CASE REPORTS AND TECHNICAL NOTES

CEREBRAL SCHISTOSOMIASIS

REPORT OF A CASE WITH SURGICAL REMOVAL OF AN INTRACEREBRAL MASS OF SCHISTOSOMAL OVA*

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The presence of American troops in the islands in the southwest Pacific and in Japan, Formosa, the Celebes and Burma has focussed a good deal of attention on the problem of fluke infestations in humans. A large number of such infestations have been encountered and will doubtless continue to be encountered in our forces. In the case that is to be reported in this communication, a mass of schistosomal ova was found, surgically, in the brain. In view of the frequency of human infestation with schistosomes and the relative infrequency of the cerebral complication, this case is herewith presented for analysis.

REPORT OF CASE

J.J.F., a 22-year-old white male soldier with no significant past or family history, first landed on Leyte in the Philippine Islands sometime in November 1943. The area in which he was stationed was later discovered to be a source of schistosome infection. Two men in his company were evacuated to the rear echelons 2 months later with a diagnosis of schistosomal dysentery. He, himself, was perfectly well, without any clinical evidence of early schistosomiasis until Mar. 27, 1945 when he suddenly had a severe grand mal seizure, observed by a medical officer. He felt perfectly well after this, until the next day when he suddenly began to complain of a bizarre taste in his mouth. This lasted only a few moments and was followed again by a severe grand mal seizure. Immediately after this seizure he had a severe generalized persistent headache, radiating into the cervical region. At the same time he noted the onset of diplopia and began to fall to the right when walking. This unsteadiness rapidly became so severe that walking was impossible. Three weeks after the first seizure, he began to notice slurring of his speech. On May 16, 1945 he was admitted to the Mayo General Hospital.

Examination revealed bilateral papilledema, measuring 3 D. in the right eye and 1 D. in the left. He had alternating convergent strabismus due to bilateral external rectus paresis and causing homonymous diplopia, bilateral corneal anesthesia, anisocoria (left greater than the right), bilateral enlargement of the blind spots and faint horizontal nystagmus in extreme lateral gaze to the left. The other pertinent findings were mental dullness, positive Romberg sign with falling to the right, mild intention tremor in both upper extremities, adiakokinesia in the left upper extremity, patchy sensory loss of the entire left side of the body and bilaterally positive Babinski signs. The remainder of the clinical examination was negative except for the fact that the patient was somewhat confused and disoriented.

X-ray examination of the chest was negative. X-ray films of the skull revealed sharpening and erosion of both anterior clinoids, most marked on the right with some reduction in size of the latter. Electroencephalogram revealed, on a low voltage fast background, much 2 to 6 per second activity of moderate voltage in all leads. The right mid and posterior temporal leads showed higher voltage than the left. The most marked difference was noted in the anterior temporal leads, the right showing baseline sway and 1 to 3 per second waves and the

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left showing high voltage 2 to 4 per second waves (Fig. 1). Bipolar leads showed no definite phase reversal. This pointed to a lesion deep in the temporal region.

Operation. On May 23, 1945 a ventriculogram was performed, revealing a shift of the entire ventricular system to the left, most marked anteriorly (Fig. 2). Accordingly, a large right frontotemporal osteoplastic craniotomy was performed exposing the dura, which was normal in appearance but under markedly increased pressure. A portion of the temporal bone at the hinge of the flap was rongeured away to leave a subtemporal decompression. On opening the dura, the cortex appeared pale and flattened with the characteristic appearance of cortex overlying tumor. At a depth of 1.5 cm. below the surface of the cortex, a greenish-pink mass about the size of a peanut was exposed and was easily shelled out. Frozen section revealed many characteristics of a granuloma on a parasitic basis. In view of this the entire area, consisting of many such masses varying in size from that of a wheat seed to that of a walnut, and totaling about the size of a tangerine orange, was resected by shelling out some portions and aspirating others. Careful examination of the cavity thus produced revealed no gross evidence of further involvement and the wound was closed in the usual manner without drainage.

Course. The patient made an uneventful recovery. Immediately following operation, there was a complete left hemiplegia. In 3 weeks he was able to walk perfectly well and in 6 weeks could use the entire left upper extremity quite well except for some clumsiness and "stiffness" of the fingers. Six weeks following operation 50 cc. of fuadin were administered intramuscularly in doses of 5 cc. every other day. At the present time (4 months postoperative), there is no diplopia and no papilledema. The blind spots are normal in size. There is no swaying in the Romberg position. The deep reflexes are hyperactive throughout and there is a positive Babinski on the left side. There have been 3 grand mal seizures.

Following operation stool examinations revealed the presence of schistosomal ova. The white blood count was 10,300 and there were 3 per cent eosinophiles. There were no ova in repeated urine specimens. Before operation the white blood count was 11,100 and there were 9 per cent eosinophiles. Cerebrospinal fluid from the ventricles showed 15 mgm. total protein

![Electroencephalogram. Note the difference in the anterior temporal leads.](image)
per 100 cc., 93 mgm. sugar per 100 cc., 2 polymorphonuclear leucocytes and 8 lymphocytes per c.mm.

Pathological Examination.—Gross. The tissue was found to be hard, almost of the consistency of cartilage. The cut surfaces of each mass were studded with many tiny abscesses, each with a soft necrotic center and a glistening, very firm, translucent, thin border. Direct scraping of the tissue revealed parasitic ova (Fig. 3), most of them swollen and measuring up to 100 μ in diameter. The parasites in the histological sections showed much more detail than in the scrapings (Fig. 3). They revealed a clumped and folded outer shell and their interior was seen to be filled with a pale mass of cytoplasm containing blue, round bodies, apparently gonadal structures, and occasionally a small mass of brown pigment.

Microscopic. On a connective-tissue background somewhat resembling Wharton’s jelly, there were many geographical areas of necrosis, which had appeared as tiny abscesses grossly (Figs. 4 and 5). Surrounding the dense central mass of cellular debris undergoing coagulation necrosis was a broad band of epithelioid cells or macrophages and rare giant cells occasionally associated with ova. Thoroughly infiltrating the general connective-tissue background were large numbers of lymphocytes, plasma cells, macrophages and occasional polymorphonuclear leucocytes and eosinophiles, the dominant cells being the plasma cells. Lying in the necrotic center and at the junction between the center and the epithelioid border were many ova, some of which had become completely necrotic and were represented only by the distorted shell filled with phagocytic cells.

Occasionally in the necrotic center, commonly in the epithelioid border and frequently in the diffuse scar tissue away from the granulomatous structures, small tubercles were seen surrounding individual parasites. These tubercles consisted of a mass of macrophages arranged in approximately 5 to 10 layers radiating outward from the central parasite, this structure being identical with the more commonly seen schistosomal pseudo-tubercles characteristic of the liver reaction to these ova.
The centers of the necrotic areas showed the ghosts of intensely infiltrated and thrombosed blood vessels. The same reaction was seen in the diffuse scar tissue and consisted of a dense infiltration of the entire vessel wall by inflammatory cells, among which the plasma cells were predominant. It was not possible to ascertain throughout the specimen the exact nature of all these blood vessels, but in general it appeared that the arteries had been completely spared, and the veins were involved.

In the adjoining brain the sulci were seen to be filled with plasma cells, lymphocytes and edema fluid. The cortex revealed considerable astrocytic proliferation with myelin degeneration and the production of gitter cells.

The appearance of the ova clearly placed them in the fluke family. Since the ova were not operculated and since gonadal structures were visible, they belonged to the schistosome species. The lack of visible spurs in the scraped preparation made S. japonicum the most likely infecting organism.*

* Lent C. Johnson, Major, M.C., Chief of Laboratory Service at the Mayo General Hospital, prepared and described the laboratory specimens.
The details of the life history of the schistosomes and clinical manifestations of schistosomiasis are well known. They are described in all the standard textbooks and need no elaboration here. However, the highlights of the parasite's life history and non-neurological clinical manifestations need to be mentioned in order to facilitate an understanding of the ensuing discussion.

Briefly, the adult parasites of the fluke family, of which the schistosome species is a member, are tiny flat worms, all of which are hermaphroditic with the exception of the schistosome species. The male schistosomes are shorter and thicker than the females. The sides of the posterior part of the body curl ventrally to form a groove in which the female worm is enclosed during most of her life. The female deposits the eggs in the small venules of the intestinal wall. Some of these eggs gradually are extruded into the lumen of the gut and are discharged in the feces. The eggs hatch within a few hours liberating a ciliated free-swimming larva known as a miracidium. This miracidium invades the soft tissue of a mollusc and undergoes asexual multiplication into free-swimming, fork-tailed cercariae which emerge from the snail over a period of months. On contact with the skin or mucous membranes of man, they drop their tails rapidly, penetrate the tissues and enter the venous circulation. The young worms after passing through the lung and heart mature, pair off in the portal circulation, and then

![Image](image-url)

Fig. 4. Low power magnification of the specimen showing the tubercle-like formations.
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proceed against the blood stream to small branches of the mesenteric veins where they settle down, copulate and produce ova. Four to six weeks following infection, ova appear in the stools and may continue to do so for up to 20 years.57

"The disease is divided into three stages, each of which merges into the other. The first stage corresponds to the period from the penetration of the body by the cercariae to the settling down of paired matured worms in the mesenteric venules. The second stage corresponds to the period in which eggs are deposited by female worms in the small vessels of the intestinal wall. Many of these are extruded into the gut. Others are carried . . . into the liver, mesenteric lymph nodes and to other abdominal organs . . . the third stage is associated with proliferation and repair of damaged tissue and includes thickening of the intestinal wall and formation of papillomata, cirrhosis of the liver, splenomegaly and ascites."

The early symptoms are often transient and include papular rash, fever, unproductive cough, neck stiffness, crampy pains in the abdomen and pains in the back of the legs. Diarrhea may be present. At this stage signs of involvement of the central nervous system appear, including confusion or stupor, muscular palsies, changes in the reflexes, and occasionally convulsive seizures. The lymph nodes may show enlargement, the liver and spleen are often palpable and the lungs may show scattered areas of infiltration. At first there is no anemia, but a rapidly increasing white count and eosinophilia is noted. As time goes on anemia ensues, the white count drops and the eosinophilia disappears.

A survey of the literature reveals involvement of the central nervous system by parasitic flukes to be uncommon in the Occident. Kawai,16 without stating specific references, mentioned that at least 100 cases of P. westermanii involving the brain had been reported in Japan. Several other descriptions of involvement of the brain by P. westermanii are present in the literature,4,28 the earliest being that of Musgrave28 in 1907, who described 9 cases. Nine authors3,8,13,14,21,23,25,29,30 reported a total of 11 cases of S. japonicum infestation of the brain.

Fig. 5. High power magnification of the specimen revealing a typical ovum.
No patients with *S. japonicum* or *P. westermanii* infestation of the spinal cord have been reported. *S. hematobium*, on the other hand, seems to attack both the brain and the spinal cord.\(^3,7,12,15\) Infestation of the central nervous system with *S. mansoni* is rare and only one report\(^19\) could be found in the literature. The same is true of cerebral infestation by *Heterophyes brevicecaea* and *Fasciola hepatica*, the former being reported only once\(^17\) and the latter being reported twice.\(^1,3\)

Three cases of surgical removal of a mass of *S. japonicum* ova are reported in the literature, one by Shimizu\(^25\) and two by Greenfield and Pritchard.\(^14\) Kawai\(^16\) reported a case (diagnosed preoperatively) of surgical removal of a mass of paragonimus ova from the brain.

Most of the authors reporting cerebral infestation by schistosomes have concerned themselves with the route that is taken by the parasites to reach the brain. Shimamura and Tsunoda\(^25,26\) were the first to report the presence of *S. japonicum* ova in the brain. They found them at autopsy in the cortex, meninges, basal ganglia, and choroid plexus of a patient who had died of this infestation and assumed from the widespread seeding that the ova had reached the brain by embolic phenomena. Fujinami,\(^13\) who was the second author to report such a case, did not agree with the embolic explanation of brain infestation and to emphasize his point described the finding of an encapsulated group of schistosome worms in the cerebral vein of a monkey. Tsuchiya\(^26\) appears to have been one of the first to bring out the theory that the adult schistosoma proceeded through the inferior vena cava and the jugular vein to the cerebral sinuses where they deposited their eggs. Faust and Melene\(^1\) mentioned that the presence of ova in parts of the body other than the alimentary canal and liver might be attributed to embolism from the lung. The case described by Shimizu,\(^25\) the two cases of Greenfield and Pritchard\(^14\) and our surgical specimen, all showed an inflammatory reaction about small veins in the brain lesions and no reaction about arteries. Shimizu emphasized the fact that the ova in his case were localized to one area in the brain. This was the impression in the two cases of Greenfield and Pritchard, and certainly in our case there was every reason to believe that the disease was sharply localized. This circumstance would, of course, be impossible if the ova reached the brain as arterial emboli. The most likely reason for deposition of ova in the brain, in the opinion of Greenfield and Pritchard, is that the female is lying in one of the cerebral sinuses and deposits her eggs in the smaller venous radicles entering the sinus. Yokogawa is quoted by Kawai\(^16\) as stating that the adult worms ascend from the lungs to the brain in the perivascular lymph spaces. Vitug, Cruz and Bautista\(^29\) reported necropsy findings in a case of cerebral schistosomiasis japonicum which revealed plugging of many capillaries in the choroid plexus with ova. This finding and the description of the case of Tsunoda and Shimamura\(^25,26\) seem to point to arterial embolism as the basis for at least some cases of cerebral infestation.

Cerebral infestation with schistosomiasis seems to render the patients particularly prone to the development of seizures, as evidenced in the history in several of the reported cases of cerebral schistosomiasis\(^8,14,29,30\) and in our own case. It has been noted also by several authors that, as in our own case, confusion and disorientation\(^14,15,29\) are commonly seen when the brain is involved by schistosoma.

It is of interest to note that in all three reported cases\(^8,14,23\) and in our case of surgically proven *S. japonicum* infestation of the brain the patients did not remember having had any of the usual symptoms of early or late schistosomiasis. On the other hand two authors report the finding of *S. japonicum* ova in the brain at autopsy\(^3,13\) without history of neurological symptoms before death.

These observations would seem to indicate that a history of early systemic schistosomiasis is not necessary in the diagnosis of cerebral schistosomiasis and that the absence of neurological findings is not positive proof that central nervous system infestation has not occurred.

**TREATMENT**

The treatment of cerebral infestation with *S. japonicum* is exactly the same as the treatment of the systemic disease.\(^27\) If the ova exist as a space-occupying lesion in the brain it
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appears from the previous reports\textsuperscript{4,14,29} and from our case that excellent results may be expected if the mass is surgically removed and a course of antimony administered. In those instances\textsuperscript{15,21,29} where the diagnosis of cerebral schistosomiasis was made by inference and could not be proven other than by the presence of ova in the urine and stools, and by the therapeutic test of a course of antimony, the authors concluded that the cerebral schistosomiasis had been “cured” by the antimony.

According to Faust\textsuperscript{10}, the most satisfactory therapeutic results are obtained by administering tartar emetic (0.5 per cent solution) over a period of four weeks with a total of 320 cc. of the solution or 0.576 gm. of the drug. This is a rather low concentration of the drug and it is, therefore, well tolerated. He further states that studies carried out at a large military installation specializing in the treatment of schistosomiasis indicate that even a total of 105 cc. of fuadin containing 0.941 gm. of metallic antimony is not invariably curative. It must be mentioned, however, that numerous authors\textsuperscript{13,29} have reported complete cures using fuadin alone.

SUMMARY AND CONCLUSIONS

1. Infestation of the central nervous system by trematodes and more specifically by schistosoma has been reported but it occurs rather infrequently.

2. There is evidence that the adult parasites may reach the brain either by ascending against the venous stream to the cerebral sinuses, or by travelling with the blood stream to the brain as arterial emboli. The former is the stronger possibility, though both routes may be possible.

3. The pathological picture of cerebral schistosomiasis resembles that of schistosomiasis in any other part of the body.

4. The neurological picture of infestation of the brain and spinal cord does not differ in any way from other infections in the central nervous system except that in cerebral involvement there appears to be a tendency to convulsive seizures, confusion and disorientation.

5. Where infestation exists as a space-occupying lesion, gratifying results may be expected from surgical removal of the mass of ova, followed by the use of antimony compounds intra-muscularly and intravenously.

REFERENCES


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EXTRASPINAL LUMBAR MENINGOCELE*

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Extraspinal meningoceles in the upper lumbar or thoracic region are a great rarity. Poli reported a meningocoele in the thoracic cavity in a 47-year-old woman. On the basis of roentgenological examination of the chest, the patient was thought to have a neurofibroma. At operation, however, a large sac of spinal fluid was found in the thoracic cavity communicating through an opening, 2 cm. in diameter, with the spinal canal at the level of the 4th thoracic vertebra. The patient unfortunately developed an empyema and died. At autopsy a synostosis of the 3rd thoracic vertebra was found. The intervertebral canal at that level was widened and communicated through a walnut-sized hole presumably at the intervertebral foramen with the meningocele in the chest.

Ameuille, Wilmoth and Kudelski reported a somewhat similar case in 1940. In both of these cases the meningocele within the thoracic cage was found by roentgenography of the chest. In the case reported here the paraspinal meningocele was present in the lumbar region and a visible, palpable mass was present in the loin.

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