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Letter to the Editor: New Observation

Eosinophilic Meningitis with Unique Imaging Changes Diagnosed by Next-Generation Sequencing

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Angiostrongylus cantonensis, a zoonotic pathogenic nematode, occasionally causes human angiostrongyliasis characterized by eosinophilic meningitis.[1] Because of the severity, achieving definitive diagnosis and receiving appropriate treatment as early as possible is essential for patients to survive.[2] Unfortunately, clinical manifestation and imaging findings of eosinophilic meningitis frequently are atypical, and that the less effective definitive laboratory tests have been a great challenge for clinicians to diagnose. However, next-generation sequencing (NGS) is an emerging method with the potential of pan-pathogen detection for central nervous system infections and has been successfully tested in proof-of-concept case studies.[3] Here, we report a case of eosinophilic meningitis caused by *A. cantonensis* with unique imaging changes and diagnosed by NGS finally. According to the data of Ningbo Center for Disease Control, this is the first case of angiostrongyliasis in Ningbo Zhejiang.

A 56-year-old female was admitted to the neurology department with headache associated with fever (38.0°C) for 1 week. She had medical history of hypertension. On initial neurological examination, only neck stiffness was observed. Acute computed tomography showed no obvious abnormalities. Subsequently, enhanced magnetic resonance imaging (MRI) of the brain revealed abnormal signal in the right frontotemporal cortex but no enhancement. And electroencephalogram suggested a moderate abnormality. Therefore, the initial diagnosis of meningitis was suspected and lumbar puncture was carried out. Cerebrospinal fluid revealed 443 leucocytes/μl, total protein 0.936 g/L, and laboratory tests for herpes virus, cytomegalovirus, bacteria, acid-fast bacilli, cryptococcosis, human immunodeficiency virus, and autoimmune encephalitis antibody-associated were negative. However, we found that the serum eosinophil count increased from 2.63 to $5.10 * 10^9$/L (reference level $<0.52 * 10^9$/L) within 2 days. Meanwhile, the patient became unresponsive and unable to establish a response. Moreover, neurological examination indicated muscle strength of the extremities decreased progressively to grade two, but signs of pyramidal tract dysfunction was not observed. Whereafter, reexamination of brain MRI was arranged immediately and indicated multiple abnormal signals in the right frontotemporal cortex and bilateral deep white matter, and the lesions were migratory compared with previous images (Figure 1). The diagnosis of parasitic meningitis was highly suspected and NGS for pathogenic microorganisms of cerebrospinal fluid implemented instantly. High-throughput sequencing disclosed *A. cantonensis* infection (Figure 2). We further asked family members whether the patient eat any raw food recently and they answered that there is a folk prescription eating raw slugs treatment for hoarseness in local area. So the patient ate a little of raw slugs within 2 months. Taken together, the diagnosis of eosinophilic meningitis caused by *A. cantonensis* was definite, and the patient received treatment with oral administration of albendazole (200 mg/day for 2 weeks), as well as intravenous dexamethasone (10 mg/day) followed by oral prednisone and mannito. After 2 weeks of treatment, the patient's headache was relieved and muscle weakness improved significantly.

Angiostrongylus cantonensis is one of the most common pathogens to cause eosinophilic meningitis characterized by headache (95%), neck stiffness (46%), paraesthesia (44%),vomiting (38%), and fever (32%).[4] It is transmitted by definite hosts of rats, intermediate hosts of snails or slugs, and some other transport hosts such as frogs, lizards, and crabs.[5] People can be infected by eating, both deliberately and inadvertently, undercooked or raw intermediate hosts. This patient becomes infected through intentionally consuming raw slugs. Radiologic abnormalities in eosinophilic meningitis is described rarely because of the location and size of lesions varied, which is probably related to the number of larvae and their movements.[6] In this case, the brain MRI indicates migration trajectories of larvae and lesions are migratory compared with previous images. NGS, an unbiased molecular diagnostic technology, is increasingly being applied to investigate central nervous system infections, especially unexplained infections.[7] In the case, antibody-detecting ELISA for parasites in cerebrospinal fluid was negative. The reason probably that antibody detection could not reveal the early stage of infection or the limitations in sensitivity of ELISA. Compared to traditional detection method (ELISA), NGS can simultaneously detect thousands of pathogenic microorganisms including parasites, bacteria, fungi, and viruses within a short time and have a sharp specificity and a high sensitivity.[8,9] This case confirmed the diagnosis without delay being based on

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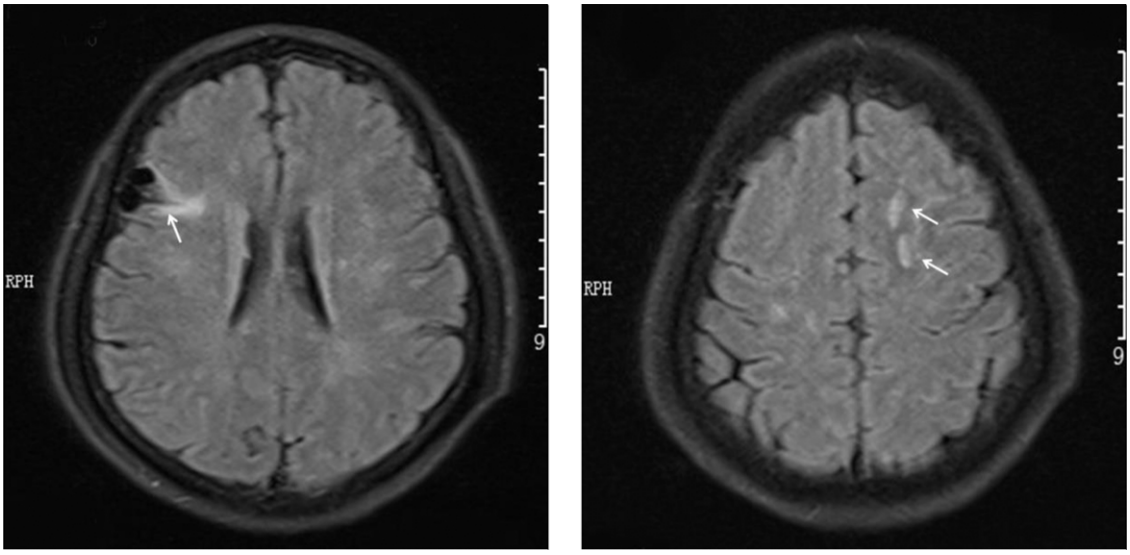

Figure 1: T2-FLAIR magnetic resonance imaging showed abnormal signal in the right forntotemporal cortex-like track sign and in the left centrum semiovale as oval shape sign (white arrow).

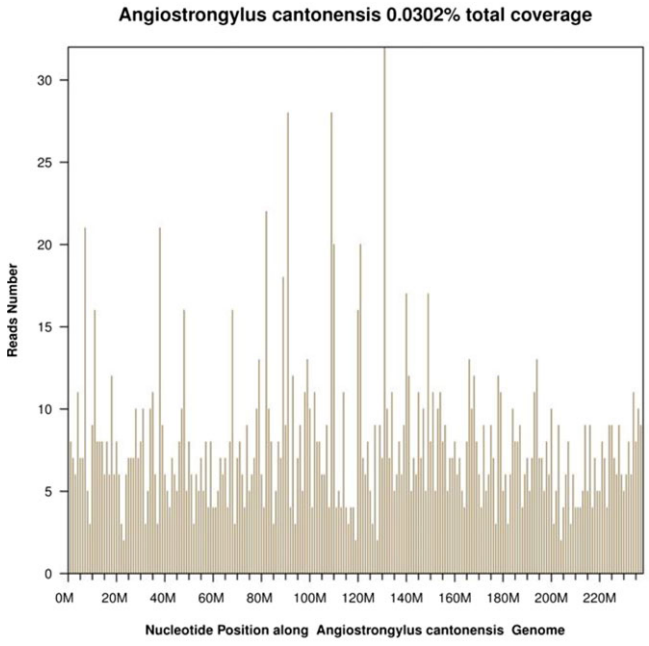

Figure 2: Next-generation sequencing (NGS) of Angiostrongylus cantonensis in the patient's cerebrospinal fluid and the result of NGS showed 1151 reads corresponding to the parasite with a coverage of 0.0302%.

NGS and achieved a favorable prognosis finally. In conclusion, parasitosis should be considered when the patient had eosinophil elevation and migratory intracranial lesions. NGS of cerebrospinal fluid will enable a timely and accurate etiological diagnosis.

Conflict of Interest. The authors have no conflicts of interest to declare.

Statement of Authorship. JQC and WNF were all involved with the drafting and editing of this manuscript.

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