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Cerebral Filariasis Caused by Acanthocheilonema Perstans

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Although in the past authorities have tended to regard *Acanthocheilonema perstans* infestation as harmless, today there is a growing body of medical opinion which is beginning to doubt this. Earlier workers may have been misled because of the number of different parasites harboured coincidentally by the African and tended to regard an eosinophilia, for example, as due to one of them. Further, although the parasite was detected in the peripheral circulation, many of those harbouring it seemed to enjoy good health. However, when its symptoms or signs appeared in Europeans, in whom parasitic disease is less common, they assumed a greater significance.

As early as 1937, Bourgignon claimed that the infestation was responsible for an acute and fatal hepatitis in an African. Another remarkable case was reported by Foster (1955) in the French Cameroons. An African male, aged 20 years, died of pericarditis with effusion, and before death sanguineous fluid, containing large numbers of microfilariae, was demonstrated. Strohschneider (1956) mentioned that pruritus, fever, enlargement of the liver and spleen and pains and aches in the joints and bones were caused by the infection. Stott (1962) found transient swellings similar to the Calabar type not uncommon. Gelfand and Wessels (1964) described a case in a European woman who had hepatitis, fever, epigastric pain with possible heart failure.

There are even references to possible neurological and psychiatric effects from the parasite. Adolph *et al.* (1962) record such a case in a European woman, aged 37 years, after she had returned to the U.S.A. following a long sojourn on the Ivory Coast. In 1960 she developed a momentary paralysis of the left arm and a numbness of the left cheek. Several weeks later she began to experience difficulty in pronouncing words. She also suffered from a varied psychiatric picture. The E.E.G. showed minimal changes in the fronto-parietal region. Microfilariae were found in the blood, but a lumbar puncture was apparently not performed. Another interesting reference to mental symptoms which may follow *perstans* infestation was made by Reis (1955) from Mozambique, who mentioned the development of psychiatric symptoms in an African patient, aged about 50 years, but when the microfilariae disappeared from the blood the patient recovered.

Enzer (1949) specially drew attention to the headache, drowsiness and fatigue in four Africans from Kenya who had heavy *perstans* infections. In Rhodesia itself a number of cases have been recorded in recent years; the main features stressed were an arthralgia, fever and a high blood eosinophilia (Gelfand and Bernberg, 1959; Baker *et al.*, 1967).

As far as we are aware, the microfilariae of *A. perstans* have not previously been demonstrated in the cerebrospinal fluid in man, and its occurrence in a European male (seriously affected with a neurological disorder), and also in an African male (with possibly mild cerebral symptoms), has prompted us to publish the findings, especially as the microfilariae were demonstrated on three separate occasions during the acute illness of the European patient and had disappeared when he recovered. The African complained of headache and drowsiness for a time and seemed to recover on his own from these complaints.

Illustrative Cases

Case 1

T.C., a young European male, aged 19 years, was very fit until he became ill on active service in the Zambesi Valley, which is about 1,000 feet above sea level with an intensively hot and humid

atmosphere. On 25th September, 1967, he first observed that he had difficulty in sleeping for more than two hours at a time. He then became aware of a headache with pains across his forehead. Although not severe, it became continuous, lasting throughout the day and becoming worse at night. The second day he was unable to sleep for pain and troubled by some minor dizzy spells. He spent the morning on patrol, but the pains in his head increased and he now noticed that he had difficulty with micturition. He complained that his neck was stiff and he found it hard to focus. He vomited anything he took by mouth. Throughout that day and night the headache and biliousness increased and codein had no effect on him. On the morning of the third day he passed urine for the first time in 24 hours. He was taken to one of the sergeants, who offered him some treatment for 'flu. A tsetse fly research official also saw him and suggested that he be sent to hospital for a blood test, as he suspected "tryps." The evening of that day he was flown by helicopter to Sinoia hospital, where he was treated for malaria with four tablets of Camaquin. However, the blood smears were negative and he was no better. The following morning (the fourth day) he was unable to keep down his food, and injections to help him pass urine were unsuccessful.

The fifth day he passed urine after an interval of 48 hours. The severe head pains continued, and as he was apparently worse he was transferred to a camp hospital in Salisbury, where he developed muscular spasms in his hands and feet; he received an intravenous injection of calcium for these symptoms. That evening he was given quinine by mouth. He found it very difficult to fall asleep; his vision was now blurred and his headache excruciating. On the sixth day the muscular spasms became more frequent and he felt nauseous and vomited. He was admitted that night to the casualty department of the Central Hospital.

When he was seen there his mental state resembled that seen in uraemia. He was stuporose but could be roused, and was only able to give a very brief account of his movements in the Zambesi Valley or in Sinoia, as his interest waned very rapidly. Very suggestive, too, of uraemia were his bouts of sighing respirations. When we were able to communicate with him he frequently expressed concern that he could not pass urine—the last time being 48 hours previously. On percussion of his abdomen, no bladder dullness was detected. His neck was not stiff and he said that he did not feel warm (his temperature at the time was 99° F.). The blood pressure was 130/80. He could scarcely walk more than a few paces at a time, after which he had to be put to bed. There was no localised paralysis. The oculomotor movements were full and equal. The fundi were normal. There was no facial weakness and all the tendon reflexes were either absent or depressed and the plantar responses flexor. Repeated palpation of the abdomen failed to reveal an enlarged spleen and the lymph nodes were not palpable. He remembered often being bitten by tsetse flies, and as proof of this he pointed to a brown circular stain about a quarter of an inch in diameter on the outside of his right leg.

At first we suspected that the young man had acute renal failure following severe malaria. Blood was taken for a blood urea estimation, but while we were waiting for the result a lumbar puncture was performed, and to our surprise the fluid shot out with tremendous force, as if from a tap. However, when we managed to take the pressure it was 250 mm. of water. When it was known that the blood urea was 32 mg. per cent. we decided to treat the patient for cerebral malaria. He was given 10 gr. quinine intravenously every six hours, and by morning was vastly improved. As he seemed mentally clear and able to empty his bladder on his own, we were satisfied that the diagnosis of cerebral malaria was probably correct. However, he still complained bitterly of a severe frontal headache. His temperature had subsided. The blood sugar was 131 mg. per cent., sodium 112.8 m.Eq./l. potassium 2.8 m.Eq./l. and chlorides 119 m.Eq./l. The intravenous drip was continued for another day, and as the patient's condition was greatly improved he was put on oral quinine three times a day. However, the headaches remained severe and were so distressing that we decided to do another lumbar puncture. The fluid was crystal clear, but its pressure was 350 mm. and the cell count 80 per c.mm. The V.D.R.L. reaction (for syphilis) was negative.

Repeated blood smears were examined for malarial parasites without success. Blood cultured for typhoid gave negative results. We were concerned in case he had tuberculous meningitis or even a cerebral tumour. An E.E.G. was performed on 6th October and Mr. L. F. Levy reported the record as possibly mildly abnormal. We were concerned by the pleocytosis and high pressure of the spinal fluid, and became even more suspicious of trypanosomiasis of the nervous system. So another lumbar puncture was performed at 10 o'clock on the night of 8th

October. The pressure of the fluid was 120 mm. water, but this time numerous microfilariae, closely resembling *A. perstans,* were found in it. The cell count was 180 per c.mm., 92 per cent. being lymphocytes and 8 per cent. polymorphs. Fig. 1 shows the filarial parasites in wet preparations made up by adding to the spun C.S.F. sediment one-tenth volume of C.S.F. diluting fluid (0.2 per cent. crystal violet in 10 per cent. v/v aqueous acetic acid).

In one case the microfilaria is seen folded and enclosed in an egg membrane (Fig. 2), which seemed highly suggestive that the adult worm was within the ventricular system of the central nervous system. All the other filariae were almost straight, averaging 170 microns in length and five microns in breadth. In fresh preparations of the first C.S.F. to contain the parasite no sheath was seen, but on ageing for a few hours a body membrane became apparent at both ends of the parasite, representing perhaps nuclear shrinkage within the body membrane. In a later C.S.F. on 25th October, taken after treatment with diethylcarbamazine, many of the filariae appeared autolytic in the fresh specimen and the body membrane at each end was constant. These proved difficult to photograph, but could be seen well by phase-contrast microscopy.

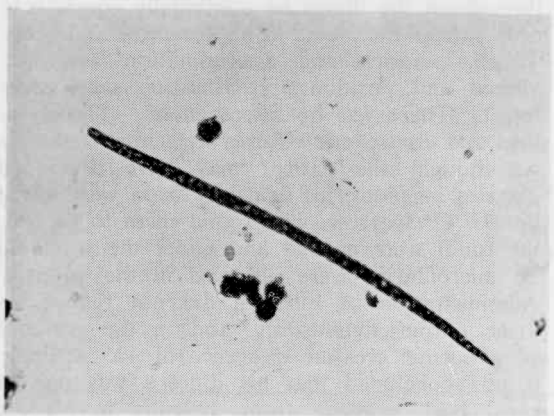

Fig. 1—Showing microfilaria as seen in C.S.F.

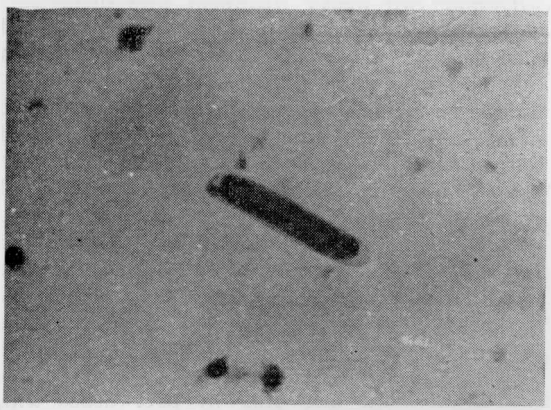

Fig. 2—The only specimen observed within the egg membrane.

Morphology of the Microfilariae.—Fifteen larvae were examined in detail and the measurements summarised in Table I.

Table I
(Total microfilariae measured = 15.)

	Range	Mean
Length	165-187.5 μ	172.3 μ
Breadth	4.5-5.0 μ	4.6 μ
Distance of nuclei from anterior end	1.5-12 μ	4.8 μ
Distance of nuclei from posterior end	0-7.5 μ	3.2 μ

The microfilariae were not in a good state of preservation and no nerve ring or other details could be observed.

No evidence of the presence of spicules was noted in any of the larvae examined. It was difficult to see details of the nuclei clearly, but they seemed to form two longitudinal rows along the length of the body. At the anterior end they were solidly demarcated and at the posterior end there appeared to be a single elongated nucleus (Fig. 3).

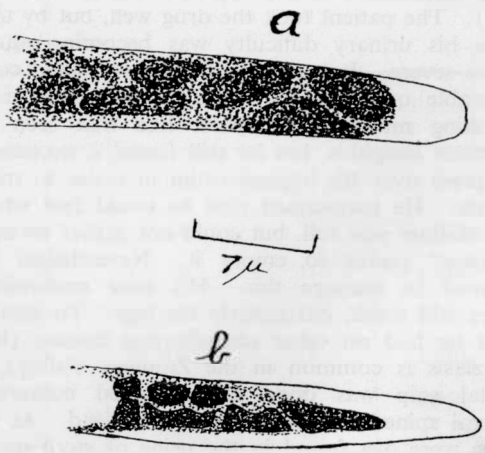

Fig. 3—Drawings of the anterior (a) and posterior (b) ends of the microfilaria.

Most of the larvae had died stretched out in contrast to the curved positions taken up by most microfilariae. However, this could have been a function of the medium in which they were mounted or the stain.

Although the distance of the nuclei from the tip to the tail varied from 0-7.5 μ, they actually reached the posterior end of the tail in only 20 per cent. of the larvae.

The larvae appeared to be unsheathed; the clear area around the nuclei at the anterior and posterior ends seemed to be body wall, not sheath, as they were too short and unfolded in the specimens observed. One larva was noticed to be still enclosed in its egg membrane. Being unsheathed with no spicules differentiated the microfilariae from those of *Wuchereria bancrofti*. The microfilariae appeared midway between the small form (100 μ x 4 μ) and the large form (200 μ x 4.5 μ) of *A. perstans*. Measurements of *A. perstans* larvae from the blood of infected African patients in Harare hospital show that both large and small forms of *A. perstans* occur here.

The finding of one of the microfilariae still enclosed in its egg membrane, together with the fact that few erythrocytes were noted in the C.S.F. specimen, would suggest that the adult worms were actually in the central nervous system, since an enclosed larva of this nature would be unable to penetrate from the blood stream to the C.N.S. This is also suggested by the fact that no microfilariae were demonstrated in the blood stream.

Course and Treatment.—We decided the correct procedure would be to prescribe two tablets of diethylcarbamazine every six hours (17th October). The patient took the drug well, but by this time his urinary difficulty was becoming much more severe. It is true that he now passed considerable quantities of urine, at the same time drinking much fluid, almost like that seen in diabetes insipidus, but he still found it necessary to press over his hypogastrium in order to micturate. He maintained that he could feel when his bladder was full, but could not gather enough "motor" power to empty it. Nevertheless he seemed to manage this. His four extremities were still weak, particularly his legs. To ensure that he had no other complicating disease (bilharziasis is common in the Zambesi Valley), a rectal snip was done and revealed numerous lateral spined ova both viable and dead. At no time were ova found in the urine or stool specimens. A search for *A. perstans* in the peripheral blood was continued, but without success.

The patient did not improve on diethylcarbamazine, so on 25th October the lumbar puncture was repeated. The fluid pressure was 250 mm. water. It was crystal clear and microfilariae were still present in it. The cell count was 25 per c.mm. The total C.S.F. amino acid nitrogen 0.9 mg./100 ml. (normal range 1-3 mg./100 ml.). When we examined his nervous system that day there seemed to be a lesion in the cord between T9 and 10. The cranial nerves were normal and there was some past pointing of the right arm. All the tendon reflexes were greatly diminished, especially on the right side. Both plantar responses were flexor. Both quadriceps were noticeably weak, especially that on the right side. There was a level of hyperaesthesia between lower T9 and 10, with hyperaesthesia below to touch, especially on the lateral aspect of the calves, soles of the feet and thighs and over the right pectoral region (T2). The patient also noticed this numbness and throughout the illness he continually complained of a similar numbness in his forearms and arms. Touch, pinprick and discrimination were unaltered and position and vibration sense were intact. There was no astereognosis. The abdomen and cremasteric reflexes were unaltered. As we thought the patient may have developed diabetes insipidus, his fields of vision were tested by Dr. C. Sparrow, who found them to be full; the fundi were normal and under the slit lamp no microfilariae were observed in the aqueous. Administration of pitressin did not reduce his urine output significantly, and in the presence of a normal creatine clearance of 125 ml./min. it was concluded that his diuresis was due to renal back pressure from difficulty in bladder emptying.

Despite two weeks' treatment with diethylcarbamazine, as the patient had not improved and especially as microfilariae were still present in the fluid, we did not think the drug had penetrated the C.N.S. We decided to try a course of Melarsen. The dose was 6.5 ml. administered intravenously daily from 27th October for four days. From the time he had received the second course of Melarsen the patient improved steadily. The headaches became much less frequent and intense. After a week he was beginning to move from his bed and a week later was frequently walking in the grounds of the hospital. The sensations of numbness in the thighs and upper extremities, though still present, were much less noticeable. He was able to pass urine with greater ease, although at times he still found it necessary to push on his bladder to empty it.

On the last lumbar puncture (20th November) the pressure of the fluid was 150 mm. of water. The protein was 49 mg. per cent., but the cell count was 30 per c.mm. The cells were composed of either mononuclears or polymorphs. A careful search for microfilariae was made, but none was found. The patient continued to make a fine general recovery except for a slight bladder weakness and numbness in the areas of the body already mentioned. A repeat rectal snip revealed non-viable ova of *S. mansoni.*

He was discharged from hospital at his own request and soon took part in the social life of his contemporaries. About three weeks later he was re-admitted to hospital after being involved in a fight in a youth club. However, we found he had recovered almost completely. We kept him under observation and stopped the oral diethylcarbamazine he was taking. His micturition was now practically normal, and he said that though he still had a little numbness in his arms and thighs, it was hardly noticeable. The administration of pitressin now produced an urine concentration with the normal value of 950 m Osm./K. He had put on weight—10 lb. The final lumbar puncture on 31st December showed two cells protein 45 mg. per cent. and no microfilariae (Table II).

Cystoscopy carried out by Professor Mynors showed diffuse injection of the bladder mucosa, with a prominent anterior wall of the neck. A patch of mucosa suspicious of bilharziasis was found adjacent to the intimal urethral meatus, but no bilharzial ova were found in the snip.

Table II

SHOWING C.S.F. CHANGES OVER SEVEN WEEKS

Filaria	C.S.F.	Sugar	Prot.	Cl.	Glob.	W.B.C.	R.B.C.
N.P.S.	1.10.67	62	68		—ve	4	66
N.P.S.	4.10.67	49	44	700	—ve	80	76
Perstans	8.10.67	49	50	680	—ve	180 (L)	1
N.P.S.	12.10.67	61	44	710	—ve	11	71
Perstans + +	25.10.67	53	57	610	—ve	25	3
Perstans few	6.11.67	58	41	730	trace	10	25
N.P.S.	20.11.67	51	49	680	—ve	30	4

N.B.—All C.S.F. specimens sterile.

Table III

HAEMATOLOGICAL CHANGES

Blood	Hb.	Total W.B.C.	N.	L.	M.	E.	Eosins. per c.mm.
2.10.67		12,800					
8.10.67		9,000	70	23	2	5	450
12.10.67	14.6 gm. %	9,200	64	18	7	11	1,010
16.10.67	14.8 gm. %	7,300	57	16	4	23	1,680
21.10.67		6,300	45	24	15	16	1,010
3.11.67		7,900	54	17	7	21	1,650
14.11.67		6,600	42	29	8	20	1,320

N.B.—No blood parasites seen at any time.

The blood picture during his stay in hospital revealed a drop in white cells after the initial count on 2nd October and a sustained rise in eosinophils. These results are plotted in Table III. The E.S.R. was 9 mm./hr. (Westergren) and the haemoglobin 14.8 g./100 ml. The serum protein 6.6 g. per cent., S. Alb. 3.9 g. per cent., S. Globulin 2.7 g. per cent., A/G ratio 1.4: 1. Alkaline phos. 9 K.A.U. per cent., thymol turbidity 1.4, thymol flocculation negative, cholesterol 225 mg. per cent. Electrophoresis: albumin normal, globulin slight relative $\alpha 2$ increase. Despite repeated searching for the embryos of *A. perstans* in the peripheral blood, we were only able to demonstrate them in the spinal fluid.

Case 2

K.C., an African male aged about 43, in the employ of the Tsetse Control Department, was stationed at Kariba, on the Zambesi. He was referred to Harare hospital on 22nd December, 1967, as having *perstans* filariasis. Two other African men working on the same station were also sent in because this parasite had been found in their blood.

The patient stated that he was perfectly fit until three months previously, when he began to experience a feeling of drowsiness, headache, tiredness and a burning sensation or pain in the epigastrium. Although none of these symptoms were marked they were sufficiently noticeable to mention them to different doctors. He also had sore eyes, a sore throat and pains in his arms and legs. He said that he felt shivery towards evening, when his body became slightly warm, and also mentioned that his vision blurred, especially towards midday. Further, he was troubled by an unusual thirst.

On examination, the patient looked fit and reasonably well covered. He weighed 143 lb. There was no fever or evidence of anaemia. The liver was enlarged to three inches below the right costal margin, but its surface was smooth and it was not tender. The lymph glands were not palpable. The central nervous system was normal in every respect. The fundi were normal; the power, sensation and reflexes in the limbs were normal.

The blood smears (wet preparation) revealed no microfilariae, although they had been demonstrated in his blood before he was admitted to hospital. The haemoglobin was 13.0 g. per cent. and the leucocyte count 3,700 per c.mm., the differential count being neut. 36 per cent. lymph. 42 per cent. mon. 12 per cent. and eosin. 10 per cent (370 per c.mm.). The urine was clear of albumin, sugar and blood. The serum bilirubin was 0.3 mg. per cent., alkaline phosphatase 15 K.A. units. Total serum protein 6.7 g. per cent., albumin 3.7 g. per cent. and globulin 3.0 g. per cent. The blood Wassermann reaction was positive. The stool showed ova of hookworm and cysts of *E. coli*. The blood urea was 10 mg. per cent. and the blood sedimentation rate 7 mm. in one hour. In view of his mild cerebral complaints a lumbar puncture was performed. The fluid was crystal clear and its pressure 120 mm. of water. The tap was non-traumatic. The leucocyte count was less than 10 per c.cm., red cells six, and microfilariae resembling *A. perstans* were seen in the wet film as well as in the centrifuged deposit. The Wassermann reaction was negative.

DISCUSSION

The most striking feature in Case 1 is the repeated demonstration of *A. perstans* microfilariae in the spinal fluid. Other features pointing to an encephalitic state were the severe constant headaches, vomiting, blurring of vision and the drowsy or stuporose state which ensued a few days after the rather acute onset of the illness. The greatly increased pressure of the spinal fluid usually present when the spinal fluid was tapped, together with the pleocytosis and the raised protein content of the fluid, supported a diagnosis of encephalitis. The presence of microfilariae strongly suggests that the encephalitis was caused by the filarial infestation. The fact that the patient improved with Melarsen and that the improvement coincided with the disappearance of the microfilariae from the spinal fluid and a reduction in the cell count and its protein might all be considered in favour of a filarial encephalitis. The weakness in his legs and arms, patchy numbness in his thighs, legs and trunk, together with a neurogenic type of bladder weakness, made us consider the possibility of a lesion in the cord. Indeed, at one time there seemed to be a level at D10, but he also showed a patchy numbness in the upper limbs associated with diminished reflexes and a definite weakness with ataxia, which would not support a lesion confined to only D10. We stress these neurological signs since the finding of ova in the rectal snip might have suggested a bilharzial myelitis. However, his disorder was mostly sensory and there was nothing to indicate an upper motor lesion in the lower limbs—rather the reverse. The lesions were too patchy for a single lesion on the spinal cord and we would have expected a clear transverse lesion in bilharziasis instead of a patchy numbness and such a widespread effect on the nervous system. Further,

an attack on the cord would not have been accompanied by so raised a spinal fluid pressure. This high pressure together with very severe headaches suggest that the main reason for the signs was an encephalitis. At first we were inclined to favour a hypothalamic lesion on account of the thirst and polyuria, but this seems doubtful. More likely the effect of the filarial parasite was very widespread, invading both brain and cord.

It is interesting to note that the case recorded by Adolph *et al.* (1962) showed certain symptoms very similar to our case—a patchy numbness, blurring of the vision and weakness in a limb.

We consider, therefore, that the bilharzial ova in this case were purely coincidental to the attack on the nervous system by *A. perstans*. We believe that this case is unique in that the microfilariae were repeatedly recovered from the fluid, a fact that has not previously been recorded. Further, it is reasonable to assume that the cerebral and myelitic lesions were also the result of a direct attack over a widespread area of the brain and cord rather like that found in disseminated encephalomyelitis.

The second case is also of interest, since this patient too complained of headache, drowsiness and fatigue, but these symptoms cleared spontaneously within a month. Even though no complaint was mentioned at the time we examined him, there were still microfilariae *perstans* in his spinal fluid.

Far from being an innocent infestation, we believe *A. perstans* to be a serious parasite which can attack several vital organs, including the pericardium, liver and central nervous system. If a patient is seen with the microfilariae in his peripheral blood it would be wise, especially if he complains of a persistent headache or drowsiness, even if these are not prominent, to examine the spinal fluid for their presence. It is quite possible that a number of patients with those vague complaints are labelled as having an anxiety state or even a psychiatric disorder.

Summary

In two patients, one a European and the other an African, microfilariae resembling those of *A. perstans* were found in the cerebrospinal fluid. The European showed evidence of a serious and diffuse lesion affecting the brain and probably the spinal cord, the disorder being best described as an acute encephalomyelitis. Although this patient also had ova of *S. mansoni*, reasons are advanced as to why we favoured a filarial encephalitis. The African had a temporary and mild illness characterised by headache, drowsiness and fatigue and his symptoms cleared spontaneously.

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