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Original Article

Imaging manifestations and diagnosis of a case of adult cerebral paragonimiasis with the initial symptom of hemorrhagic stroke

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Abstract: This study is to investigate the clinical features, neuroimaging and diagnosis of adult cerebral paragonimiasis. One case of patient with cerebral paragonimiasis as retrospectively analyzed in this study. Analysis included medical history, clinical manifestations and neuroimaging. Blood test, body fluid examination, immunological test, stool examination and imaging examination were performed. Many symptoms such as headache, hemiplegia, chest pain, cough, and pleural effusion were detected in the patient. The features of "tunnel-like shape" and "ring-like shape", the intracranial hemorrhage and edema were shown by CT and MRI imaging. Chest CT examination revealed pleural effusion. Eosinophil count of peripheral blood and pleural effusion increased. Lung fluke ELISA test was positive and anti-parasitic treatment was effective. The typical clinical manifestations of MRI of cerebral paragonimiasis, such as the "tunnel-like shape" and "ring-like shape", were of high diagnostic value. And, blood eosinophil count examination and paragonimiasis antibody test could also help the diagnosis value.

Keywords: Cerebral paragonimiasis, neuroimaging, eosinophilic granulocyte

Introduction

Paragonimiasis is a zoonotic parasitic infection caused by the lung fluke, which is widely distributed around the world. Cerebral paragonimiasis is the most serious form of extra-pulmonary paragonimiasis. About 20-45% patients with paragonimiasis have cerebral paragonimiasis. Humans are infected by the lung fluke through eating raw or undercooked freshwater crabs or crayfish (which are the second intermediate host of bronchial fluke) that are infected with metacercariae of the fluke, or directly drinking lung fluke polluted water.

The metacercariae exocyst in the duodenum, penetrate through the intestinal wall into the peritoneal cavity, then through the abdominal wall and diaphragm into the lungs, where they become encapsulated and develop into adults. Both of the adults and larvae of the lung fluke have the invasive and harassing habits. They can invade many organs (such as the lung, the thoracic cavity, the abdominal cavity, the pelvic cavity, the diaphragm, and the brain) and the subcutaneous tissues, thus causing corresponding symptoms [1, 2]. Once in the lung or ectopic site, the worm stimulates an inflammatory response that allows it to cover itself in granulation tissue forming a capsule. These capsules can ulcerate and heal over time. The larvae and adults of the lung fluke may cause direct mechanical damage or indirect damage caused by immunopathologic responses to the human body.

In this study, the clinical manifestations of a case of patient diagnosed as paragonimiasis were investigated. The process of diagnosis and treatment were analyzed by studying the characteristics of brain imaging and cerebrospinal fluid.

Materials and methods

Patients' data

A male patient of 35 years old was enrolled in this study. He had the hobby of eating raw

crabs, raw crayfish or drinking raw stream water. He was admitted to the hospital because of "sudden weakness in left limb and numbness with a headache for 1 day". Once admitted, physical examination was carried out. The general condition was listed as follows. Temperature: 36.7°C, Pulse: 76 times/min, Respiration: 20/min, and Blood pressure: 130/87 mmHg. The neurologic examination showed that he was conscious while taking the examination, with neck stiffness (-), Klinefelter syndrome (-) and cranial nerve (-). The left nasolabial groove was shallow. The muscle strength of the left upper limb was grade 0 and that of the left lower limb was grade IV. The muscle tension of the left limb decreased and the left upper limb showed hypoalgesia. The bilateral tendon reflex showed symmetric (+ +). The pathological signs of the left side were (+) and of the right side were (-). Blood pressure was in the normal range. Chest pain and paroxysmal dry cough appeared during the hospitalization, with no fever or night sweats.

Prior written and informed consent were obtained from the patient and the study was approved by the ethics review board of the First Affiliated Hospital of Wenzhou Medical University.

Blood tests

Peripheral white blood cell, eosinophilic granulocyte, erythrocyte sedimentation rate (ESR), and levels of IgE and C-reactive protein (CRP) in the serum were measured. Bone marrow cytology and biopsy was performed.

Body fluid examination

Pleural effusion and cerebrospinal fluid examinations were performed.

Immunological test

Diagnoses were confirmed by IgG enzyme-linked immunosorbent assays. ELISA test for the lung fluke was performed. IgG and IgM in the serum, the pleural effusion and the cerebrospinal fluid were examined.

Stool examination

Stool examination aimed at detection of the egg of the lung fluke was carried out.

Imaging examination

Conventional imaging examinations including chest CT, chest x-ray, head CT and head MRI were performed.

Therapeutic regimen

Pathogenic therapy was taken on the basis of symptomatic treatment.

Results

Changes of the blood

To find the cause of eosinophilia and exclude diseases such as leukemia, blood test was carried out. Progressive increase in the peripheral white blood cell and eosinophil counting were observed. The minimum and maximum value of white blood cell count was 8.33 × 10^9/l and 43.9 × 10^9/l. The minimum and maximum value of eosinophil count was 0.8 × 10^9/l and 37.0 × 10^9/l. The minimum and maximum values of ESR, CRP and serum IgE were 9 mm/h-63 mm/h, 9.79 mg/L-23.5 mg/L, and 187.56 IU/ml-3000 IU/ml, respectively. The bone marrow biopsy result did not support the diagnosis of eosinophilic leukemia. The results of blood test indicated that this patient was not leukemia and might have allergic diseases.

Result of body fluid examination

To identify whether or not the symptom was caused by tumor or microorganisms, body fluid examination was carried out. The pleural effusion was coffee color and cloudiness. The number of nucleated cells was 12160/ul and most of these nucleated cells were eosinophils (accounting for 76%). No tumor cells, acid fast bacilli, fungi or bacteria were found and carcinoembryonic antigen detection was negative. In the cerebrospinal fluid, the number of nucleated cells was up to 48/UL. Among these nucleated cells, the polymorphonuclear cells accounted for 2%, the eosinophils accounted for 8% and the lymphocytes accounted for 90%. And, up to 72.1% of these lymphocytes were activated. Number of red blood cell was 1/UL and cerebrospinal fluid (CSF) protein level was 655 mg/L. The content of glucose and chloride was normal. There were no bacteria, fungi, or cryptococcus neoformans in cerebrospinal fluid. In addition, acid fast bacilli smear and bacterial culture all were negative. These

Figure 1. The pleural effusion analyzed by chest CT imaging. Representative chest CT images were shown. The pleural effusion on the left side of chest was shown Arrows indicate pleural effusion. Chest CT imaging showed bilateral pleural effusion in the thoracic cavity (A, B). At 2 weeks after onset of the disease, the volume of the pleural effusion increased (C, D) and the volume of the pleural effusion increased larger at 1 month after onset of the disease (E, F).

results indicate that the symptom is caused neither by tumor nor by microorganisms.

Result of immunological test

To test whether the symptom was caused by the lung fluke, immunological test was performed. ELISA test showed that Paragonimus-specific IgG was both positive in serum and pleural effusion. However, Paragonimus-specific IgG was negative in cerebrospinal fluid. These results suggest that the patient may be infected by the lung fluke.

Result of stool examination

To further diagnose the infection of the lung fluke, stool examination was taken. No eggs were detected in the stool. By this result, the diagnosis of lung fluke infection could not be confirmed.

Imaging examination results

To observe the dynamic evolution of pleural effusion and brain lesions in the patient, chest X-ray, chest CT, brain CT and MRI were carried out. Chest CT imaging showed bilateral pleural effusion in the thoracic cavity (**Figure 1A** and **1B**) at 2 weeks after onset of the disease and the volume of the pleural effusion increased (**Figure 1C** and **1D**), at 1 month after onset of the disease, the volume of the pleural effusion increased larger (**Figure 1E** and **1F**). Head CT imaging showed no vascular malformations or aneurysms. Head CT imaging showed that there was hemorrhage in the right parietal lobe (**Figure 2A**). And, the hematoma was absorbed gradually as shown in head imaging at 1and 2 weeks of disease onset (**Figure 2B** and **2C**). However, the edema around the hematoma was obvious and the morphology of the edema was irregular. As shown by MRI imaging, at the onset of the disease, T1WI signal was surrounded by a low signal intensity ring (**Figure 3A**). High signal intensity with middle patch of low signal intensity and surrounding slight edema signal was seen in T2WI (**Figure 3B**). At 1 month after the disease onset, low signal intensity with peripheral ring-shaped high signal intensity was seen in T1WI (**Figure 3C**). High signal

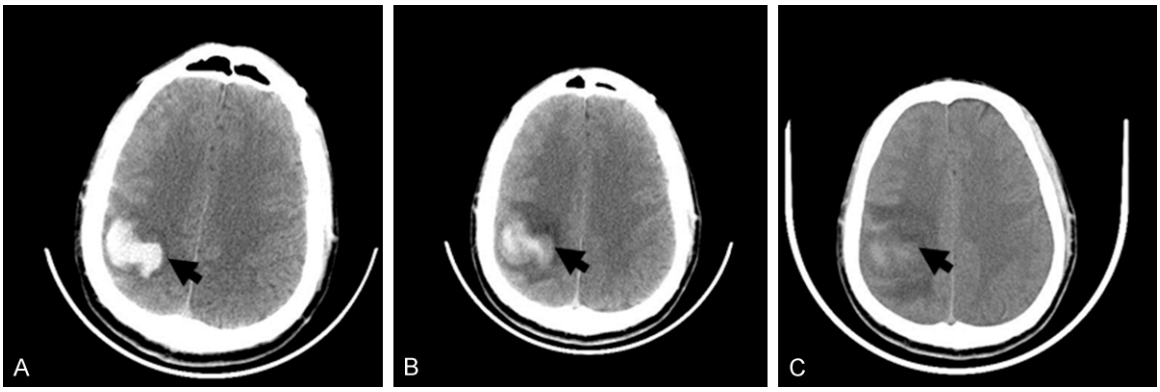

Figure 2. The hematoma analyzed by head CT imaging. Representative head CT images were shown. A. Head CT image at the onset of the disease. The hematoma (arrow) in the right parietal lobe was shown. B. Head CT image at 1 week after the onset of the disease. The hematoma (arrow) in the right parietal lobe was absorbed partly and the edema was obvious. C. Head CT image at 2 weeks after the onset of the disease. The hematoma (arrow) in the right parietal lobe was absorbed and edema was more obvious.

intensity with peripheral visible annular low signal intensity was seen in T2WI (**Figure 3D**). The head MRI study showed that the lesion had progressively extended, with obvious surrounding edema and irregular "tunnel-like shape" and "ring-like shape", which were typical characteristics of cerebral paragonimiasis. To sum up, these results indicates that the patient has positive lung results, which includes visible pleural effusion lung lesions.

Treatment efficacy and follow-up data

To acquire treatment efficacy and timely handle sudden incident or emergence occurring in the patient, the patient was followed up after discharge. After treatment, the symptoms of cough and chest pain disappeared. Blood eosinophilia decreased gradually. Cranial CT showed that edema around the hematoma reduced and chest CT showed that pleural effusion gradually reduced. After the condition was improved, the patient was discharged with continuous anthelmintic treatment. No relapse occurred after follow-up of six months. These results showed that the patient got good therapy result.

Discussion

The lung fluke mainly infects the two lower lobes of the lung, which are close to the mediastinal and diaphragmatic surfaces. It also can spread to the pleura, leading to localized pleurisy and production of the pleural effusion. Li et al [3] and Zheng et al [4] reported that the pleural effusion was mostly found in paragonimus infection. In this study, localized pleurisy and pleural effusion was found, which, was consistent with their reports. However, there are no specific clinical manifestations of pleural effusion but just the nonspecific index of eosinophilia, as a result, pleurisy caused by the lung fluke are easily misdiagnosed as tuberculosis and other diseases. Bilateral pleural effusion of the patient increased progressively. After excluding tuberculosis, malignant tumor and eosinophilic leukemia, pleurisy caused by the lung fluke was considered. However, the intradermal test showed negative results, which increased the possibility of misdiagnosis [5].

The worm of the lung fluke mainly invades the lungs. However, its larvae can penetrate the mediastinum and migragte through the internal carotid artery into the brain. And, the lesions caused by lung fluke infection are mainly located in the occipital and temporal lobes of the brain. Meanwhile, invasion of the white matter, the basal ganglia, the brainstem, the cerebellum and the cerebral ventricle are also found [2, 6-10]. This phenomenon is associated with the invasive and harassing habits of the lung fluke. In this study, the onset manifestation of the patient was stroke-like symptom, suggesting that the lesion was located in the frontal and parietal lobe. With head CT imaging showing high density lesion in the right parietal lobe and chest X-ray revealing normal results at early onset (data not shown), the patient was misdiagnosed as acute cerebral hemorrhage [11]. However, with the gradual increase of

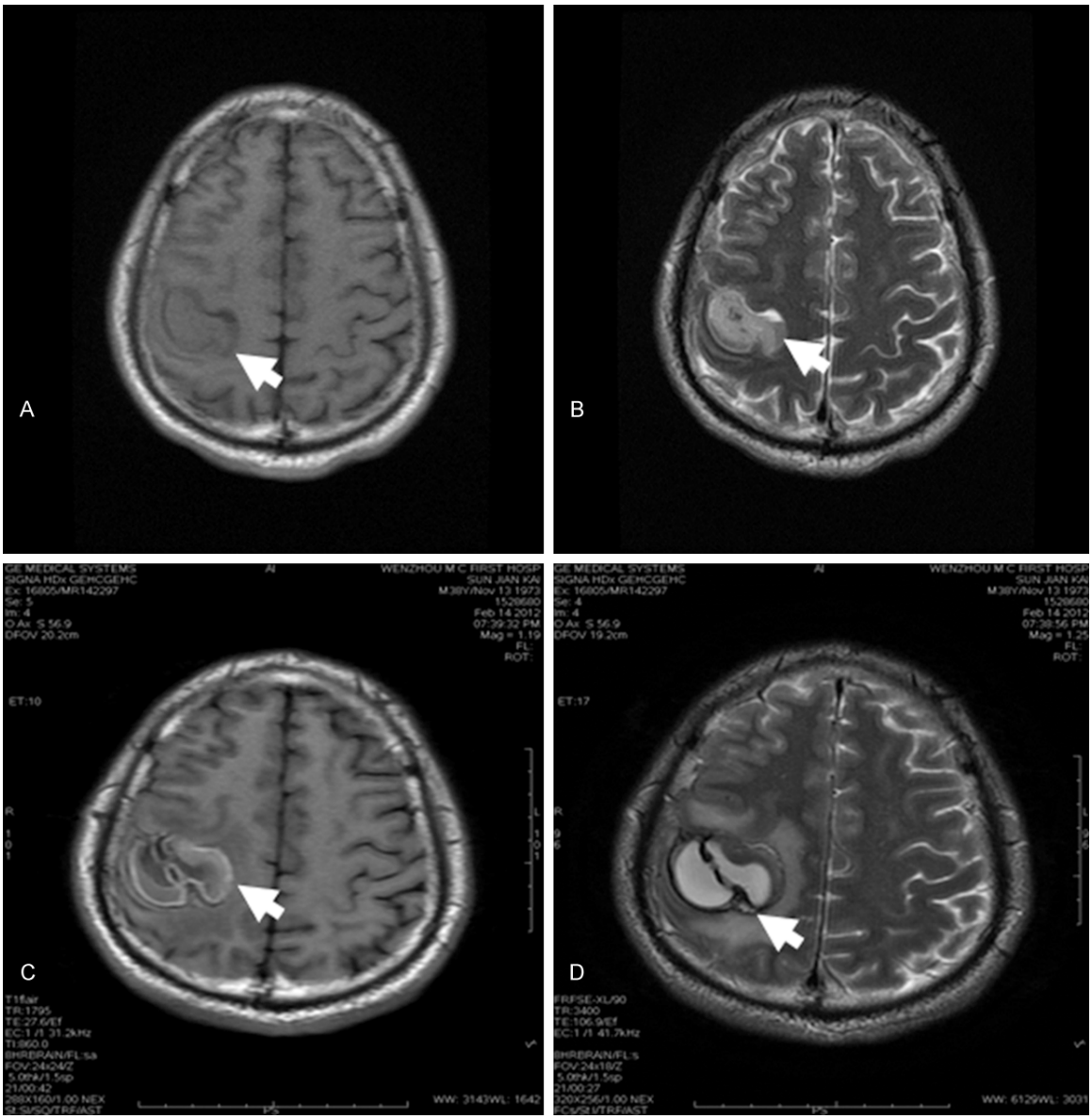

Figure 3. The edema analyzed by MRI imaging. Representative head MRI images were shown. A. T1WI signal was surrounded by a low signal intensity ring (arrow) at the onset of the disease. B. High signal intensity with middle patch of low signal intensity and surrounding slight edema signal (arrow) was seen in T2WI at the onset of the disease. C. Low signal intensity with peripheral ring-shaped high signal intensity (arrow) was seen in T1WI. D. High signal intensity with peripheral visible annular low signal intensity (arrow) was seen in T2WI at 1 month after the onset of the disease. The massive edema zone showed "ring-like shape" around the hematoma and "tunnel-like shape" in the hematoma.

peripheral blood eosinophils and progressive increase of bilateral pleural effusion and acidophilic cells in it, the diagnosis of "cerebral hemorrhage" was not accurate. Head CT and MRI imaging showed that the edema around the irregular hematoma gradually increased. The massive edema zone showed "ring-like shape" around the hematoma and "tunnel-like shape" in the hematoma. This was another feature of imaging manifestations of cerebral paragonimiasis and was consistent with typical image feature previously reported [6, 7, 12, 13]. Because that the patient refused to be further examined by the enhanced MR, enhanced MR performance were not observed.

Another important basis of diagnosis in this case was that the detection of the antibodies

against the lung fluke was positive. At first, the intradermal test screening for the lung fluke antigen was negative. Considering the great possibility of the false negative results, the detection of the antibodies against the lung fluke in the serum, the pleural effusion and the cerebrospinal fluid were performed. The results showed that the anti-fluke antibodies were positive in the serum and the pleural effusion, which supported the diagnosis of paragonimiasis. However, the anti-fluke antibodies were negative in the cerebrospinal fluid. We speculate that the paragonimiasis in the patient may be caused by adult worm recently migrating to the brain. Although the brain tissue was damaged, the immune response was not induced yet. After anthelmintic treatment, clinical symptoms disappeared and imaging examinations showed improved conditions of the patient, which further supported the diagnosis.

In conclusion, the diagnosis thinking of this case was briefly summarized as follows. The patient had a long history of eating raw crab or crayfish or drinking raw water from the stream. The lung fluke infection may affect multiple organs in the human body. Eosinophil cells in the serum and the pleural effusion increased. The edema showed “ring-like shape” and “tunnel-like shape” in the imaging of cerebral paragonimiasis. Paragonimiasis antibody test was positive and anthelmintic treatment was effective.

Disclosure of conflict of interest

None.

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