Original Article

Case series of eosinophilic meningoencephalitis from South India

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Abstract

Eosinophilic meningoencephalitis (EM) is a rare type of meningoencephalitis. The objective of this report is to describe a series of EM identified in a specific geographic area over a short period of time. **Materials and Methods:** This series of cases are described from a neurological center in Central Kerala occuring in the period between February 2004 and June 2006. **Results:** During this period we had identified ten patients (eight males and two females) with EM. Their mean age was 37.1 years (range 15-60 years). Main symptomatologies were fever, severe headache, body pain, abdominal pain and arthralgia. One patient was in akinetic rigid state with coma. All patients had peripheral eosinophilia. The cerebrospinal fluid (CSF) of all patients showed eosinophilic pleocytosis. The mean CSF white cell count was 588 cells. CSF differential count showed 50-70% eosinophils. CSF glucose levels were normal but proteins were markedly raised (mean CSF protein was 180 mg/dl). MRI brain showed T2 hyperintensities diffusely in periventricular white matter in the comatose patient. Contrast enhanced CT scan of the brain was normal in others. All eight male patients gave history of eating "raw flesh of Monitor Lizard" (Iguana) some three to fourteen days prior to the onset of symptoms. There was no such history for the female patients. Considering the history of exposure and eosinophilic meningitis we suspected a meningoencephalitis with *Angiostrongylus cantonensis* and treated them with albendazole, steroid and other supportive measures. All of them recovered. **Conclusion:** Eosinophilic meningitis (EM) is a rare condition and in this locality, a CNS infection with *Agiostrongylus cantonensis* is highly likely. AC is a parasite in monitor lizard. Human infection occurs from consumption of uncooked flesh or blood of infected lizards. Physicians need to maintain a high index of suspicion and enquire for any exposure to uncooked meat or blood of monitor lizard when faced with EM. Specific therapy with albendazole offers excellent response.

Keywords

Angiostrongylus cantonensis, eosinophilic meningitis

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Ann Indian Acad Neurol 2006;9:217-22

Eosinophilic meningoencephalitis (EM) is a rare variety of meningoencephalitis. CNS infection with *Angiostrongylus cantonensis* (AC) or other parasites is the most common cause of EM but rarely there can be other causes. AC is the most common parasite causing the disease worldwide. Angiostrongyliasis is a parasitic disease affecting both man and animals. Human infection occurs after ingestion of the infective larva found in 'raw snails' (which serve as intermediate host) or Monitor lizard's liver (which act as transport host). The parasite was first described in 1935 in China in the pulmonary artery of rat.[1] Since then more than 5000 cases have been reported in various parts of the world. Most cases are prevalent in Asian countries namely, Thailand, Japan, Taiwan and China. This is the first report of EM in Indian literature. There are some unique presentations of EM, making the clinical diagnosis very difficult. These features include minimal meningeal signs and normal neuroimaging studies in the early stages of the disease.

Materials and Methods

This study was carried out in Indo American Hospital, Brain and Spine Center, Vaikom, in Central Kerala. During the period between February 2004 and January 2006, we had identified 10 patients with characteristic EM. All patients underwent lumbar puncture and cerebrospinal fluid (CSF) was examined for cells, proteins and glucose. Detailed work up for any specific bacterial, fungal and tuberculous etiology was carried out in all patients. Contrast enchanced CT scan was performed in nine patients and an magnetic resonance imaging (MRI) of brain was done in another patient. The clinical

profile, laboratory investigation findings and outcome are described below.

Results

During the study period we had identified ten patients (eight males and two females) with EM. Their age ranged from 15- 60 years (mean 37.1 years). All male patients gave a history of consumption of raw flesh of Monitor lizard some three to fourteen days prior to the onset of symptoms. The presenting symptoms for these patients included fever (100%), severe headache (100%), body pain, abdominal pain (80%) and arthralgia (70%). One patient each presented with radicular pain and seizures. One patient was in comatose state with rigidity of all four limbs. Their clinical profile is given in Table 1.

Case 1

A 51-yr-old man got admitted in the neurology department after an initial one-month treatment as salmonella septicemia in a local hospital. He was absolutely healthy previously with no other risk factors. He ate raw liver of monitor lizard (as suggested by local indigenous physician to strengthen his power) and became severely ill on the ninth day of consumption of the raw flesh. He had severe body ache, arthralgia, prolonged fever, abdominal pain and headache. At the time of admission to this hospital he was in coma and had akinetic rigid state with multiple bedsores. During the hospital stay he had several generalized seizures. Lumbar CSF showed plenty of eosinophils. Extensive work up for EM including CSF polymerase chain reaction (PCR) for TB, HSV, CSF acid fast bacilli (AFB), stain, AFB culture, fungal stain and culture, neurocysticercal serology work were negative. MRI showed multiple periventricular white matter hyper intensities in T2W images. His neurological state slowly improved on treatment with albendazole and steroids. At the end of the first year he achieved complete cognitive, motor recovery and started to work independently.

Case 2

A 15-year-old boy, son of 'Case no 1', had consumed raw flesh of monitor lizard along with his father. He had consumed lesser quantity of raw flesh. He developed body pain, fever, arthralgia, abdominal pain and headache on the ninth day after eating raw flesh of lizard. LP CSF study showed eosinophilia. He slowly improved and became completely normal by three to four weeks.

Case 3

A 30-yr-old, previously healthy male, presented with severe holocranial headache of one-month duration. He had low-grade fever lasting few days at the onset. He consulted several physicians and ENT surgeons during that one-month period for his recent onset of severe headache. He had also tried many combinations of NSAIDS and antibiotics without any success. He had no meningeal signs, papilledema or any other neurological deficits. CECT scan of brain was normal. CSF showed severe eosinophilia. On probing, he recalled that the headache started very clearly within one week of eating the "raw liver of monitor lizard". He improved and became completely asymptomatic within three days of treatment.

Case 4

A fifty-year-old man came with headache of one-month duration and severe multiple area body pain. On examination he had signs of cervical and lumbosacral radiculopathy. CECT scan of brain was

Table 1: Clinical features of eosinophilic meningitis

Sr. No.	Age/ sex	Incubation period	Presenting symptoms	Signs	Other systems	Outcome
1	51/M	9th day	Headache, bodyache, arthralgia, fever, abdominal pain, headache, seizures	Coma, akenitic rigid mute state	Hepatitis, Pneumnitis	Recovered
2*	15/M	9th day	Fever, abdominal pain, severe headache	Nil	Nil	Recovered
3	30/M	7th day	Headache, fever	Nil	Nil	Recovered
4	50/M	7th day	Headache, body pain, fever	Cervical and lumbar radiculopathy	Nil	Recovered
5	30/M	3rd day	Abdominal pain, myalgia, headache, vomiting, arthralgia, fever	Nil	Hepatitis	Recovered
6	60/F	No definite exposure	Headache, fever	Nil	Nil	Recovered
7	28/M	7th day	Body ache, arthralgia, headache, fever	Nil	Nil	Recovered
8	26/M	14th day	Fever, headache, body ache, arthralgia	Nil	Nil	Recovered
9	44/F	Indigenous medication for rheumatoid arthritis	Headache, body ache, vomiting, fever	Nil	Rheumatoid arthritis	Recovered
10	32/M	7th day	Headache, fever	Nil	Nil	Recovered

*= Case 2 was the son of case 1

normal. Lumbar CSF showed eosinophilia. Retrospectively, he recalled consumption of raw liver of monitor lizard one week prior to the onset of symptoms. Work up for chronic meningitis, including CSF PCR for tuberculosis, herpes simplex virus, was normal. CSF direct smear for AFB, fungi, culture for bacteria, tubercle bacilli and fungi were negative. CSF serology for neurocysticercosis was negative. He recovered completely within one week of specific therapy.

Case 5

A thirty-five-year old man consumed raw liver of monitor lizard and he presented on the third day with fever, severe body pain, abdominal pain, vomiting, arthralgia and severe headache. LP CSF showed eosinophilia. CECT scan brain was normal. He became asymptomatic within two days of specific therapy.

Case 6

A sixty-year-old lady presented with severe headache of two weeks duration. She had a history of tension type headache for nearly forty years. She was treated for tension type headache without any improvement. Her headache and general condition worsened rapidly. There were no focal neurological deficits. CECT scan of brain was normal, but CSF showed severe EM. She responded well on specific treatment.

Case 7

A twenty-year-old male presented with severe holocranial headache of two weeks duration. He had consumed lizard's raw flesh one week prior to the onset of symptoms. He had severe body ache, fever and arthralgia at the onset, which spontaneously subsided within three days. But he continued to have severe holocranial headache. He did not have any meningeal signs, papilledema or focal neurological deficits. There were many eosinophils in his CSF. He improved well on the third day of therapy with steroids and Albendazole.

Case 8

A twenty six-year-old male presented with severe body ache, arthralgia and abdominal pain and holocranial headache of three weeks duration. He had consumed uncooked meat of lizard two weeks earlier. CECT scan brain was normal but CSF showed plenty of eosinophils. He recovered completely on treatment with steroids and albendazole.

Case 9

A forty four-year-old lady presented with fever, severe holocranial headache, vomiting and generalized body ache of one week duration. She had chronic deforming seropositive rheumatoid arthritis for the last the twenty years. She had recent relapse of arthritis and was on indigenous medication for two weeks prior to onset of symptoms. CECT head was normal, CSF showed many eosinophils. She recovered fully within one week of treatment with steroid and albendazole.

Case 10

A 32-year-old man was admitted with holocranial headache on a background of low-grade fever of one-month duration. He showed no focal neurological deficits, meningeal signs or papillodema. He had consumed uncooked meat of lizard seven days prior to onset of fever and headache. His CECT scan brain was within normal limit. All other biochemical work up were negative. His CSF showed severe EM. He recovered completely on treatment with albendazole and steroids.

Discussion

In this series, all eight male patients developed the illness after consumption of uncooked meat of monitor lizard. There is prevalent belief that raw flesh, particularly the tongue and the liver of monitor Lizard (iguana) has rejuvenating properties and is a good aphrodisiac. Monitor lizard is well known for its strong grip. People tend to take bits of uncooked meat (mainly tongue or liver) of the lizard sandwiched between slices of bread or banana. These patients developed the clinical symptoms about three to fourteen days after the ingestion of offending meat.

It is interesting to note that the second patient is the son of patient number one described in the Table 1. Both of them consumed the offending meat together and both became symptomatic on the ninth day itself. Both patients were having severe systemic symptoms and got admitted in a local hospital. Son improved spontaneously while father's condition deteriorated. Father (case 1) was treated for leptospirosis initially and subsequently he was labeled as having salmonella septicemia and not even suspected to have EM. He became comatose and was in akinetic rigid state with recurrent seizures. He got admitted at the neurology department nearly one month later in very sick state. LP CSF study showed pleocytosis with eosinophilia even after one month.

There were no focal neurological deficits, meningeal signs or papilloedema for nine patients. One patient (Case 4) had feature of lumbar and

Table 2: Laboratory findings in eosinophilic meningitis

Patient	Peripheral eosinophilia %	CSF cells/mm³	CSF differential count	CSF protein (mg%)	CSF sugar/ BS
1	30	45	L70%, E30%	65	60/90
2	40	200	E40%, L60%	120	50/80
3	45	380	P3% L44%, E53%	70	49/90
4	30	758	E50%, I50%	200	70/120
5	44	738	P12%, L31%, E57%	140	50/90
6	30	1600	P5%, L15%, E80%	250	
7	15	300	P10% E70% L20%	200	60/90
8	10	654	E50% L50%	256	48/90
9	20	956	E 80%, L20%	350	50/90
10	15	250	E30%, L70%	150	56/90

BS= Blood glucose corresponding to CSF study, E= Eosinophils, L= Lymphocyte, P= Polymorph, CSF - Cerebrospinal fluid

cervical radiculopathy additionally.

All patients had peripheral eosinophilia [Table 2]. Other metabolic and biochemical work up were negative. All had CSF eosinophilia (30-80%). The CSF cell count ranged between 45 to 1600 cells [Table 2]. The CSF protein was markedly elevated and average CSF protein was 180 mg%. CSF sugar was normal. CECT scan head were normal in nine patients (which were done in the early stage of disease). In one patient (case no 1) who was severely affected showed bilateral symmetrical white matter changes in MRI. The serum and CSF were investigated extensively for other causes of chronic meningitis in Patients No. 1, 2 and 4. Serological work up for cysticercosis and tuberculosis were negative. Microbiological tests for ameobiasis, fungal stain, fungal culture, AFB stain, AFB culture and PCR test for tuberculosis and herpes simplex encephalitis were carried out on the CSF samples and were negative. Serological test for or angiostrongylosis cantonensis, Gnathostoma spinegera or Paragonimus westermani were not done due to lack of availability.

Our patients had symptoms and signs typical of eosinophilic meningitis due to Angiostrongylus cantonensis. We were unable to confirm the diagnosis because the specific immunological test was not available locally. Repeat CSF examination after four weeks of therapy was carried out in eight patients and was normal in all of them.

All the patients were treated with Albendazole and steroids. Even though the Case no 2 had started improving spontaneously; he was also given the benefit of albendazole and complete recovery ensued. Steroids were administered only for the initial five days of therapy. Albendazole therapy (10-15 mg/kg body weight/day) was continued for 21 days. All patients recovered and became asymptomatic within three to four days of initiating therapy. The severely affected comatose patient made a gradual recovery and he was back to normalcy by one year

All these patients had fairly typical clinical features. All (except one) of them were had no previous illnesses of importance. All male patients gave a history of ingestion of uncooked meat of monitor lizard that was probably infected with the parasite. Parasitic infection of the CNS is the most common cause of EM although rarely it can be due to other etiologies [Table 3].

We could exclude most other causes of EM in these patients by respective laboratory investigations.[2] It is difficult to confirm the diagnosis in India, because the specific serological test for *A. cantonensis* is not available in India. But the several pointers strongly suggest *A. cantonensis* as the etiology of the EM in this series. 1) Very clear temporal relationship with the onset of disease and consumption of raw flesh of lizard. 2) Dramatic and prompt response to treatment with albendazole and steroids. 3) Similarity with the clinical presentations of the published proven previous cases.

Table 3: Causes of eosinophilic meningitis in human

1) CNS parasitic infestation
   - *Angiostrongylus cantonensis*
   - Neurocysticercosis
   - Gnathostoma spinegerum
   - Trichinella spiri
   - Toxaplasma gondi
   - Toxacara infestation
2) Other CNS infections
   - Subacute sclerosing pan encephalitis
   - Rickettsial fever
   - Lympho cytic choreomeningitis virus
3) Non infectious causes
   - Non Hodgkins lymphoma
   - Hodgkins lymphoma
   - Eosinophilic leukemia

CNS - Central nervous system

The locality is predominantly a waterlogged area with a variety of flora and fauna. Monitor Lizard (iguana) is a wild reptile that encroaches in to human habitat fairly frequently in this area. There is a prevalent superstitious belief among the local community that the raw flesh of monitor lizard is a very good promoter of health and is an aphrodisiac. Monitor lizard is very popular for its strong grip. People used it in the olden days to climb trees and tall structures. They used to tie the lizard to a rope and throw it over the structure they wanted to climb. The lizard would cling to the wall or the high structure and the person would climb up along the rope.

Angiostrongylus cantonensis, the rat lungworm, is the most common infectious cause of EM in humans. Rats serve as the definitive hosts of the nematode (roundworm), whereas humans can get infected by ingesting third-stage larvae in raw or inadequately cooked intermediate hosts, such as snails and slugs or transport hosts, such as freshwater prawns, frogs, fish and monitor lizards. Eosinophilic meningitis has been reported even in vegetarians who consumed improperly cleaned raw vegetable or vegetable juices that had snail tracking. Lizards have infective third stage larva and act as infective transport host by eating infected snails. There are several other infective agents also. Fresh water snails (Ampularium canaliculus), when eaten raw, are the main source of human infection in some areas.[3] In *V. bengalensis* (a yellow tree monitor lizard), which can also be a host for *A. cantonensis,* the third stage larvae are found mostly in the liver.[2,4] It has been reported that patients who consume lizard liver are affected more severely with EM than those who consume snails, probably because the lizard carries more advanced infectious stage of *A. cantonensis.*[4]

When third-stage larvae get ingested by humans, they penetrate the vasculature of the intestinal tract and eventually reach the meninges, where they usually die shortly thereafter. An eosinophilic reaction develops in response to the dying larvae and is manifested as aseptic meningitis. Although many cases of infection are self-limited, neurologic sequelae can occur in some cases and even deaths have been reported. In the present case series, three patients were severely affected and one patient was comatose at the time of admission. Only one child (case no 2) showed signs of spontaneous remission. All other cases were progressively worsening at the time admission to hospital. Most cases of *A. cantonensis* meningitis have been reported in Southeast Asia[5] and the Pacific basin but sporadic cases have been reported in many other regions. Although most cases occur singly, outbreaks and epidemics have also been reported.[6] Diagnostic criteria had been proposed for diagnosis of EM in suspected persons who had traveled to endemic areas.[6]

The neuropathology of human angiostrongyliasis had been well described earlier.[7-11] *A. cantonensis* larvae can be recognized in the brain tissue, the meninges and sometimes in the blood vessels or perivascular spaces. In some of the above reports the larvae were densely distributed in the cerebellum and brain stem. Both dead and alive worms were found at necropsy. Cellular reaction was minimal around the living worms but more pronounced around the dead worms. Cellular reactions were also observed along the meninges and intracerebral vessels.[9-11] One of the characteristic pathologic features was that of multiple microcavities or numerous tracks (usually smaller than 150 μm) in the brain and spinal cord, representing the passage of migrating worms.[12] The presence of migratory tracks may be of diagnostic value in some cases. One striking microscopic feature was vascular dilatation, both arterial and venous, in the subarachnoid spaces. Autopsies of the patients revealed the presence of worms in the subarachnoid spaces over the frontal cortex, pons, tip of the temporal lobes and paraventricular areas of the lateral ventricle.[9] The subarachnoid space was widened and edematous and the arachnoid membrane was thickened with marked vascular dilatation in the subarachnoid space.

Radiologic abnormalities in EM have been described rarely.[13,14] The size and location of imaging abnormalities were varied and probably related to the number of larvae and their movements. MRI of the brain during the acute phase of the illness can show multiple discrete white matter lesions in both cerebral hemispheres and the cerebellum on T1- and T2-weighted images.[13] MRI findings suggested tissue reactions to dead worms and local vasodilatation associated with minimal thrombus formation. In the present case series all patients underwent radiological investigations. CECT scan of brain study were normal in all the 10 patients. MRI was done only in one severely affected patient (Case No. 1) and MRI findings revealed T2 hyperintensities in bilateral periventricular region, due to deeply located lesions. These are nonspecific findings that may indicate demyelination, small vessel ischemic changes or gliosis.

Conclusion

We report ten patients with EM possibly due to angiostrongylus cantonensis. Eight of them had the exposure through consumption of uncooked meat of monitor lizard (Iguana). Many case of EM were often under diagnosed as some of the cases were mild and self-limiting. Sometimes they were misdiagnosed either due to physician's unawareness or failure of laboratory tests to identify eosinophilia in CSF. This is the first report of EM most probably due to *AC* in Indian literature.

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Received: 29-08-06, **Revised:** 13-10-06, **Accepted:** 30-10-06

Source of Support: Nil, **Conflict of Interest:** None declared.