Sri Lanka Journal of Medicine **SLJM**

Case Report

Citation: Kankananarachchi I, Vithanage ND & Silva KDN, et al., 2021. Childhood Eosinophilic Meningitis: Two case reports. Sri Lanka Journal of Medicine, pp 133-137.
DOI: http://doi.org/10.4038/sljm.v30i2.296

Childhood Eosinophilic Meningitis: Two Case Reports

Kankananarachchi I[1], Vithanage ND[2], Silva KDN[3], Liyanarachchi N[4] & Jayantha UK[5]

[1,4,5]Faculty of Medicine, University of Ruhuna
[2,3]University Paediatric Unit, Teaching Hospital Karapitiya

Correspondence: Kankananarachchi I
Senior Lecturer Paediatrics
Faculty of Medicine, University of Ruhuna
E-mail: imalke462@gmail.com
: https://orcid.org/0000-0002-9351-2966

Abstract

Introduction: Eosinophilic meningitis (EM) is a rare form of meningitis caused by parasitic infestations, Hypereosinophilic syndrome and neoplasms.

Case Presentation: We present two EM cases with no clear evidence of parasitic infestation or malignancy, who responded well to steroid treatment. Both of the patients presented with high-grade fever and features of central nervous system involvement. Both patients had moderate to severe Eosinophilia in blood and cerebrospinal fluid. The patients were treated with broad-spectrum intravenous antibiotics and anti-helminthic drugs with no improvement. However, there was a marked clinical improvement after commencing steroids.

Discussion: Even though the diagnosis of EM was made easily, we could not find an exact aetiology. However, both patients showed a remarkable improvement with our management and no deterioration was observed during the follow-up.

Keywords: Eosinophilic Meningitis, Steroids', Angiostrongyliasis, Hype eosinophilic syndrome

INTRODUCTION

Eosinophilic meningitis (EM) is an uncommon presentation in children, usually secondary to parasitic infestations. To diagnose EM, either absolute Eosinophils count in CSF should be >10/ Cu mm or percentage of Eosinophils should be >10%[1]. Angiostrongylysis and Gnathostomiasis are the most typical parasitic infestations leading to EM[2]. Hypereosinophilic syndrome and neoplasms are the other known causes of EM[2]. We report 2 cases of EM without any identifiable Parasitic infections who responded well to steroids.

CASE 01

A 9-month old baby presented with a history of fever of 5 days, and a left-sided focal seizure that lasted for 3 minutes. He had been having fever, irritability and vomiting for the last three days. On examination, he had bulging fontanelle without focal neurological signs. He was empirically started on IV Cefotaxime and IV Acyclovir for probable meningoencephalitis. His initial blood

Received: 2021-08-27 **Accepted revised version: 2021-11-22** **Published: 2022-01-25**

investigations revealed severe Eosinophilia (7174/µL) and elevated C-reactive protein (CRP) levels (96 mg/L).

Following the day of the admission, he developed another left-sided focal convulsion which lasted for 40 minutes. He was managed according to the standard advanced paediatric life support protocol. He was intubated and taken to the Intensive care unit for ventilation. A brain CT scan was done, which showed no abnormality and Magnetic Resonance Imaging (MRI) was not performed. He was extubated in 2 days and subsequently had a Lumbar puncture. The lumbar puncture which was done on day 4 of admission showed elevated white cells (1300 Cumm) with marked Eosinophilia (572/µL). With the given presentation, focus history was obtained to rule out a possible parasitic infestation.

Table 1: Investigation summary of Case 01

		Day1	Day 4	Day 22	Day 25
FBC	White cell count (/µL)	21100	25400	16700	12300
	Eosinophil count (/µL)	7174	8116	7980	1500
	Haemoglobin (g/dL)	8.4	9.4	9.1	10.2
	Platelet (10^3x µL)	522000	518000	498000	356000
CSF	WBC (µL)		1300		36
	Lymphocytes (/µL)		574		18
	Eosinophils (/µL)		570		08
	Neutrophils (/µL)		156		10
	Protein (mg/dL)		73		44
	CSF glucose (mg/dL)		44		65
	Random Blood sugar (mg/dL)		82		108

The child was from an average social-economic background, and there was no history of ingestion of pork, lizard meat or snails. The mother denied any history of Pica or the possibility of ingestion of rat faeces. There was no history of eczema, hay fever or atopy. There was no contact history of tuberculosis. There was no recent history of travel abroad. His immunization is up to date and the last vaccine was given at the age of 6 months. There was no family history of Eosinophilia. There was no evidence of pigmented lesions suggestive of melanoma. He did not have positive antibodies for Filaria, Mycoplasma, Toxoplasma and Toxocara. Microfilariae were not isolated in thin and thick films done at night. CSF was stained for parasites but none were isolated and the CSF cytology did not reveal any malignant cells. Fungal studies were not done in the CSF. His HIV screening was negative, and there were no features to suggest congenital immunodeficiency. Vasculitis screening was not carried out since there were no other supportive findings. His urine full report did not show any red blood cells or proteinuria. His Chest X-ray (CXR) was normal. The stool smear did not show amoeba, cysts or ova. However, the child was given a course of Antihelminthic (AH) treatment with Diethyl Carbamazine (DEC) and Mebendazole.

His blood, urine and CSF cultures did not grow any organisms. He continued to have a fever and remained ill despite being on IV antibiotics and AHs. His subsequent FBCs showed persistent severe Eosinophilia even after commencing on AHs. (Table 01)

He underwent bone marrow examination which was in favour of reactive Eosinophilia without any features suggestive of haematological malignancy. His Ultrasound scan of the abdomen and 2D Echo cardiograph were normal. Antibiotics and AHs were stopped, and he was started on Prednisolone on day 22 of admission. Within 48 hours of steroid therapy, his fever subsided, and peripheral Eosinophilia was improved. He had another lumbar puncture one week after steroids and which showed an Eosinophil count of 08/ µL. The steroids were continued for two weeks at a dose of 2mg/kg/day and then tailed off over another 2 weeks. He was followed up in the clinic for another 1-year duration, and his serial blood counts remained normal.

CASE 02

A 2-year-and-10-month-old boy presented with fever for 7 days and drowsiness, headache and vomiting for three days' duration. On admission, he was drowsy and ill-looking, but neck stiffness or Kernig signs were not there. He did not have any focal neurological signs, and on admission, he was started on IV Cefotaxime. His full blood count on admission revealed moderate Eosinophilia (1203/µL).

He had a lumbar puncture on day 2 of admission, which showed a high WBC (905 Cumm) count with an Eosinophil count of 498/µL. His CRP and ESR levels were 5mg/L and 08 mm/1st hour respectively.

Similar to case number 1, history was negative for contaminated food consumption, atopic diseases, recent travel history, contact history of tuberculosis or features of congenital immunodeficiency. Screening with antibodies, microscopy of blood and faecal smears for possible infectious aetiologies were also negative for the organisms mentioned in case one. His immunization was up to date and the last vaccine was given at the age of 18 months. Parents denied any family history of Eosinophilia. There was no evidence of pigmented lesions suggestive of melanoma. CSF was stained for parasites but none were isolated and the CSF cytology did not reveal any malignant cells. Fungal studies were not done in the CSF. He had no positive antibodies for Filaria, Mycoplasma, Toxoplasma and Toxocara. Thin and thick blood films done at midnight did not isolate any Microfilariae. His HIV status was negative, and he had no recurrent infections in the past. His stool smear did not show amoeba, cysts or ova. Vasculitis screening was not carried out and the urine full report did not show any haematuria or proteinuria. Though there was no identifiable parasitic aetiology, he was started on Albendazole 15mg/kg for five days for which he had no clinical improvement.

A CT scan of the brain was carried out and did not show any abnormality and an MRI scan of the brain was not performed. There was no abnormality found in the CXR. Bone marrow examination showed no features of haematological malignancy. On day 14 of admission, he was started on Prednisolone 2mg/kg for which he made a remarkable clinical and haematological improvement. Her repeat lumbar LP and FBC done two weeks later (day 28) showed no Eosinophilia. (Table 02). Steroids were tailed off and follow in the paediatric clinic was arranged.

Table 2: Investigation summary of Case 02

		Day1	Day 2	Day 10	Day28
FBC	White cell count (µL)	121600		8050	7890
	Eosinophil count (µL)	1204		1047	450
	Haemoglobin (g/dL)	14.1		13.8	13.9
	Platelet (10^3x µL)	522000		388000	423000
CSF	WBC (µL)		585	905	05
	Lymphocytes (µL)		310	389	04
	Eosinophils (µL)		262	498	00
	Neutrophils (µL)		13	18	01
	Protein (mg/dL)		585	520	34
	CSF glucose (mg/dL)		49	54	62
	Random blood sugar (mg/dL)		91	96	101

DISCUSSION

The most common cause of EM is parasitic infestations; Angiostrongylysis is the leading cause of EM worldwide[2]. The definitive host of the Angiostronglysis is rats, whereas land snails and slugs act as the intermediate host. Prawns, crabs and frogs are considered paratenic hosts of the parasite. Ingestion of raw meat of intermediate or paratenic host results in the human transmission of Angiostrongylysis[3]. However, in both cases, there was no history suggestive of the ingestion of

suspected animals. Gnathostomiasis is another common cause of EM. Cats and dogs are the definitive hosts of Gnathostoma infection, whereas fish, snakes, frogs, fowl and pigs are the paratenic hosts. Both children consume cooked fish and denied ingestion of any other suspected food Apart from the parasites mentioned above, Toxocariasis, Schistosomiasis, Hydatidosis and Strongyloidiasis are identified as potential EM causes[4]. There was no serological evidence of Toxocariasis. However, the serology, microscopy of the blood and faecal smears were negative for common pathogens as mentioned above.

In EM, identifying the parasite in the CSF is challenging since the organisms are not easily isolated in the CSF. In a case series reported by Tsai et al. in 2000, only 2 out of 50 taps in 17 patients had isolated Angiostrangylysis species in CSF. Similarly, it is unusual to identify a larve of Gnathostomiasis in the CSF[5]. Though serological tests can be used to identify parasites, these tests are not available in Sri Lanka. Both these patients were treated with anti helminthics empirically, but there was no clinical response. However, both patients showed significant improvement after starting steroids. The lack of response to anthelminthic treatment and subsequent response to steroids may indicate a primarily steroid-responsive process other than infection. However, eosinophilia may be driven by an inflammatory/allergic response to parasitic infection and the antigens released by the dying organisms due to anthelminthic medication may have maintained the CNS inflammation. Even a degree of paradoxical worsening of clinical status upon parasitic treatment is described in the literature. The lack of response to AH treatment in our cases may represent the above phenomenon. The one-year follow up in case one without recurrence may be due to empirically completely treated unidentified parasitic infection with subsequent resolution of inflammation with steroids, any other monophasic steroid-responsive illness as the patient is stable off steroids or any steroid-responsive illness with possible long term remission in-between episodes. Fungal infection is less likely given the non-worsening of the clinical picture despite steroid treatment in absence of antifungal treatment.

Malignancies, drug reactions and hypereosinophilic syndrome are possible non-parasitic causes of EM[2]. Rarely fungal infections can cause EM (coccidioidal or cryptococcal meningitis)[1] and Primary CNS vasculitis with EM is described in the literature in an adult patient[6]. Neurosarcoidosis rarely can show eosinophilic CSF despite the usual norm of lymphocytic response. We have ruled out haematological malignancy by doing bone marrow examinations of both children. There was no history to suggest drug-related eosinophilia. CXR and serum calcium levels were not suggestive of sarcoidosis which is a steroid-responsive condition that is very rare in the Sri Lankan context and rarely known to cause CSF eosinophilia.

Since there was an excellent response to steroids and non-apparent alternative causative factors, hypereosinophilic syndrome (HES) should also be entertained as a differential diagnosis. The diagnosis of HES should be made when there is no aetiology found for severe Eosinophilia irrespective of end-organ damage[7]. Under the umbrella term of HES, there could be various subcategories such as myeloproliferative, lymphocytic form, organ restricted Eosinophilia, chronic eosinophilic Leukemia, FIP1L1-PDGFRA(F/P)-associated clonal hypereosinophilia and Idiopathic forms[8]. Specific investigations used in the diagnosis of HES are F/P fusion gene using real-time Polymerase chain reaction (PCR), fluorescence in situ Hybridization (FISH) to look for the CHI2 locus, lymphocyte phenotyping, and analysis of T cell receptor (TCR) gene rearrangement patterns[8]. None of these investigations was performed on these two children due to financial constraints. HES can present with many neurological manifestations, and there are few reported cases of EM secondary to HES [9,10]. Corticosteroids, Hydroxycarbamide, Imatinib, Humanized and interferon-alpha are recognized modes of therapeutic modalities in HES[8].

Based on the current diagnostic criteria, there is a possibility to make the diagnosis of HES in these two patients; however, specific investigations to exclude parasitic and other secondary causes were not available in our resource-limited setting. Moreover, specific investigations to support the diagnosis of HES were not done due to limited

resources. Considering the overall picture, it is still possible that these two children had parasitic infestations and in the clinical context of our setup, empirical treatment covering the parasitic infection with added steroids may be needed based on the clinical judgement with close monitoring of response.

Author declaration
Acknowledgements
The authors would like to thank patients and their parents and the Department of Parasitology, Faculty of Medicine, University of Ruhuna.

Author Contributions
Imalke Kankananarachchi was involved with the management and writing of the manuscript. N D Vithanage and KDN Silva engaged with the management and the follow-up of patients. ND Liyanarachchi and UK Jayantha were involved with diagnosing the condition and revising the manuscript. All three authors revised the final manuscript.

Funding sources
No sources of funding were involved in this paper

Ethics approval and consent to participate
Informed written consent to publish the details of the patients were obtained from parents.

Competing interests
We declare no competing financial interests

REFERENCES

1. Re III VL, Gluckman SJ. Eosinophilic meningitis. The American journal of medicine. 2003; 114 (3):217-23. https://doi.org/10.1016/S0002-9343(02)01495-X
2. Ramirez-Avila L, Slome S, Schuster F, Gavali S, Schantz P, Sejvar J, et al. Eosinophilic Meningitis due to Angiostrongylusand Gnathostoma Species. Clin Infect Dis 2009; 48:322-7. https://doi.org/10.1086/595852
3. Cross JH, Chen ER. Angiostrongyliasis. InFood-borne parasitic zoonoses 2007 (pp. 263-290). Springer, Boston, MA. https://link.springer.com/chapter/10.1007/978-0-387-71358-8_8
4. Graeff-Teixeira C, da Silva AC, Yoshimura K. Update on eosinophilic meningoencephalitis and its clinical relevance. Clinical Microbiology Reviews. 2009;22(2):322-48. https://doi.org/10.1128/CMR.00044-08
5. Tsai, H. C., Y. C. Liu, C. M. Kunin, S. S. Lee, Y. S. Chen, H. H. Lin, T. H. Tsai, W. R. Lin, C. K. Huang, M. Y. Yen, and C. M. Yen. 2001. Eosinophilic meningitis caused by Angiostrongylus cantonensis: report of 17 cases. Am. J. Med. 111:109–114. Doi: 10.1016/S0002-9343(01)00766-5
6. Hirano K, Fukae J, Hieda S, Fujimaki M, Ishii H, Tsuboi Y, Kawamura M, Arai H, Hattori N. Eosinophilic meningitis caused by primary angiitis of the central nervous system. Internal Medicine. 2013;52(12):1393-6. PMID: 23774554 DOI: 10.2169/internalmedicine.52.9578
7. Simon HU, Rothenberg ME, Bochner BS, Weller PF, Wardlaw AJ, Wechsler ME, Rosenwasser LJ, Roufosse F, Gleich GJ, Klion AD. Refining the definition of hypereosinophilic syndrome. Journal of allergy and clinical immunology. 2010; 126(1):45-9. https://doi.org/10.1016/j.jaci.2010.03.042
8. Roufosse FE, Goldman M, Cogan E. Hypereosinophilic syndromes. Orphanet journal of rare diseases. 2007; 2(1):1-2. http://www.OJRD.com/content/2/1/37
9. Weingarten JS, O'Sheal SF, Margolis WS. Eosinophilic meningitis and the hypereosinophilic syndrome. Case report and review of the literature. The American journal of medicine. 1985; 78(4):674-6. https://doi.org/10.1016/0002-9343(85)90412-7
10. Chou CW, Hsu SP, Chen MT, Chen MH, Shih YH, Lee LS, Lin CF. Idiopathic hypereosinophilic syndrome with infiltration of cerebrospinal fluid by immature eosinophils: a case report and literature review. Surgical neurology. 2007;68:S52-5. PMID: 17963925, DOI: 10.1016/j.surneu.2007.01.077