Two Further Cases of Spinal Bilharziasis

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Whereas the neurological consequences of the invasion of the central nervous system by *S. japonicum* are well documented,[1] the fact that the schistosomes of this continent (*S. haematobium* and *S. mansoni*) may also damage the neural axis is less well known. As far as we can see, 110 cases of infection of the brain due to *S. japonicum* have been reported in the world literature, while only two cases of this particular schistosome invading the spinal cord have been observed.[2-6] By contrast, *S. mansoni* has been reported only 11 times within the brain and 30 times within the spinal cord, while S. *haematobium* has been reported five times within the brain and 11 times within the spinal cord. Of the 41 reported cases of *S. mansoni* and *S. haematobium* infection of the spinal cord, 29 were diagnosed by autopsy or biopsy, while the remaining 12 were diagnosed by inference. In these latter cases the patient suffered a paraplegia usually with a pleocytosis in the cerebrospinal fluid in the presence of an acute bilharzial infection frequently with resolution of the condition after treatment of the bilharziasis. Five other cases in which the ova could not be classified have been reported.[1, 2, 4, 7-35]

We report two further cases, one infected with *S. haematobium* and the other with *S. mansoni*. Both of these are cases in which the diagnosis has been made by inference.

Case No. 1

J.T.S., a 14-year-old European child, was referred for opinion in December, 1967. Two months prior to examination in Salisbury the patient tried to get out of bed one morning and found that his legs were extremely weak. He had no sensory loss nor urinary nor bowel disability. He was admitted to the Gwelo hospital under the care of Dr. J. Quinlan, where a blood count performed the same day showed a haemoglobin of 107 per cent. There were 10,000 leucocytes per c.mm. containing 2,050 neutrophils (20.5 per cent.), 2,900 lymphocytes (29 per cent.), 4,300 eosinophils (43 per cent.), 500 monocytes

(5 per cent.), 200 basophils (2 per cent.) and 50 Turk cells (.5 per cent.). A lumbar puncture performed on the same day (17th August, 1967) showed 80 W.B.C.'s/c.mm. (mainly mononuclears), 1,100 R.B.C.'s/c.mm. and a protein of 120 mg. per cent., blood sugar 69 mg. per cent. and chlorides 720 mg. per cent. Culture was sterile. Examination of the urine showed a few leucocytes, but no ova.

Blood count was repeated six days later (23rd August) and showed an Hb of 100 per cent. with an E.S.R. of 8 mm. in one hour. The total white cell count was 16,000/c.mm. containing 7,840 neutrophils (49 per cent.), 6,240 lymphocytes (39 per cent.), 1,600 eosinophils (10 per cent.) and 320 monocytes (2 per cent.). On the following two days viable ova of *S. haematobium* were found in the urine. No ova were found in the stools. The patient, who was a very big boy, was given 1 gm. of Ambilhar morning and night for seven days with an immediate improvement in his condition. He was then given six intravenous injections of Triostam.

Lumbar puncture was repeated on the 30th August—that is, during the course of his treatment. On this occasion the protein was 60 mg. per cent. and there were 40 W.B.C.s and 260 R.B.C.s/c.mm. The W.B.C.s were predominantly mononuclears and no eosinophils were seen. On the 28th August non-viable ova of *S. haematobium* were noted in the urine, but on the 31st August only one non-viable ovum could be seen, while on the 1st September a few viable and non-viable ova were noted.

The patient's knee and ankle jerks remained very brisk, and three weeks later he was given a further and similar course of Ambilhar. Two weeks after the conclusion of this latter treatment he suffered a brief relapse when his legs became weak, but he soon recovered. Lumbar puncture performed on the 27th November showed a protein of 46 mg. per cent. with 2 W.B.C.s and blood sugar of 67 mg. per cent.

The patient was examined in Salisbury on the 12th December, 1967. At that time he showed no physical or neurological abnormality. X-ray of the spine and myelography were normal, while the cerebrospinal fluid showed a protein of 40 mg. per cent. with no cells. At that time he had a Hb. of 14.4 gm. per cent. and a white cell count of 6,900 c.mm. (4,150 neutrophils (60 per cent.), 2,620 lymphocytes (38 per cent.) and 130 eosinophils (2 per cent.)). Three specimens of stool and urine showed no ova and a rectal snip was negative. The patient was asymptomatic on arrival for his investigations, having recovered quickly from his second episode, and was discharged without any complaints.

Case No. 2

E.M.J., a 26-year-old European district officer from the Kariba district, was referred for opinion by Dr. A. Shulman. The patient stated that he was well and active up to three days before his admission to the Salisbury Central Hospital on the 27th April, 1967. At that time he developed a severe low backache which was sufficient to disturb his sleep. This was followed by a sensation of pins and needles, and at times he suffered spasms of pain in his back and legs and he had some difficulty in passing his urine.

On examination at the time of admission he was found to have a total urinary retention, while the right plantar reflex was questionable. There was no other abnormality. An indwelling catheter was inserted. Lumbar puncture performed on the day after admission showed a normal pressure with a protein of 90 mg. per cent., 150 R.B.C.s, 95 lymphocytes and 15 polymorpho-nuclear leucocytes/c.mm. V.D.R.L. reaction was negative. Examination of the blood performed on the same day showed a Hb. of 17.4 gm. per cent. with 10,000 white cells/c.mm. (5,400 neutrophils (54 per cent.), 2,300 lymphocytes (23 per cent.) and 2,300 eosinophils (23 per cent.)). E.S.R. was 2 mm. in one hour. The following day the lumbar puncture was repeated, when normal C.S.F. dynamics were once again found. Examination of this fluid showed a protein of 180 mg. per cent. with 270 polymorphs (50 per cent. of which were eosinophils), 80 lymphocytes and 59 erythrocytes/c.mm. Examination of the urine showed leucocytes but no ova. A rectal snip showed *S. mansoni*. A diagnosis of bilharzial myelitis was made. The patient was started on a course of $\frac{1}{2}$ gm. Ambilhar twice daily, together with prednisolone 5 mg. four times daily for seven days.

Despite the administration of the drug the patient's neurological condition deteriorated, and on the 4th May, 1967, both legs were seen to be very weak and a sensory loss to pinprick was found at L.5 downwards on the left and L.4 on the right. Nonetheless a lumbar puncture performed on the 5th May showed a protein of 60 mg. per cent. with three lymphocytes and 36 R.B.C.s/c.mm., so that by contrast a considerable improvement in his clinico-pathological condition was noted. The first course of Ambilhar ended on the 7th May. Lumbar puncture was repeated on the 12th May and showed a recrudescence of the disorder

with a C.S.F. protein of 140 mg. per cent. and 37 polymorphs, 12 lymphocytes and 20 erythrocytes/c.mm. This was associated with a further decline in his neurological status in that he was now extremely weak in both legs, while his sensory level to light touch had ascended to L.1 and to pinprick to L.2 bilaterally. He had vague position and vibration sense in both limbs. He had considerable difficulty with bowel function, but his bladder had improved to the extent that it could be emptied by abdominal pressure.

On the advice of Dr. D. M. Blair he was then given a six-day course of Ambilhar 1 gm. in the morning and 1.25 gm. in the evening from the 14th to the 20th May to a total of 13.5 gm. Thereafter he slowly started to improve. A lumbar puncture on the 24th May showed a protein of 90 mg. per cent. with one lymphocyte and 80 erythrocytes. Nonetheless the spinal cord improvement was not accompanied by an improvement in his blood picture, which on the 28th June still contained 1,133 eosinophils (21 per cent.) in a total of 5,400 W.B.C.s. The patient was given a third course of Ambilhar, 1.25 gm. per day for three days from the 4th to the 6th August (3.75 gm. total), which was increased to 2 gm. per day for five days from the 7th to the 11th August (total 10 gm.). In all the patient received 34.25 gm. He has made a slow but steady improvement, but even now (April, 1968), a year later, he still has some slight weakness of the legs. His most recent white blood count totalled 6,500/c.mm. and contained 780 eosinophils/c.mm. (12 per cent.), so that it is still possible that he is suffering some active infection despite a seemingly adequate treatment.

Comment

Without visualisation of the cord one can only surmise as to the nature and cause of the lesion in these two cases. In both patients, however, there was a proven bilharzial infestation, and when this was controlled the patient's condition improved. It can be argued that this was purely coincidental and that there was another cause for the myelopathy. None was found, however, while the presence of eosinophils within the cerebrospinal fluid of one of the patients points strongly to a parasitic cause for the disturbance. The fact that both cases exhibited substantial recovery of function shows that the infection did not occasion widespread destruction and that the disturbance here was transient. This is not always so and a number of reported cases have been left severely disabled.

The nature of the lesion in these cases and its mode of action in the production of symptoms are as yet not completely clear. Three forms of lesion have been described, viz., transverse myelitis, granulomatous tumour and radiculitis. In the first many small granulomata may be seen, often with one or more dead ova in the centre surrounded by lymphocytes, giant cells, polymorphs, epithelioid cells and eosinophils with areas of necrosis—an apparently permanent lesion which is bound to result in considerable neurological disability at best. In the second type large solitary granulomata produce direct pressure as well as infiltration and may involve the meninges as well.[15, 35] Their pathology does not appear to be greatly different except in size from that of the smaller granulomata lying within or on the spinal cord itself. In the third type involvement of the spinal roots by multiple small granulomata produce a varying disability.[27] Necrotic areas may be related to numerous clumps of ova lying within the spinal cord which form the basis of a granuloma or to an acute necrotising vasculitis, with the ova actually lying within the vessels of the spinal cord itself.[2]

It would be reasonable to expect, in all of these three types of effect, that if the lesions were large enough to produce a total paraplegia they would be too large to allow a total or even partial resolution of signs when the disorder was controlled, yet cases are reported (e.g., Case No. 2) in which a surprising degree of recovery ensues. This leads one to suspect that either there is a sufficient variation in the pathological picture to permit almost complete regression of the process after the ova have died and their toxins dissipated themselves, or that the three lesions described may not be the only possible ones.

It seems quite possible that altogether different mechanisms may be at work in some cases. There appears to be general acceptance that gross eosinophilia tends to occur early rather than late in the disease, possibly as part of an allergic response to the dissemination of the cercaria throughout the body. It may well be that if a few eggs enter the spinal cord at this time there will be an exaggerated response to the presence of the toxins, with the rapid appearance of severe neurological signs, yet a good return of function provided the disease is treated rapidly enough. If the reaction is very severe or if it is left too long the nerve fibres of the spinal cord may undergo such destruction as to be unable to recover. Such may have been the mechanism in Zilberg's[24] case and our second case. The dura-

tion of infection in Zilberg's case is not known, but in our second case it seems to have been around 30 days. Both patients had an acute onset, but Zilberg's case was paraplegic by the time she reached medical help. This patient was explored by one of us and the cord was seen to be grossly inflamed, but no granulomata were seen on the surface, though they might have been present deep inside. The arachnoid was infiltrated with inflammatory cells. Possibly this represents an acute inflammatory reaction to the presence of a few ova in the cord during the stage of maximum body sensitivity to the disease, a stage which resolved rapidly enough in one case to permit recovery after the bilharziasis was treated and the ova died, but not in the other.

Another possible hypothesis, yet to be resolved, is the likelihood of the vessels of the cord being blocked, not only by eggs, as has been noted, but actually by adult worms. That adult worms can migrate is indisputable. El Gazayerli[36] found a male *S. haematobium* in the circumflex branch of the coronary artery, while Badir[37] removed a tumour from the conjunctiva of the left eye and found a pair of worms in a branch of the opthalmic vein. Fujinami and Nakamura[38] discovered a male worm in the middle cerebral vein of an experimentally infected monkey (*S. japonicum*). Raper [11] reported seeing an adult fluke in the extradural veins of the spinal cord. The adult worms could therefore get to the spinal cord to lay eggs themselves by migrating through the vertebral venous plexuses or alternatively the eggs could be carried there by the patient coughing and straining. Once in the vessels of the cord, the worms may not only lay their eggs there, but in so doing may block some of the vital draining vessels. The blood supply of the spinal cord is notoriously tenuous and the temporary blockage could cause severe malfunctioning of the cord. When Ambilhar is exhibited the worm is believed to migrate back to the liver before being destroyed by the drug; at that moment normal drainage would be re-established and the patient could recover.

Abbott and Spencer,[17] reporting a case from the Sudan, comment as follows: "Although there are so few reported cases, it is probable that the invasion of the cord by *S. mansoni* is not as uncommon as the few recorded cases would suggest. Cases of paraplegia are not infrequently seen in the Sudan, both in the northern irrigated areas where *S. mansoni* and *S. haematobium* are common, but in the Southern Province, where *S. mansoni* alone exists. The majority are diagnosed as being due to syphilitic meningo-myelitis, a diagnosis which the high incidence of syphilis supports. Nevertheless, if *post-mortem* examinations were more frequently performed we are sure that many more cases would be revealed." A brief look at local medical history suggests that the same statement holds good for this part of Africa. The following cases are almost certainly bilharzial in origin. Miss M.F. was a healthy girl of 19 when she developed a severe pain in the back and shortly afterwards became paraplegic. She had a laminectomy by Mr. Huggins (later Lord Malvern), but nothing was found. She died 18 months later in 1936. *Post-mortem* examination is reputed to have shown bilharziasis of the spine. Miss M., a Southern Rhodesian hospital matron, died in 1945 from "bilharziasis of the spine." Mr. de B. developed a bilateral flaccid paralysis and died in Johannesburg of ? bilharziasis of the spine. C.M.J., a 14-year-old boy from Kitwe, developed a sudden pain in his back and became paraplegic in 1963. At operation the cord was seen to be swollen and reddened. No granulomata were seen. His blood count showed 17 per cent. of eosinophils in 5,900 white cells. *S. haematobium* was demonstrated in his urine. He made an incomplete recovery. G.T., a 16-year-old boy from Umtali, suffered an attack of transverse myelitis of undiagnosed aetiology and then partially but incompletely recovered. *S. haematobium* was isolated from his urine. A.J., a 22-year-old man, was on a boat travelling to the United Kingdom. He developed bladder difficulty and weakness of the legs. He was found to have eosinophils in the C.S.F. He was diagnosed as having spinal bilharziasis in London.

None of these cases are authenticated; all are highly suspicious. Probably there is more bilharzial involvement of the central nervous tissue both pathological and non-pathological than we appreciate. This being so, it follows that in all cases of paraplegia where a pleocytosis is found in the cerebrospinal fluid, special staining for eosinophils must be made as a routine procedure. Furthermore, where bilharziasis can be incriminated, vigorous treatment must be instituted. If a granuloma has already been established, this may not be successful. On the other hand, if the signs are due to the presence of a pair of adult worms causing interference with the blood supply to the cord, treatment may encourage them to leave this site, thus restoring or at least not aggravating the blood supply to the cord.

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