MRI findings and differential diagnosis in children with cerebral paragonimiasis

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Abstract

Objective: To analyze the clinical characteristics and MRI features of cerebral paragonimiasis in children.

Methods: Twenty-four patients (17 males and 7 females, ages: 5–14 years; mean age: 9.67 years) with cerebral paragonimiasis were recruited from June 2012 to December 2015. The diagnosis was confirmed by IgG enzyme-linked immunosorbent assays or pathologic examination. The clinical and MRI findings of all patients were analyzed retrospectively. Pre- and post-contrast MR imaging of the brain were performed using a GE Signa HDxt 3.0T scanner in all patients, and diffusion and susceptibility weighted imaging were obtained in 3 patients.

Results: Consumption of raw or undercooked fresh water crabs or crayfish within one year prior to the presentation was confirmed in 18 cases. The most common presenting symptom was headache, followed by vomiting, seizures, hemiparesis, hypesthesia and blurred vision. Twenty-two cases had high eosinophil counts (>0.5 x 10^9/L), and the paragonimus serum antibody were positive in 23 cases. The lesions were surgically removed in 2 cases and the diagnoses were confirmed by pathologic examination. Of 24 cases, 17 cases manifested with cerebral hemorrhage, showing short T1 and long T2 signal intensities, most of which were located in cerebral cortex and subcortical areas. Of 17 cases with cerebral hemorrhage, 2 cases showed nodular and ring-like enhancement, while the other 15 patients revealed no enhancement. Seven cases of encephalitis type showed multiple conglomerate, and ring-like enhancements. The “tunnel” sign was found in 3 cases. Most patients showed small lesions surrounded by extensive vasogenic edema that was isointense on diffusion weighted imaging.

Conclusions: The clinical manifestations of cerebral paragonimiasis are nonspecific in children while the MRI findings of cerebral paragonimiasis are characteristic, including irregular hemorrhage, ring-like enhancement and disproportionately large areas of surrounding edema. Brain MRI plays an important role in the diagnosis of cerebral paragonimiasis in children.

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1. Introduction

Paragonimiasis is an uncommon parasitic disease caused by infection of paragonimus spp. There are approximately 2.3 million paragonimiasis patients distributed in China, Korea, Japan of Asia and Latin America [1], especially prevalent in East and Southeast Asia. Infection in human often occurs via ingestion of infected raw or undercooked fresh water crabs or crayfish. Paragonimus species are most commonly associated with ectopic migration. The most common extrapulmonary location is the brain, which accounts for 2%—27% of all paragonimiasis cases [2,3]. Patients with cerebral infection commonly present with headache, seizures, hemiparesis, hypesthesia, blurred vision and meningitic symptoms. Cerebral paragonimiasis would be easily missed or misdiagnosed due to the lack of specific clinical manifestations and the awareness of
the disease by the clinicians. Early diagnosis is crucially important as early paragonimiasis can be treated successfully by chemotherapy with bithionol or praziquantel [4]. The delayed treatment and misdiagnosis of cerebral paragonimiasis often result in severe sequelae and even death [1]. In this article, we retrospectively analyzed the imaging findings of 24 pediatric cases of cerebral paragonimiasis and explored the relationship between imaging findings and pathology, and sought to strengthen the awareness of cerebral paragonimiasis.

2. Methods

2.1. Subjects

Twenty-four patients with cerebral paragonimiasis were reviewed in Affiliated Hospital of Zunyi Medical College from June 2012 to December 2015, including 17 males and 7 females (ages: 5–14 years; mean age: 9.67 years). The research protocol was approved by the ethics committee of our institution. Clinical diagnostic criteria for paragonimiasis included: 1) a history of eating raw or undercooked fresh water crabs or crayfish, 2) the presence of eggs of paragonimus in the sputum, feces or lesions on the pathologic examination, 3) an increase in peripheral blood eosinophil count, 4) a positive ELISA reaction for paragonimus-specific antibody in serum, 5) symptoms, signs and imaging findings caused by paragonimus and, 6) an effective drug treatment with anti-paragonimus.

2.2. MRI scan

Conventional pre- and post-contrast MRI scans were performed in all patients using a GE Signa HDxt 3.0T scanner, and diffusion weighted imaging (DWI) and susceptibility weighted imaging (SWI) were performed in 3 patients, respectively. MRI protocols consisted of axial T1-weighted imaging (TR 400–600 msec, TE 18–25 msec) and T2-weighted imaging (TR 2800–4500 msec, TE 90–120 msec, slice thickness 5 mm, field of view (FOV) 240 × 240 mm), DWI (slice thickness 5 mm, FOV 230 × 230 mm, matrix 128, b value 0, 1000 s/mm²), SWI (TR 27 msec, TE 20 msec, flip angle 15°, slice thickness 2.0 mm, FOV 220 × 160 mm). SWI processing used inline real-time online technology to automatically generate intensity maps and phase diagrams. Thickness of minimum intensity projection was 12 mm. The post-contrast T1WI images post intravenous application of contrast medium (Dimeglumine Gadopentetate Injection, 0.2 ml/kg) were obtained in all patients. To exclude cerebrovascular disease, 6 patients underwent digital subtraction angiography (DSA) and 3 patients underwent 3D time-of-flight (TOF) magnetic resonance angiography (MRA). Twelve patients also had chest CT and/or radiographic examinations.

3. Result

3.1. General appearances

Twenty-four patients (17 males and 7 females, ages: 5–14 years; mean age: 9.67 years, standard deviation: 2.85) with cerebral paragonimiasis were included in this study. Consumption of raw or undercooked fresh water crabs or crayfish was confirmed in 18 cases within 1 year of presentation. All patients came from rural areas of Guizhou province of China. Seventeen patients showed symptoms of paroxysmal headache, of which 12 patients had simultaneous vomiting. Seizures or paroxysmal convulsion occurred in 8 cases. Contralateral hemiparesis was present in 7 cases, of which 5 patients had markedly improved due to timely treatment, although hemiparesis with myodynamia grade 3–4 remained in 2 subjects. Other symptoms included hypesthesia and blurred vision. Among the 24 cases, 9 cases had a history of fever (ranging 37–39.6 °C), and 12 patients with respiratory symptoms, mainly presented with chest pain, chest tightness, intermittent dry cough with a duration of 1–8 months. Three of the patients with respiratory symptoms also had bloody sputum. Twenty-two cases had high eosinophil counts (≥0.5 × 10⁹/L), ranging between 0.5 × 10⁹/L and 25.31 × 10⁹/L. The paragonimus-specific antibody was positive in 23 cases.

3.2. MRI findings

Most lesions involved unilateral cerebral hemisphere in this study, 10 cases with lesions on the right, 12 cases with lesions on the left and only 2 cases with bilateral involvement. Almost all lesions are located in cerebral cortex and subcortical areas, including 19 cases in the parietal lobe, 11 cases in the occipital lobe, 8 cases in the frontal lobe, and 5 cases in the temporal lobe, 3 cases in corpus callosum, 1 case in the basal ganglia and mesencephalon, respectively. Seventeen patients demonstrated punctate, sheet-like, cordlike or oval hemorrhage of variable sizes, ranging from a few millimeters to 8.1 cm in diameters. Cerebral hemorrhage manifested as short T1 and long T2 signal intensities, surrounded by extensive vasogenic edema which is isointense on DWI (Fig. 1A–C). Two cases showed nodular and ring-like enhancement (Fig. 1D), while the other 15 cases had no enhancement. SWI detected multiple spot-like low signal intensities in the lesions which showed small punctate isointense foci on T1WI (Fig. 2A–C). SWI sequence was more sensitive than conventional MRI sequences in detecting small amount of bleeding in the sub-acute and chronic phases [5]. Of 24 cases, 6 patients had DSA and 3 patients had MRA of the brain, which were normal (Fig. 1E). The lesions were surgically removed in 2 cases and were confirmed by pathological examination, with hematoxylin-eosin staining (× 100) revealing a large quantity of eosinophils infiltration accompanied with hemorrhage (Fig. 1F). Seven cases were encephalitis type, which showed multiple conglomerate, ring-shaped enhancements. The wall of partial “ring” is isointense on T1WI and isointense or hypointense on T2WI (Fig. 3A–C). The “tunnel” sign was observed in 3 cases, with a tubular structure measuring 17 mm long and 3 mm wide. The “tunnels” were hypointense on both T1WI and T2WI with tubiform enhancements and the walls of “tunnels” were hyperintense on T1WI (Fig. 4A–D). All cases demonstrated as small lesions surrounded by...
disproportionately prominent vasogenic edema. Twelve cases had pulmonary paragonimiasis simultaneously, and 9 cases showed multiple hypodense cystic lesions (Fig. 3D) or small and cord-like hyperdense lesions while 3 cases demonstrated a small amount of pleural effusion.

4. Discussions

Cerebral paragonimiasis is caused by lung fluke in pleural and peritoneal cavities, migrating along the loose tissues around the carotid arteries, and then through the carotid canals or foramen lacerum into the brain. Focal neurological deficits caused by injury to the brain tissue mainly manifest as visual abnormalities, mental disorders, motor dysfunction, speech disturbances, and sensory impairment. Intracranial hypertension secondary to extensive inflammation may cause headache, vomiting, fever, seizure, vertigo and ataxia [4]. Cerebral paragonimiasis is more likely to occur in children than in adults [5–7], with 75% of the cases under 20 years old [6], which probably is due to comparatively shorter necks, thinner soft tissues surrounding carotid arteries and relatively thinner walls of the blood vessels in children [5]. The brain is the most common extrapulmonary organ involved by paragonimiasis, accounting for about 2%–27% of all cases [2,3]. Its main pathologic changes include infiltrative aseptic inflammation, hemorrhage or infarction. Cerebral paragonimiasis are
frequently misdiagnosed or diagnosed with delay due to the lack of characteristic clinical manifestations. Therefore, brain MRI plays an important role in the diagnosis of cerebral paragonimiasis in children.

The MRI manifestations of cerebral paragonimiasis were divided into two types, including the hemorrhage type and the encephalitis type according to this case series. MR findings of the hemorrhage type included punctate, sheet-like, cordlike or oval lesions of short T1 and long T2 signal intensities, mostly located in cerebral cortex and subcortical areas. Pathological basis of hemorrhage type may be attributed to the migration of lung fluke into brain parenchyma and the resultant mechanical damages and contrafluxion, vasculitis, capillary breaking, as well as infarction or hemorrhage [8]. The hemorrhage type can easily be misdiagnosed as vascular malformations, subarachnoid hemorrhage, spontaneous intracerebral hemorrhage, tumor apoplexy, or cavernous hemangiomas initially in these patients [9,10]. In fact, none of 17 cases in our series was initially diagnosed as cerebral paragonimiasis by either the pediatricians or the radiologists. Hemorrhage type accounted for 70% in this study, which is higher than the previously reported [2,3]. This may be related to the study population of children and the availability of resources in the southwestern regions of China [4,11]. Other locations of infection in the brain including cerebrum and brainstem were also seen in this study series, which may be not contributory to diagnosis.

Encephalitis type of cerebral paragonimiasis manifests as multiple conglomerate or, ring-like or nodular enhancements with extensive vasogenic edema in the cerebral cortex and subcortical areas. The so-called “tunnel” sign, which is formed when the lung fluke migrates inside of brain tissue [2,12], a characteristic, insensitive but specific finding of columnar or tubiform hypointense structures on both T1- and T2-weighted images, was found in 3 cases. In this study, 7 cases demonstrated single or multiple nodular, ring-like, tunnel-like enhancements. The apparently different enhancement patterns may be related to the different pathological stages [8]. Toxic effect and mechanic damage from metabolite of lung fluke may cause inflammatory reactions in the brain tissues. If the worm remains alive for a long period of time or the eggs...
conglomerate, abscesses, cysts or granulomas may develop before the worm dies. If the adult worm dies or has been dead for a long period of time, focal atrophy or calcification will happen. Cystic lesions often manifest as ring-shaped enhancement, while lesions with a nodular or dot-shaped enhancement may imply an inflammatory reaction of the vessels or formation of granulation tissue. SWI is more sensitive than conventional MRI sequences in detecting microbleed [5]. Another image feature is small lesions surrounded by prominent vasogenic edema [12], which may be due to severe anaphylactic reaction resulting from toxic metabolite secreted by the worm, and the increased vascular permeability of the focal brain tissue.

Hemorrhage type of cerebral paragonimiasis should be differentiated from vascular malformations, tumors or venous thrombosis. DSA or MRA is helpful in detecting abnormal vessels and excluding other cerebrovascular diseases. Post-contrast MRI and Magnetic Resonance Spectrum may be beneficial in the differentiation paragonimiasis from tumor. Encephalitis type of cerebral paragonimiasis should be differentiated from viral encephalitis, tuberculosis, and fungal infection. Herpes simplex virus encephalitis often involves the temporal lobes without cluster or aggregated ring-like enhancement. Brain tuberculosis or fungal infections can also have ring-like enhancing lesions but rarely with hemorrhage.

Fig. 4. A 7-year-old girl presented with paroxysmal headache. Conventional MR imaging shows multiple ring-like lesions hypointense on both T1WI (A) and T2WI (B) in the right parietal lobe. The wall of the “ring” is isointense on T1WI. Post-contrast sagittal and coronal T1WI (C, D) demonstrate the “tunnel” sign, with a tubular structure of 17 mm long and 3 mm wide (black arrow).
In conclusion, MRI characteristics of pediatric cerebral paragonimiasis mainly include multiple hemorrhage lesions, ring-like enhancements and the “tunnel” sign, as well as small lesions surrounded by extensively vasogenic edema. When these MRI features were detected in a patient from an epidemic region, together with proper history, pulmonary symptoms and abnormal findings on chest radiographs or CT, cerebral paragonimiasis should be a primary differential consideration. Multi-parametric brain MRI examination plays an important role in early diagnosis of cerebral paragonimiasis.

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