Eosinophilic Meningitis without Peripheral Eosinophilia

Dokyung Lee Sang-Hwa Lee Sung Sang Yoon Tae-Beom Ahn

Department of Neurology, Kyung Hee University College of Medicine, Seoul, Korea

Dear Sir,

Eosinophilic meningitis (EM) may be diagnosed if there are more than 10 eosinophils (Eo)/ μ l or 10% leukocytes in the cerebrospinal fluid (CSF) [1]. EM is commonly associated with peripheral eosinophilia (PEo), and the most common cause of EM is parasitic infestation [2]. Few patients with EM have presented without PEo, and in those patients parasite infestation and drugs were identified as the culprits [3–5]. There have been no reports of idiopathic EM without PEo.

Case Reports

Case 1

A 30-year-old female was admitted to the hospital because of sudden-onset right facial palsy. She had neither fever nor headache. Her medical history, including medications such as analgesics and antibiotics, was unremarkable.

On neurologic examination, she had sensorineural hearing loss of the right ear on the Weber and Rinne tests in addition to a peripheral type right facial palsy. Impedance and pure tone audiometry showed no abnormalities. Two days after admission, she complained of double vision. The red glass test revealed right lateral rectus palsy. No other abnormal neurologic features were noted.

PEo was within normal limits (100/ μ l, 0.7%). CSF analysis showed a value of 26 white blood cells (WBCs) per microliter with predominant Eo (91%) (table 1) and the CSF/serum albumin ratio [CSF albumin (mg/dl)/serum albumin (g/dl)] was normal (4.91). Extensive workups for infectious diseases including viral, bacterial and fungal agents were unremarkable. No malignant cells were detected in the CSF. Parasite studies such as stool examination and enzyme-linked immunosorbent assay (ELISA) for parasite infestations including neurocysticercosis, paragonimiasis, and sparganosis were negative. Brain magnetic resonance imaging (MRI) with gadolinium enhancement was normal.

Clinical symptoms improved with methylprednisolone (48 mg/day p.o. for 5 days). No Eo was detected in the follow-up CSF study after 13 days. No additional neurologic illness appeared for over 3 years.

Case 2

A 70-year-old woman with diabetes presented with fever and headache that had persisted for 2 days. She had not taken any medications except her usual drugs for diabetes. Her neurologic examination was normal except for a finding of neck stiffness.

PEo was absent (Eos = 30/ μ l, 0.7%). CSF examination showed 150/ μ l WBCs with 78% Eo (table 1). The patient's CSF/serum albumin ratio was elevated (22.95). The CSF oligoclonal band was absent. Diagnostic workups for viral, bacterial, parasitic and fungal diseases including a stool examination and ELISA for parasites were unremarkable. Brain MRI with gadolinium enhancement was normal.

Her clinical symptoms spontaneously disappeared without any specific treatment such as steroid pulse therapy. A follow-up CSF study was normal. She reported no neurologic illness afterwards.

Case 3

A 23-year-old female was admitted to the hospital for headache and fever. She had no significant medical history and did not take any medications before her illness.

Although she was normal on neurologic examination, a CSF study was performed due to severe headache, showing 450/ μ l WBCs with predominant Eo (43%). PEo was absent (370/ μ l, 3%) (table 1). Further workups for causative agents were unremarkable, including stool and ELISA studies for parasite infestation. An enhanced brain MRI was normal. Serologic tests showed the presence of anti-SSA antibodies (60 and 52 Kd) without any symp-

Table 1. Major clinical manifestations and laboratory findings of previously reported cases of EM without PEO

Related conditions of EM	Blood		CSF			Major clinical manifestations	
	WBC n/ μ l	Eos n/ μ l (%)	protein mg/dl	glucose ^a mg/dl	WBC n/ μ l	Eos %	
<i>Angiostrongylus cantonensis</i> [5]	7,560	302 (4.0) ^c	54	0.63 ^b	477	50	headache
Ciprofloxacin [3]	6,700	402 (6.0) ^c	54	52/109	147	24	fever, headache, neck stiffness
Ibuprofen [4]	11,400	114 (1.0) ^c	60	44/99	576	60	fever, headache, neck stiffness
Ventriculoperitoneal shunt, Coxsackie B4 virus [11]	10,600	0 (0)	140	76/107	407	11	prolonged generalized seizure, fever, nuchal rigidity
HL [6]	5,300	0 (0)	160	8/NA	163	39	HL stage IVB, headache, fever
HL [7]	NA	0 (0)	72	46/NA	22	35	HL stage IIB, fever, headache
HL [8]	NA	0 (0)	392	10/NA	490	80	Headache, weakness, diplopia
HL [9]	6,500	0 (0)	mildly elevated	NA	133	PC	HL stage IIA, fever, generalized seizure
None (case 1)	11,800	100 (0.7)	29	66/170	26	91	facial palsy, sensorineural hearing loss, diplopia
None (case 2)	4,500	30 (0.7)	115	84/134	150	78	fever, headache
None (case 3)	12,130	370 (3.0)	58.5	46/87	450	43	fever, headache, nuchal rigidity

NA = Not available; PC = pathologically confirmed (exact Eo count was not specified). ^a Values are CSF/serum except for ^b CSF/serum ratio; ^c calculated number of Eos.

toms or signs suggesting connective tissue diseases such as Sjögren's syndrome. Anti-nuclear antibodies and anti-Sm antibodies were absent.

Conservative treatment with adequate hydration and analgesics (ketorolac and tramadol hydrochloride) was administered. Her symptoms and follow-up CSF study improved (Eo 27% and WBC count 140/ μ l). She suffered no neurologic problems over the next 2 years.

Discussion

The predominance of Eo in CSF was not accompanied by PEO in our series. As no specific etiologies were identified and latent etiologies were excluded by benign clinical courses and uneventful follow-ups, our cases were designated as idiopathic EM without PEO.

Symptomatic cases of EM without PEO are rarely reported in the literature [3–9]. Etiologies include *Angiostrongylus cantonensis* infestation, Hodgkin's lymphoma (HL), and medications such as ciprofloxacin and ibuprofen.

In a case series of *A. cantonensis* infestations, only 1 out of 17 cases could be classified as EM without PEO [5]. Although Coxsackie B4 virus infection was found in one patient with a ventriculoperitoneal shunt, intra-ventricular administration of antibiotics could not be excluded as the cause of isolated CSF Eos [10]. In HL, EM without PEO was associated with CNS invasion and poor prognosis [6–9].

The blood-brain barrier may limit Eo proliferation within the CSF in cases receiving intra-ventricular drugs [11]. In HL, some reports have indicated that isolated CSF Eos may be mediated by interleukin production by tumor cells such as IL-5 and/or IL-3 [12]. However, the pathomechanism of isolated Eo proliferation within CSF remains uncertain in non-HL cases and in our idiopathic cases. Although immunologic derangement could be considered in case 3, isolated CSF Eos was not explainable by peripheral anti-SSA antibody in addition to the presence of the antibody in normal population [13].

Most reported cases of EM without PEO presented with headache and fever and were treated conservatively [5], or by the discontinuation of offending drugs [3, 4], except HL. The clinical features of our cases were similar to those of symptomatic cases besides multiple cranial neuropathies in case 1, which was not reported in the literature. Although one patient (case 1) was treated with steroids, as other patients showed spontaneous improvement, steroid treatment may be reserved for later use in idiopathic EM without PEO.

To our knowledge, idiopathic EM without PEO has not been reported previously. Further studies are needed to investigate the mechanism of isolated CSF Eos without PEO.

Disclosure Statement

The authors declare that they have no vested interest that could be construed to have inappropriately influenced this study.

References

- Kuberski T: Eosinophils in cerebrospinal fluid: criteria for eosinophilic meningitis. *Hawaii Med J* 1981;40:97–98.
- Lo Re V 3rd, Gluckman SJ: Eosinophilic meningitis. *Am J Med* 2003;114:217–223.
- Asperilla MO, Smego RA Jr: Eosinophilic meningitis associated with ciprofloxacin. *Am J Med* 1989;87:589–590.
- Quinn JP, Weinstein RA, Caplan LR: Eosinophilic meningitis and ibuprofen therapy. *Neurology* 1984;34:108–109.

- 5 Tsai HC, Liu YC, Kunin CM, Lee SS, Chen YS, Lin HH, Tsai TH, Lin WR, Huang CK, Yen MY, Yen CM: Eosinophilic meningitis caused by *Angiostrongylus cantonensis*: report of 17 cases. *Am J Med* 2001;111:109–114.
- 6 Strayer DR, Bender RA: Eosinophilic meningitis complicating Hodgkin's disease. A report of a case and review of the literature. *Cancer* 1977;40:406–409.
- 7 Patchell R, Perry MC: Eosinophilic meningitis in Hodgkin disease. *Neurology* 1981;31:887–888.
- 8 Hollister D Jr, Clements M, Coleman M, Petito F: Eosinophilic meningitis in Hodgkin's disease. report of a case and review of the literature. *Arch Intern Med* 1983;143:590–592.
- 9 Calame JJ, van't Wout JW, van Dijk JG, Bots GT: A case of eosinophilic meningo-encephalitis accompanied by eosinophilic inflammation of the myenteric plexus in Hodgkin's disease. *Histopathology* 1986;10:535–539.
- 10 Weller PF, Liu LX: Eosinophilic meningitis. *Semin Neurol* 1993;13:161–168.
- 11 Chesney JC, Hoganson GE, Wilson MH: CSF eosinophilia during an acute coxsackie B4 viral meningitis. *Am J Dis Child* 1980;134:703.
- 12 Simon D, Simon HU: Eosinophilic disorders. *J Allergy Clin Immunol* 2007;119:1291–1300; quiz 1301–1302.
- 13 Franceschini F, Cavazzana I: Anti-Ro/SSA and La/SSB antibodies. *Autoimmunity* 2005;38:55–63.