norman F. Conant, of Duke University, for their generous assistance in identifying the organism in the first case and for their suggestions in reference to therapy.

REFERENCES


CEREBRAL PARAGONIMIASIS

R. S. Hooper, M.S., F.R.C.S.
Royal Melbourne Hospital, Victoria, Australia

(Received for publication November 14, 1953)

Cerebral abscess caused by fluke infestation is a rare event outside the areas where these parasites are endemic. Though invasion of the brain by Schistosoma japonicum is seen from time to time, and removal of these lesions has been reported by Shimizu,2 Greenfield and Pritchard,3 and Speigel,4 the related condition of paragonimiasis appears to be less frequently considered. Only a few reports of successful surgical removal of such a lesion were found in the literature. The first was by Kawai,4 who described the case of a native of Japan. A diagnosis of pulmonary infestation by Paragonimus westermanii had been made on clinical and radiological findings, when he presented signs of a cerebral lesion. Another case of successful removal was reported by Busch and Cooper.2 Their patient was a Korean, and a provisional diagnosis of a cerebral glioma had been made. Mitsuno et al.6 reported 3 additional cases. The patients were Japanese children, 7, 9½ and 14 years of age. Two (Cases 2 and 3) were still well 6 months after operation. The third (Case 1) made an excellent immediate recovery but died 3 months later from “meningitis”. A clinical diagnosis of brain tumor had been made in each instance.

The present report concerns a merchant seaman whose clinical picture was suggestive of a frontal lobe abscess secondary to a frontal sinusitis.

CASE REPORT

C.Y.C., a Chinese seaman, was admitted on Oct. 25, 1952. Although his comprehension of English was limited it was apparent that he was confused and, at times, irrational. The difficulties in obtaining a satisfactory history of his condition were thus considerable, and the information available from other sources at this time was limited.