EOSINOPHILIC MYELOMENINGOENCEPHALITIS CAUSED BY *ANGIOSTRONGYLUS CANTONENSIS*: A REPORT OF THREE CASES

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Abstract. Three members of a family developed eosinophilic myelomeningoencephalitis following ingestion of Pila snails. They were father, daughter and son and had similar clinical presentations. Two days after ingestion of snails, they developed a generalized itchy maculopapular rash followed by myalgia, marked paresthesia, fever and headache. Two days later there was weakness of the extremities which was progressive in severity involving the legs more than the arms. They later developed urine retention and cloudiness of consciousness. Two patients progressed to coma, one of whom died after 3 weeks and the other died at home 9 months after the onset. Autopsy of the fatal case revealed multiple tracks and cavities with the presence of *Angiostrongylus cantonensis* in the brain and various levels of the spinal cord.

INTRODUCTION

It has been generally well accepted that *Angiostrongylus cantonensis* is the cause of a typical form of eosinophilic meningitis characteristically presenting with severe headache with very few focal neurological signs if any and the presence of eosinophils in the cerebrospinal fluid with or without the history of Pila snail ingestion. However, there is another form referred to as eosinophilic myeloencephalitis, the clinical course of which is rather unpredictable and many cases of which are fatal. These cases usually develop focal neurological signs and cloudiness of consciousness in the course of the disease. It is this latter form in which the causative parasite has been questioned. *Gnathostoma spinigerum* was believed at one time to be the most likely agent since it was supposed to be more penetrating resulting in tissue damage and rupture of the blood vessels (Punyagupta *et al,* 1970; Punyagupta *et al,* 1975). However, *A. cantonensis* had been demonstrated in the brain of several severe and fatal cases (Jindrak and Alicata, 1965; Tangchai *et al,* 1967; Nye *et al,* 1970; Sonakul, 1978; Kliks *et al,* 1982). These latter cases had a rather different clinical presentation from the cases of gnathostomiasis, ie they usually did not present with the typical agonizing neuralgic pain and the cerebropsinal fluid was not frankly bloody.

The present report describes three members of a family who developed eosinophilic myelomeningoencephalitis following ingestion of raw Pila snails. They were father, daughter and son and had similar clinical presentations. Another member of the family (mother) ate the raw snail too but immediately vomitted the contents and had no symptoms.

CASE REPORTS

Case 1: A 20-year-old Thai male, who was admitted on 15 June 1982, presented with a history of generalized itchy rash similar to that due to mosquito bites 2 weeks prior to admission. Two days after the onset, he had myalgia and painful sensation in the extremities and trunk together with abdominal pain. On the following day, he became febrile and developed weakness of both legs which was progressive. Ten days after the onset, he had difficulty in passing urine followed by urinary retention 3 days later when he was admitted to the hospital. Two days before the onset, he ate raw Pila snail salad together with other members of the family who also had the same problem.

On examination he was alert but slightly depressed with a temperature of 38.3°C. There was no neck stiffness and the cranial nerves were normal. There was mild proximal weakness of the upper extremities but marked weakness of the lower extremities. The reflexes were normal in the

upper limbs but almost absent in the lower limbs with bilateral flexor plantar responses. The most striking features were generalized paresthesia and marked muscle tenderness along the extremities together with diminished pain sensation from the toes up to the level of T_{12}.

Investigations showed a normal complete blood count with no peripheral eosinophilia. The cerebrospinal fluid was xanthochromic with a pressure of 180 mm H_2O. There were 363 white cells per cu mm with 20% eosinophils and 80% lymphocytes. The sugar was 34 mg% (blood sugar 102 mg%) and the protein was 75 mg%.

Three days after admission, he complained of headache and became drowsy with a rise of temperature up to 40°C. The neck was slightly stiff and the level of consciousness gradually deteriorated. On the seventh hospital day, he developed bilateral horizontal nystagmus on lateral gaze with early signs of increased intracranial pressure on fundoscopic examination. The cerebrospinal fluid on that days revealed a pressure of 340 mm H_2O with 800 white cells per cu mm and 80% eosinophils. The sugar was 40 mg% (blood sugar 270 mg%) and the protein was 80 mg%. Eight days after admission, he remained drowsy with high fever and flaccid quadriplegia. On the tenth hospital day he became comatose with absence of Doll's eye sign. The clinical picture progressively deteriorated until there was no spontaneous respiration and he died 14 days after admission.

Autopsy disclosed significant pathological findings in the central nervous system. The brain weighed 1510 gms and was edematous with uncal and tonsillar herniation. There was mild generalized subarachnoid hemorrhage with focal thickening of leptomeninges between the cerebellum and occipital lobes. Several young adult *A. cantonensis* (5th stage larvae) were seen in those areas. The coronal sections of the brain revealed multiple hemorrhagic tracks in the basal ganglia and some of them contained parasites. The spinal cord was also removed and many *A. cantonensis* larvae were found, measuring 2.5 cm in length and 0.1 cm in diameter. There were multiple parasitic and hemorrhagic tracks in both grey and white matter at all levels of spinal cord extending to the sacral plexus, as well as in the cerebellum. The bodies of *Angiostrongylus* larvae were seen at the subarachnoid space and parenchyma of the cerebellar hemisphere (Fig 1) as well as in the spinal subarachnoid space and parenchyma (Fig 2). Parasitic larvae were numerous in all levels of the spinal cord parenchyma.

Many tracks were filled with red blood cells and parasites (Fig 3) or with numerous polymorphonuclear leucocytes, lymphocytes and eosinophils (Fig 4).

The surrounding tissues around these tracks in both brain and spinal cord showed necrosis and perivascular cuffing with lymphocytes, plasma cells and few eosinophils.

Fig 1—The section of cerebellar hemisphere revealing a transverse segment of *Angiostrongylus cantonensis* in the molecular layer of cerebellar parenchyma without any cellular reaction. (H&E × 400)

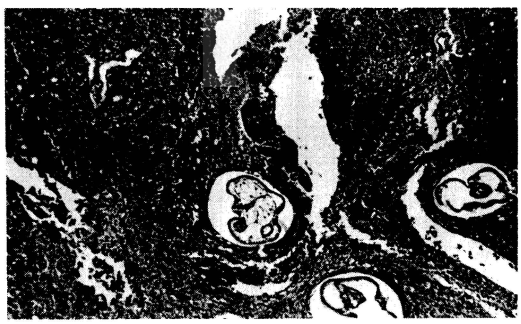

Fig 2—The section from spinal cord revealing three tracks containing three transverse segments of *Angiostrongylus* larvae without any cellular reaction (bottom and right lower corner of the picture). There were evidences of large hemorrhagic necrotic track (upper half and middle) and necrotic track (left side of the picture) without parasites. (H&E × 100)

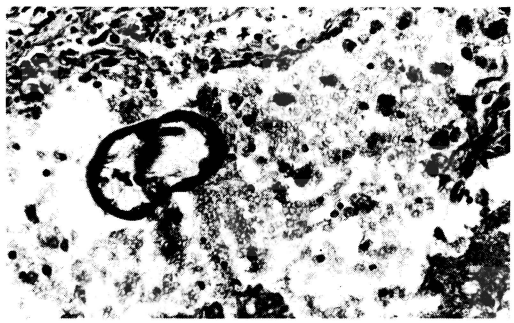

Fig 3—The microscopic finding of parasitic hemorrhagic tract containing a segment of *Angiostrongylus cantonensis* in the central portion of the track with numerous red blood cells, few lymphocytes, macrophages and eosinophils. (H&E × 400)

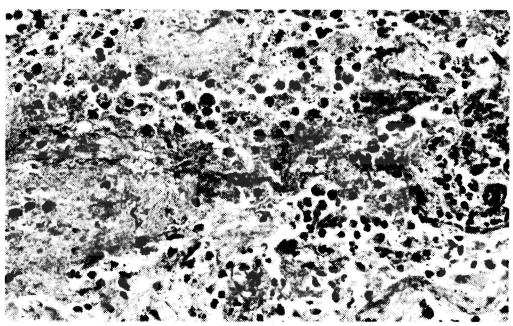

Fig 4—Photomicrograph disclosing necrotic track with numerous polymorphonuclear leucocytes, eosinophils, glitter cells, fibrin and necrotic tissue debris. (H&E × 400)

However, several tracks containing parasites without cellular reaction (as in Fig 2) were also seen: presumably the living parasites continued to move to those locations after the death of the patient. Some areas of the meninges showed a moderate degree of eosinophilic meningitis.

The pathological findings in other organs included severe pulmonary hemorrhage and acute confluent bronchopneumonia of both lungs, opisthorchiasis and centrilobular hemorrhagic necrosis of the liver, acute tubular necrosis of the kidneys and chronic cystitis. The sections of the colon revealed a chronic inflammatory process and venous thrombosis with eosinophilic plugging in the lumen and giant cells around the eosinophils which were suggestive of parasitic tracks.

Case 2: A 48-year-old Thai male (father of case 1) who was admitted on 29 June 1982, presented with a history of generalized itchy rash similar to mosquite bite 2 days after ingestion of snails. The clinical features were similar to case 1, ie, he later developed myalgia, paresthesia, fever, weakness of arms and legs progressing to quadriplegia, urinary retention, headache and cloudiness of consciousness.

On examination, he was afebrile, disoriented and depressed but could respond to simple verbal commands. The neck was stiff. The cranial nerves were normal. There was mild weakness of left arm, marked weakness of right arm and moderate weakness of both legs.

Investigations showed a hemoglobin of 13.2 g%, white blood count of 23,750 cells/cu mm with 58% neutrophils, 21% eosinophils and 21% lymphocytes. The cerebrospinal fluid was clear and colorless with pressure of 90 mm H_2O. There were 220 cells/cu mm with 50% each of lymphocytes and eosinophils. The sugar was 40 mg% (blood sugar 108 mg%) and protein 130 mg%.

On admission he had urinary tract infection, being unable to void by himself and needed urethral catheterization and antibiotic treatment. He was given dexamethasone and supportive treatment. His clinical course in the hospital gradually improved and he was eventually able to pass urine. On discharge after 3 weeks of hospitalization, there was marked improvement of the power of the arms and legs.

On follow up a year later, his mental status was apparently normal. He had no weakness of the extremities and could walk with moderate spasticity of both legs.

Case 3: A 25-year-old Thai female (elder sister of case 1) had similar symptoms to cases 1 and 2.

On examination, she was febrile, dehydrated, and comatose, not responding to painful stimuli. Doll's eye movement was present. There were minimal movements of all limbs. The tendon reflexes were all present except both knee jerks. The plantar responses were bilaterally extensor.

Investigations revealed hemoglobin of 14.1 g% and white blood count of 7,400 cells/cu mm without eosinophilia. The cerebrospinal fluid showed a pressure of 130 mm H_2O, 350 white cells/cu mm with 55% lymphocytes, 30% eosinophils and 15% neutrophils. The sugar was 84 mg% (blood sugar 196 mg%) and protein 60 mg%.

On admission, her spontaneous respiration was inadequate necessitating tracheostomy and assisted ventilation. Dexamethasone and supportive treatment were given. Her respiration gradually improved and later she could breathe properly without the respirator. Two months after admission, her consciousness and mental status slightly improved but the weakness of the extremities remained very severe. She was discharged after 4 months with quadriparesis. She could not communicate and could only move her eyes when her name was called. She eventually died at home 4 months after discharge. Autopsy was not performed.

DISCUSSION

The clinical presentations of these cases were those of lesions of spinal cord and peripheral nerves or nerve roots (myeloradiculopathy) ie urinary retention, weakness of both legs with lowered sensory levels and depressed deep tendon reflexes in the lower limbs together with hyperesthesia of hands and legs. The patients informed the physician about the snail ingestion from the beginning and related the initial symptoms to the snail including the itchy generalized skin rash resembling that from mosquito bites followed by the hyperesthesia over the extremities. This skin rash was thought to be an allergic reaction to the worm.

The snails were ingested in the family of 4 persons ie mother, father, son and daughter. Fortunately, the mother vomitted the stomach contents and was not affected. It was believed that the son who was most severely affected had eaten the greatest number of snails. The snails were collected from Tung Maha Mek district in central Bangkok.

The clinical features in these cases were rather unusual and striking for this worm in view of the profuse neurological deficits and rapid progression, in contrast to the familiar picture of self-limiting eosinophilic meningitis without focal neurological signs. In a series of 484 patients studied by Punyagupta *et al,* (1975) there were

Table 1
Frequency of symptoms in patients with eosinophilic meningitis.

	% patients	
	Punyagupta *et al,* 1975 (484 cases)	Yii, 1976 (114 cases)
Headache	99	86
Neck stiffness	64	40
Vomiting	49	
Nausea	38	
Blurred vision or diplopia	38	10
Paresthesia	37	28
Fever low grade	33	
high grade	4	
Aching of body and extremities	6	-
Impairment of sensorium	6	92
Muscle twitching	-	13
Convulsion	4	3
Weakness or paralysis of extremities	1	23
Urinary incontinence or retention	1	6
Abdominal pain	-	34

Table 2

Frequency of neurological signs in patients with eosinophilic meningitis or meningoencephalitis.

	% patients	
	Punyagupta *et al*, 1975 (484 cases)	Yii, 1976 (114 cases)
Impairment of sensorium	(5.4)	(92)
Lethargy	3.2	82
Confusion	1.4	
Semicoma	0.6	10
Coma	0.2	
Neck stiffness	15.0	-
Presence of Kernig's sign	6.0	44
Impairment of vision	(16.0)	-
Unilateral	6.4	
Bilateral	9.6	
Abnormal visual field	1.0	-
Abnormal fundi	(12.0)	-
Blurred discs	9.6	
Papilledema	1.2	
Optic atrophy	1.2	
Other cranial nerve abnormality	(7.0)	(10)
CN VI palsy	3.0	8
CN III palsy	0	1
CN VII palsy	4.0	1
Weakness or paralysis of extremities	1.0	6
Paresthesia	4.0	-
Exaggerated deep tendon reflex and spasticity	2.0	-
Extensor plantar response	2.0	-

very few cases who had severe or focal neurological deficits. Among these, 0.8% were semicomatose or comatose, 12% had abnormal fundoscopic examination (blurred disc, papilledema and optic atrophy), 7% had other cranial nerve (VI, VII) abnormality, 1% had weakness of extremities and 4% had paresthesia. This was in contrast to the cases in the series of 114 patients from Taiwan reviewed by Yii (1976) where a larger proportion of cases was fatal or had serious clinical manifestations; for example, 10% of patients were semicomatose or comatose, 10% had cranial nerve (III, VI, VII) abnormality and 6% had weakness or paralysis of extremities (Tables 1, 2). Yii pointed out that the difference in the severity of the disease may be due to heavier infections in Taiwan patients than those in other geographic locations. The presumption that parasite load was heavier in Taiwan was supported by the more frequent detection of the parasites in the cerebrospinal fluid than elsewhere and the suspected source of infection on Taiwan, the giant African snail *(Achatina fulica)* was known to harbor enormous numbers of infective larvae (Wallace and Rosen, 1969). In Thailand, the source of infection was Pila snails which usually harbor relatively fewer infective larvae.

The neuropathological findings in the autopsied case in this report were mostly similar to those previously reported. External appearance was generally unremarkable except for brain edema with thickening of the leptomeninges. Gross hemorrhages were reported to be most unusual while subarachnoid hemorrhage was noted in this case. Larvae of *A. cantonensis* were often seen on the surface of the brain or spinal

cord and in this case 5th stage larvae were detected around base of the brain where the leptomeninges were markedly thickened. The most striking findings were multiple hemorrhagic tracks representing passage of the migrating worms and the parasites in the parenchyma of the brain and spinal cord.

The interesting aspect of this report was the correlation of the neurological manifestations and the rapid progression with the documented pathological findings. Although *A. cantonensis* usually causes self-limiting eosinophilic meningitis, it can be very penetrating like *G. spinigerum,* another worm which much more frequently presents with focal neurological deficits. Clinical differentiation in these cases may be difficult. However, the presence of agonizing neuralgic pain and bloody cerebrospinal fluid suggest gnathostomiasis and the cases of angiostrongyliasis usually have history of snail consumption (Boongird *et al,* 1977).

These three cases were admitted in the period studied by Schmutzhard *et al,* (1988) but were not included in their report. Therefore, that study and discussion were incomplete and could give a false impression as to the true nature of *A. cantonensis.* That report omitted out the very important point that *A. cantonensis* can penetrate the brain and spinal cord parenchyma causing severe damage to these tissues and death.

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