PATHOLOGICAL FINDINGS IN FOUR CASES OF HUMAN ANGIOSTRONGYLIASIS

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INTRODUCTION

Fatal human angiostrongyliasis was first reported in the Far East by Nomura and Lin in 1945. The patient was a 15-year-old asthmatic Japanese schoolboy presenting with eosinophilic meningitis: 10 actively motile nematodes were recovered on the first lumbar puncture, several on the second, none on the third. No autopsy was obtained in this case. Subsequently Rosen (1962) during the course of studies on an outbreak of eosinophilic meningitis, in 1960 found at least 7 *Angiostrongylus cantonensis* larvae in the brain and meninges of a mental patient in Hawaii.

Since then, in Southeast Asia and Thailand, many clinical and a small number of autopsy cases have been reported (Promindaroj *et al.*, 1962; Jindrak and Alicata,1965; Tangchai and Nye,1967;Nye *et al.*,1970). In this report the pathological findings in 4 fatal cases of angiostrongyliasis are presented.

REPORT OF CASES

Case 1: A 21-year-old Thai man gave a history of eating raw *Pila* snails 3 days prior to admission; that night he had high fever, abdominal pain, headache and aching over the whole body. This meal was shared with several other people who also had similar symptoms; however these people later recovered. In this patient paralysis and urinary incontinence ensued.

Lumbar puncture yielded turbid fluid with protein 100 mg/100 ml, 884 cells/c.mm, 63% eosinophils, 33% lymphocytes, 4% polymorphs; 3 *Angiostrongylus* larvae were recovered.

The patient was treated with steroids with little improvement. Later he developed bed sores, pneumonia and septicaemia and died 51 days after admission. Total length of time between onset of symptoms and death was 54 days.

Main autopsy findings related to angiostrongyliasis: a 5th stage larva was found on the surface of the right frontal lobe (Fig. 1)

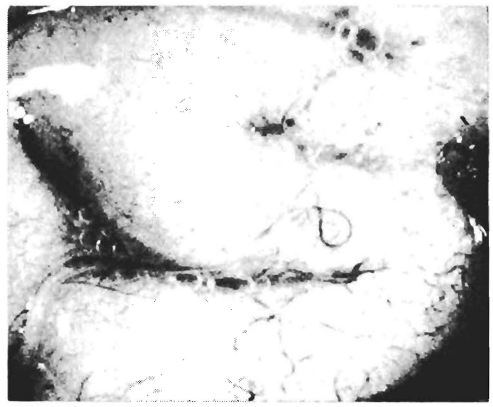

Fig. 1—Case 1 : Brain with larva. x 35.

no other parasite or remnants. There was moderately severe cerebral oedema, with the brain weighing 1,340 gm. There were a small number of old tracks in the lumbar, thoracic and cervical cord, and in the brain; these measured 0.1-0.3 mm in diameter and were bordered by gitter cells and proliferating capillaries. Cellular infiltration in the meninges and around cerebral vessels was minimal and mainly lymphocytic. The cause of death was staphylococcal pneumonia with microabsces-

ses and acute pyelonephritis with necrotising papillitis due to septicaemia.

Case 2: A 3½-year-old Thai girl presented with a history of falling off a board, followed by back pain, 9 days prior to admission; next day she was paraplegic with urinary incontinence. There was no history of eating raw snails. Lumbar puncture yielded approximately 80 *Angiostrongylus* larvae. A slight improvement followed the lumbar puncture and she was able to lift her legs; but 3-4 days later she developed weakness in the arms and legs and became stuporous. Pneumonia ensued and she died 14 days after admission. Total length of time between onset of symptoms and death was 23 days.

Main autopsy findings related to angiostrongyliasis: larvae were found in many sites: most were in the c.s.f. especially around the cauda equina; 2 worms were found in the choroid plexus of the third ventricle; others were in the sulci of the cerebellum, frontal and temporal lobes. The larvae varied in size from 7 mm to 2.5 cm. in length and up to 1 mm in greatest diameter. There was severe cerebral oedema, the brain weighing 1,000 gm. Microscopic examination showed numerous tracks meandering over all areas of the spinal cord and brain. These tracks varied 0.3-0.9 mm in diameter, consisting of disrupted brain tissue forming "microcavities", often containing gitter cells, bordered by demyelinated and swollen axons or what Nye and Tangchai called "axon retraction balls", degenerated neurones and a few glia cells and gitter cells (Fig. 2). Some of the tracks were accompanied by small focal hemorrhages. Many larvae of variable size, 80-130 μ at midgut level, were found in the brain tissue and meninges, sometimes without reaction (Fig. 3), suggesting perhaps that the larvae continued to move after patient's death. In the larger larvae the gut was pigmented and gonads were well formed although immature.

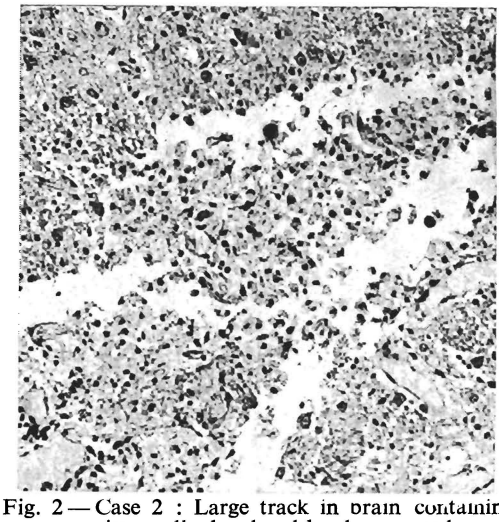

Fig. 2 — Case 2 : Large track in brain containing gitter cells, bordered by degenerated axons and neurones. H.E. x 35.

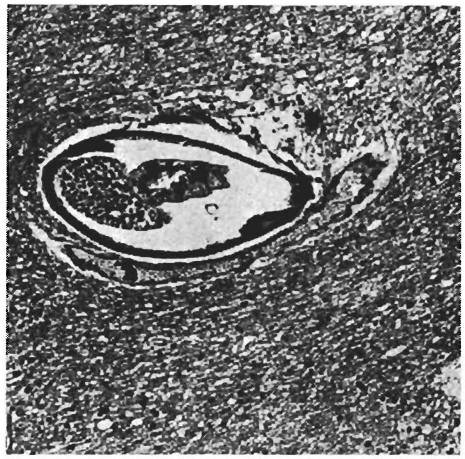

Fig. 3 — Case 2 : Cross-section of worm with pigmented gut and gonad without reaction. H.E. x 100.

The meninges and perivascular spaces were moderately infiltrated by lymphocytes including large transformed lymphocytes with a small number of plasma cells and very few eosinophils. The cause of death was a combination of confluent purulent bronchopneumonia and eosinophilc meningomyeloencephalitis.

Case 3: A 26-year-old Thai woman was admitted with a history of severe headache for

7 to 8 days prior to admission, followed by stupor and coma 2 days prior to admission. She habitually ate raw fish and *Pila* snails. Lumbar puncture on first day showed Pandy 2+; 960 cells/c.mm, 65% eosinophils, 35% lymphocytes; no parasites. On second day-Pandy 2+; 850 cells/c.mm, 60% eosinophils, 40% lymphocytes; no parasites.

The patient remained in coma and died 3 days after admission. The total length of time between onset of symptoms and death was 10 days.

Main autopsy findings related to angiostrongyliasis: the brain was very oedematous, weighing 1,250 gm and there was severe meningoencephalitis with heavy infiltration of eosinophils and smaller numbers of lymphocytes in the meninges and around the cerebral vessels (Fig. 4). Numerous tracks were

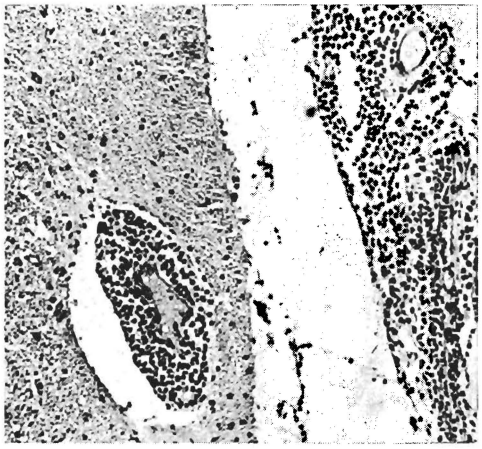

Fig. 4—Case 3 : Eosinophilic infiltration of meninges and around blood vessels. HE x 100.

found throughout the brain, most frequently in the cerebellum, brain stem and inferior surface of the cerebral hemispheres. The tracks were similar in appearance to those in Case 2, but the majority were 0.1-0.3 mm in diameter. A few of the tracks were slightly haemorrhagic.

In this case subserial blocks of the brain were taken, followed by serial sections where the worms were found, in an attempt to estimate the number of parasites. In the cerebellum and brain stem 37 larvae were found, 30 within the brain tissue and 7 in the meninges; 7 larvae were in veins (Figs. 5-6), 4 of these in

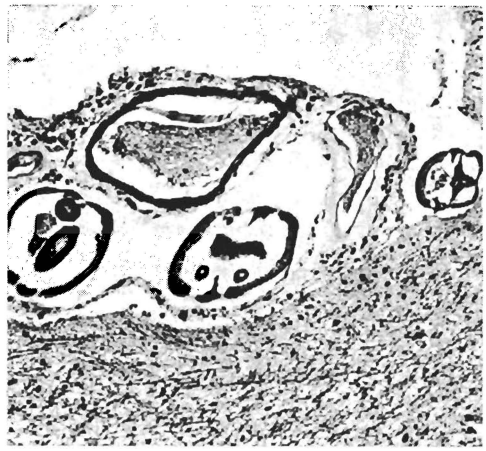

Fig. 5 — Case 3 : Cross-sections of two worms in a blood vessel, one outside, cerebellar white matter. H.E. x 100.

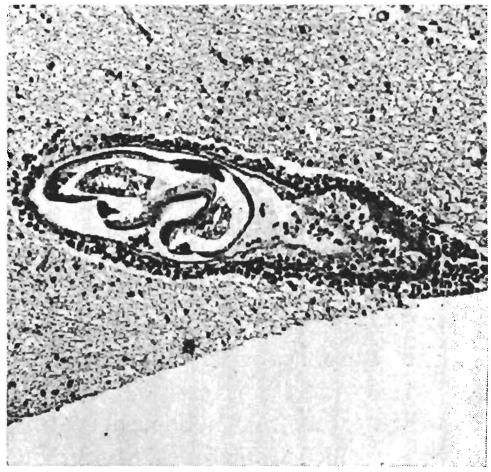

Fig. 6 — Case 3 : Tangential section of a worm in a blood vessel with heavy cuffing, mid-brain. H.E. x 100.

the meningeal veins. In the cerebral hemisphere 35 larvae were found, 8 within the brain tissue and 27 in the meninges including one dead larva in a meningeal vein, in contrast

to the cerebellum and brain stem. Total number of larvae found was 72.

The larvae varied from 50-120μ in diameter, most measuring 80-100 μ, and up to 700 μ in length. In the larger worms pigment had begun to appear in the gut and gonads were present.

A granuloma with fragments of cuticle was found in the cerebral meninges; and eosinophilic abscess was present in a cerebellar folium. Coincidentally there were changes in the liver consistent with long-standing opisthorchiasis: an eosinophilic abscess found in the liver was most likely due to this cause. The cause of death in this case would appear to be directly related to the parasites.

Case 4: No clinical data were available in this case apart from the fact that the patient was a 34-year-old Thai man who was in hospital for 19 days.

Main autopsy findings related to angiostrongyliasis: cut surfaces of the brain reportedly showed several focal haemorrhages pinhead to pea-size. Microscopic examination showed numerous tracks in all areas, varying from 0.3-0.5mm up to 1mm or more in diameter, with marked disruption of brain tissue and often quite large haemorrhages. Many larvae were found in the brain tissue and meninges, some 90-100 μ in diameter, others 130-150 μ; in these larger worms the intestine was pigmented and gonads appeared well-developed though still immature (Fig. 7). Cellular infiltration of the meninges and cerebral vessels was moderately heavy, mainly lymphocytic including large transformed lymphocytes, with small numbers of eosinophils and few plasma cells. There were 2 granulomata with fragments of dead worms in the meninges (Fig. 8).

In addition to the *Angiostrongylus* larvae found in the brain, 2 dead larvae were found in a pulmonary vessel (Fig. 9) with granulo-

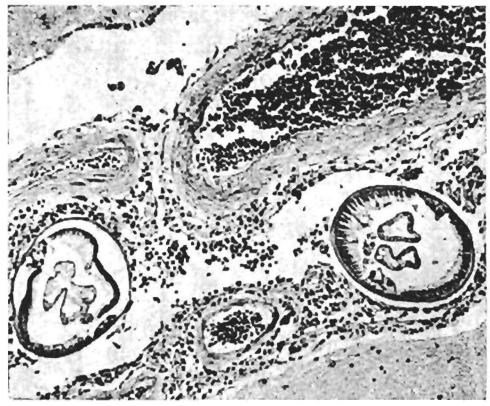

Fig. 7 — Case 4 : Cross-section of two worms in the meninges with lymphocytes and eosinophils. H.E. x 100.

Fig. 8 — Case 4 : Granuloma with dead worm fragments in meninges. H.E. x 400.

Fig. 9 — Case 4 : Longitudinal section of dead worm in a pulmonary artery. H.E. x 35.

matous reaction. Unfortunately their internal structures and real size were difficult to ascertain due to degeneration, but one of the worms appeared to be at least 9 mm long even in a contracted state. There was extensive pulmonary haemorrhage.

This patient was also found to have 5 tape worms in the intestines and numerous liver flukes in the distended bile ducts and gall bladder. The cause of death was due to cerebral, pulmonary and gastric haemorrhages.

DISCUSSION

Table 1 summarizes the clinical and pathological findings in the 4 cases. The presenting symptoms in each case were referable to the central nervous system, with back and/or headache, paralysis, followed by coma. Root pains, or "lightning-like" pain, as described in cases of radiculomyelitis associated with *Gnathostoma* (Punyagupta *et al.*, 1968a, b, Bunnag *et al.*, 1970) was not a feature, although there was paralysis in at least two cases, and in these cases tracks were present in the spinal cord in Case 1 and tracks and parasites in Case 2. Eosinophilic pleocytosis was present in all cases with clinical data, and *Angiostrongylus* larvae were recovered in the cerebrospinal fluid in 2 cases.

There was a definite history of raw *Pila* snail consumption in Cases 1 and 3. In Case 4, where no clinical data were available there was "circumstantial evidence" of a constant diet of raw food in the form of heavy liver fluke infestation and no less than 5 tape worms in the intestines. As for Case 2, who can state definitely what a child of $3\frac{1}{2}$ does or does not eat while playing outside? Is it also not possible that infective larvae might have been present in the slime left on raw vegetables as snails crawled over them?

At autopsy, *Angiostrongylus* larvae were found in all cases. In Case 1, only one 5th stage larva was found, although 3 were recovered antemortem and old tracks were present there was little reaction left. Death in this case, occurring 54 days after onset of symptoms, was due to inanition and secondary bacterial infection, rather than directly to the parasites.

In Cases 2, 3 and 4 numerous larvae were found and were a direct or contributory cause of death. There were meandering tracks throughout the central nervous system, consistent with tortuous paths taken by the parasites. The tracks, though varying in size from 0.1-0.9 mm, all consisted of disruption of brain tissue forming microcavities, some empty, some filled with shreds of degenerated brain substance and gitter cells, with peripheral demyelination, "axon retraction balls", swollen degenerate neurones and variable amount of haemorrhage. These tracks were not dissimilar to those of *Gnathostoma* though the latter are larger (0.8-over 1 mm), and massive haemorrhage as seen in gnathostomiasis (Punyagupta *et al.*, 1968, 1970) was not encountered.

There was stricking engorgement of blood vessels but no vascular necrosis or aneurysm. Cellular reaction was predominantly eosinophilic in Case 3, with the shortest duration between the onset of symptoms and death, 10 days. In Cases 2 and 4, with durations of 23 and at least 19 days respectively, lymphocytes, including transformed lymphocytes, predominated.

The larvae, judging by their size and internal structure, were probably late 4th stage and early 5th stage in Cases 2 and 3. In Case 3, where subserial blocks were taken, the larvae appeared to favour the cerebellum and brain stem; those in the cerebral hemispheres were more frequently found in the meninges. The presence of larvae in the meningeal and cerebral vessels in this case suggested the route of migration out of the central nervous system.

Table 1

Comparison of clinical and pathological findings in four cases of angiostrongyliasis.

	Case 1	Case 2	Case 3	Case 4
Clinical				
Age and sex	M 21	F 3½	F 26	M 34
Chief complaints	Generalised pain, fever, headache, paralysis	Back pain, paraplegia, urinary incontinence	Severe headache, coma	Not known
Days PTA	3	9	7-8	Not known
Raw snails eaten	+	0	+	Not known
Days in hospital	51	14	3	Not known
CSF findings	Eosinophils, 3 worms	80 worms	Eosinophils, no worms	Not known
Pathological				
Tracks	+ old 0.1-0.3 mm.	+ + 0.3-0.9 mm.	+ + + 0.1-0.3 mm.	+ + 0.3-1 mm
Haemorrhage	0	+ + small	+	+ + + large & small
Infiltrates	0	lymphocytes	eosinophils	Lymphocytes, few eosin.
No.worms found	1	Numerous	72 (7 in b.v)	Many: 2 in lungs
Immediate cause of death	Staph. pneumonia and pyelonephritis	Meningo-encephalitis; bronchopneumonia.	Severe meningo-encephalitis	Cerebral, pulmonary, gastric haemorrhages.

Lung worms naturally leave the parenchyma of the rat brain after 2 weeks (Mackerras and Sandars, 1955; Weinstein, 1963), through meningeal veins mainly, therefore small tracks and larvae should also be found in the parenchyma in human cases, and larger ones near and in the subarachnoid space, but in real life it does not appear to be that neat.

In Case 4, the larvae were generally larger, more compatible in size and internal structure with early and late 5th stage. The tracks were larger and often haemorrhagic. The interesting feature in this case was the presence of 2 degenerated, probably 5th stage larvae in the lung. Since these were dead further development in the human lung remain questionable.

SUMMARY

Three adults and a 3½-year-old child presented with eosinophilic meningitis. A history of consumption of raw snails was elicited in 2; evidence of a constant diet of raw food, in the form of opisthorchiasis and taeniasis, as well as angiostrongyliasis, was present in the third; no history of raw food ingestion was obtained in the fourth, the child.

Pathologic changes were similar in all 4 cases. There was infiltration of the meninges and around intracerebral vessels by varying proportions of lymphocytes, plasma cells and eosinophils. Numerous tracks and microcavities were found in the brains, and in the spinal cords in 2 cases, varying in size from 0.1 to 2 mm, and in age, with older tracks containing debris and gitter cells, newer tracks showing disruption of brain tissue, with and without haemorrhage. Numerous 4th and 5th stage *Angiostrongylus* larvae, alive and dead, were found in the meninges and brain tissue, sometimes in blood vessels or perivascular spaces, in 3 cases; in the fourth case a 5th stage larva was found on the surface of the right frontal lobe. In one case a degenerating larva was found in a pulmonary vessel. Cellular reaction was more often associated with dead larvae.

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