

CLINICAL CHARACTERISTICS, PARACLINICAL, AND TREATMENT RESULTS OF EOSINOPHILIC MENINGITIS IN CHILDREN: A CASE SERIES

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ABSTRACT

Background: Recognizing clinical and paraclinical reduce morbidity and mortality from this disease. **Objective:** To investigate the association of factors, clinical and paraclinical characteristics, and treatment outcomes of Eosinophilic meningitis. **Materials and methods:** Reports on a series of diseases detected with eosinophilic meningitis at the Department of Infectious Diseases at Can Tho Children's Hospital. **Results:** the cause of admission was usually intermittent headache, fever, and vomiting. Neurological symptoms include lethargy, and a stiff neck, no focal neurological damage was noted. White blood cells count in the peripheral blood slightly increased or normal; increased number of cerebrospinal fluid white blood cells; no larvae was found in the CSF; ELISA technique to find parasite antigens in blood detected all 3 cases positive for *Toxocara* spp. The drugs were treated include Ceftriaxone, Vancomycin, Imipenem, Albendazole, and Prednisolone. All cases got stable treatment results and hospital discharge after treatment **Conclusion:** Eosinophilic meningitis, although rare, can occur and it is easy to miss the diagnosis in the early stages. Treatment with anthelmintics and steroids can be effective.

Keywords: eosinophilic meningitis, *Toxocara* spp

I. INTRODUCTION

Vietnam is a favorable condition for parasitic diseases to develop, including eosinophilic meningitis. The clinical presentation of eosinophilic meningitis is diverse. Proper recognition and treatment of eosinophilic meningitis reduces morbidity and mortality from this disease. To date, clinical studies on eosinophilic meningitis in children have not been performed in the world as well as in Vietnam, so we conduct research on this topic.

II. MATERIALS AND METHODS

2.1. Materials

2.1.1 Study population: All pediatric patients were diagnosed with eosinophilic meningitis at the Department of Infectious Diseases at Can Tho Children's Hospital from June 30, 2021 to June 30, 2022.

2.1.2 Inclusion criteria: The study population inclusion criteria included a diagnosis of meningitis: fever, headache, vomiting, stiff neck, Kernig (+); consciousness disturbances (somnolence, somnolence, coma), convulsions, focal neurological signs and Cerebrospinal fluid test: CSF has > 10% eosinophils in the total white blood cell count or more than 10 eosinophils/mL.

2.1.3 Exclusion criteria: Patients with comorbidities that cause erroneous test results such as: cerebral palsy, blood diseases causing eosinophilia.

2.2. Methods

2.2.1 Study design: The study was conducted by case series reporting method.

2.2.2 Study contents: All patients who met the inclusion criteria were recorded in the prepared medical record form information on age, gender, history, time of hospitalization, place of residence, epidemiological characteristics, characteristics clinical and subclinical. Record the results of the tests: Blood count, cerebrospinal fluid test (biochemistry, cell), look for parasite antigens in the blood, drugs and dosage.

III. RESULTS

The results recorded 3 cases of eosinophilic meningitis at Can Tho Children's Hospital from June 2021 to June 2022, showing that:

3.1. Case 1

A 9-year-old male patient was admitted to the hospital because of a headache lasting 3 days, intermittent headaches on a background of bilateral temporal noises with fever (temperature unknown) and nausea-vomiting.

Undocumented about a history of contact with a patient with tuberculosis, not recently vaccinated, head trauma, ear discharge but had contact with domestic cats and dogs.

Vital signs (fever 38.9 °C, respiratory rate 41 breaths/min, pulse 62 beats/min and blood pressure 105/60 mmHg). Feeling sluggish, neck strained. The total leukocyte count in the peripheral blood was $9.99 \times 10^9/L$ with eosinophil elevation accounting for 17.9%. Cerebrospinal fluid test WC/ CSF 350/mm³, in which eosinophil accounted for 38%, protein 0.56g/L and glucose 4.3 mmol/L. The patient was started on empiric antibiotic therapy with Ceftriaxone 100mg/kg/24h intravenously, plus Vancomycin 60mg/kg/24h. Then, perform ELISA enzyme immunoassay to find parasite antibodies in the blood that are positive for *Toxocara* (canine and cat roundworm). This suggests the cause of eosinophilic meningitis by *Toxocara ssp.*

The patient was treated with Albendazole 400mg/day for 10 days and Prednisolone 1mg/kg/day. After 8 days, eosinophil counts in peripheral blood and in CSF improved. The patient showed a clinical improvement in the disappearance of symptoms. The subclinical manifestations of blood count and cerebrospinal fluid are described in Table 1. Ceftriaxone was discontinued after 10 days and vancomycin after 9 days of treatment. The patient was discharged and continued to take the prescription drug Albendazole 200mg for an additional 11 days and Prednisolone 5mg for an additional 4 days.

3.2. Case 2

A 67-month-old boy was admitted to the hospital because of vomiting, once a day, with a low-grade fever (temperature unknown) lasting 4 days, 2 days before admission, he had anorexia, and headache that did not subside. This patient has a history of exposure to domestic cats and dogs.

Vital signs are normal (temperature 38°C, blood pressure 110/60 mmHg, pulse rate 70 times/min, respiratory rate 28 breaths/min). Dizziness, infectious facial expression, stiff neck, light reflection (+).

White blood cell count is $14.3 \times 10^9/L$ with eosinophil increase accounting for 5.67%. The amount of WC/CSF 470/mm³, Eosinophil accounted for 7%, protein increased 0.6 g/l, glucose 2.9 mmol/L within normal limits. Received empiric antibiotic therapy with ceftriaxone and vancomycin. After 4 days of treatment, there was no clinical response, the patient was assigned to repeat CSF and the amount of WC/CSF 1310/mm³, eosinophil

accounted for 53%, protein increased 0.64g/L and normal glucose 2.4 mmol/L. Immunosorbent ELISA for parasite antibodies in the blood was positive for Toxocara.

Patients were treated with antibiotics Meropenem 120mg/kg/day for 14 days and vancomycin 60mg/kg/day for 21 days, a combination of Albendazole 400mg/day for 3 weeks and Prednisolone 1mg/kg/day (2 weeks). After 25 days of treatment, the patient showed clinical recovery and decreased eosinophils on the blood count.

3.3. Case 3

A 5-year-old male patient was admitted to the hospital with headache, recurrent headache on a background of bilateral temporal noise, fever (temperature unknown), and nausea-vomiting 1 day before admission. The patient has a history of contact with dogs and cats.

Vital signs were recorded (temperature 38 ° C, pulse 90 beats/min and blood pressure 90/60 mmHg). The patient had stiff neck.

White blood cell count is $9.33 \times 10^9/L$, eosinophil increase accounts for 20.8%. The amount of WC/ CSF increased by 930/mm³, of which eosinophils accounted for 22.6%, protein increased by 0.7g/L, and glucose was 2.2 mmol/L. Blood and cerebrospinal fluid cultures do not grow bacteria. The patient was treated with empiric antibiotic with Ceftriaxone 100mg/kg/24h. Detection of parasite antibodies in the blood positive for Toxocara spp by ELISA suggests Toxocara eosinophilic meningitis.

The patient was treated with Vancomycin 60mg/kg/24h for 11 days (due to day 11 of antibiotic allergy) and Imipenem 120mg/kg/24h for 21 days in combination with Albendazole 400mg/day for 21 days and Prednisolone 0.5mg/kg/day for 2 weeks. The patient's clinical symptoms improved. The clinical and subclinical manifestations of the blood count and cerebrospinal fluid are described in Table 1.

Table 1: Clinical manifestations, subclinical and treatment

Characteristics		Case 1	Case 2	Case 3
Clinical	Fever	37- 38.9 ° C	37 ° C- 38 ° C	37- 38 ° C
	Headache	Appeared 3 days before admission It gradually decreased after 4 days of treatment and ended after 8 days of treatment.	Appeared 2 days before admission Increase on the 3rd day of treatment Decrease and disappear from the 4th day of treatment.	Appeared 1 day before admission It gradually decreased after 2 days of treatment and ended after 10 days of treatment.
	Vomiting	-4 days -Done after 1 day of treatment	-5 days -Done after 1 day of treatment	(-)

Characteristics		Case 1	Case 2	Case 3	
	Constipation	(-)	(-)	-5 days - Constipation gone after 2 days of treatment	
Examination	<i>Sense Kernig</i> <i>Brudzinski</i> <i>Stiff neck</i>	Languid (-) (-) 3 days	Languid (-) (-) 20 days	Conscious (-) (-) 2 days	
Test	CBC	Increased eosinophils	Increased eosinophils	Increased eosinophils	
	C S F	<i>Appearance</i> <i>Protein</i> <i>Glucose</i> <i>White cell count</i> <i>Pandy</i>	Clear 0.56 g/L 4.3 mmol/L 350/mm ³ ; eosinophil 38% (+)	Clear 0.64 g/L 2.4 mmol/L 1310/mm ³ ; eosinophil 53 % (+)	Clear 0.7 g/L 2.2 mmol/L 930/mm ³ ; eosinophil 22.6% (+)
	ELISA for antibodies in blood	(+) <i>Toxocara spp</i>	(+) <i>Toxocara spp</i>	(+) <i>Toxocara spp</i>	
Treatment	Number of days	10	25	21	
	Medicine	Antibiotics: Ceftriaxone and Vancomycin Antihelminthic: Albendazole Anti-inflammatory: Prednisolone	Antibiotics: Imipenem and Vancomycin Antihelminthic: Albendazole Anti-inflammatory: Prednisolone	Antibiotics: Ceftriaxone and Vancomycin Antihelminthic: Albendazole Anti-inflammatory: Prednisolone	

IV. DISCUSSION

4.1. General features

Children aged 5-9 were admitted to the hospital in late August, early September. All of them were in rural areas, and children were exposed to cats and dogs frequently. In children, the habit of not washing hands before eating is also an important factor in causing illness in children.

4.2. Clinical features

Headache is a common presentation in the literature and was present in all 3 cases in this study. Location on both sides of the temples and forehead. Ho Thi Hoai Thu's study has the most headaches in the occipital and frontal areas [3].

Fever was recorded in all 3 cases with the highest temperature of about 38 - 38.9 o C. After being treated for about 1 day, the temperature decreased around 37 - 38 o C. Mild but prolonged fever. This result is different from Ho Thi Hoai Thu's study, where 63% of subjects showed fever [3].

Vomiting in all 3 children and resolved after 6 hours to 2 days after treatment. This rate is relatively high in Kittisak's study (63.2%) [5]. Mild vomiting, frequency less than once a day, may appear a few days before or on the same day of admission.

Consciousness lethargy in 2 children at the time of admission, resolved after 2 hours and 1 day, respectively. Neck strain in 3 cases; in which, 2 cases of neck strain after 3, 4 days of treatment, 1 case of neck strain after 20 days of treatment. In Kittisak's study, the occurrence of a stiff neck at the time of admission was 68% [5]. We did not record localized nerve damage. This rate is also not high in the previous study of Ho Thi Hoai Thu, which appeared to be 7% [3].

In all 3 cases, there were no symptoms of somnolence, coma, convulsions, ophthalmoscopy, Kernig (-), Brudzinski (-), light reflex (+).

4.3. Paraclinical features

White blood cells and eosinophils in the blood increased in all 3 cases, the rate ranged from 5.67 to 20.8%, the absolute number of eosinophils in the blood increased from 810-1940 cells/mm³. Thus, the absolute value and percentage of eosinophil in the blood both increased, compared with the study of Pham Nhat An was 8% [7] and Kittisak was 20% [5]. In Hwang F's study, 85% of patients had eosinophil/blood $\geq 10\%$ [4], we noted that 2/3 of patients had eosinophil/blood $\geq 10\%$. All 3 cases had eosinophil/blood > 500 cells/mm³, compared with 85.2% in Ho Thi Hoai Thu's study [3]. Thus, eosinophil/blood increase to a certain threshold will become a sign suggesting eosinophilic meningitis [2], [6].

Elevated white blood cells/CSF, ranging from 350-1310 cells/mm³, as in the case of purulent meningitis, is easy to diagnose for pyelonephritis if the treating physician does not pay attention to the suggestion of eosinophil in the patient's CSF. Eosinophil values in CSF ranged from 133-694 cells/mm³, accounting for 22.6-38%. There was 1 case at admission, eosinophil did not increase in CSF, however, after 4 days, eosinophil increased. This helps us to realize that the timing of CSF puncture is also very important, and to monitor treatment.

No larvae were found in the CSF. According to the literature, it is very rare to find larvae of *A. cantonensis*, *Toxocara spp*, and *Gnathostoma spp* in CSF and this study is no exception. This is similar to the study of Ho Thi Hoai Thu, Hwang FP found only 1 patient out of 87 eosinophil patients with *A. Cantonensis* larvae in the cerebrospinal fluid by pumping method.[2] [4]. The enzyme immunoassay technique ELISA to find parasite antigens in the blood detected all 3 cases positive for *Toxocara spp*. This helps to suggest the causative agent.

4.4. Treatment

Antibiotics are used for 14-21 days. Ceftriaxone dose is 100mg/kg/24h once a day when the patient has just been hospitalized and monitored for meningitis. After the CSF

results, Vancomycin dose is 60mg/kg/24h divided into 3 times a day in combination with Meropenem 120mg/kg/day or Imipenem 120mg/kg/24h; Albendazole 400mg/day divided into 2 times a day for 21 days; Prednisolone 5mg dose 1mg/kg/day once a day for 14 days. In the study by Chotmongkol et al. also found that 2-week use of prednisolone reduced persistent headache or less need for lumbar puncture to relieve symptoms[1]. Empiric antibiotic therapy was done because the initial diagnosis of the 3 cases above could not be identified with eosinophilic meningitis at the beginning time.

After using the above drugs at the dosage and maintenance according to the recommended number of days, the patient's general condition is stable, no headache, vomiting, soft neck. Patient is discharged.

V. CONCLUSION

Eosinophilic meningitis, although rare, can occur. History of exposure to cats and dogs may suggest the cause. Treatment with anthelmintics and steroids can be effective.

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