CASE REPORT

Encephalopathy in Henoch-Schönlein Purpura

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Background: Henoch-Schönlein purpura (HSP) is the most common vasculitis in childhood. Severe central nervous system (CNS) involvement is rare in HSP. **Case characteristics:** Three children with features of HSP presented with seizures and CNS dysfunction. **Observation**: All three children had abnormalities on neuroimaging; 2 had complete remission but one was left with severe neurological damage. **Message**: HSP patients may rarely present with CNS involvement with a prolonged course requiring aggressive treatment.

Keywords: *Convulsion, Nephritis, Vasculitis.*

Henoch-Schönlein purpura (HSP) is the most common systemic inflammatory disease of small blood vessels (capillaries) [1]. Clinical symptoms of HSP usually include non-thrombocytopenic purpura, abdominal and joint pain, and renal involvement [2]. Rarely the brain, meninges, heart, pancreas, male genitalia, lungs and pleura are also involved. It is estimated that neurologic complications may occur in one out of 14 patients with HSP [3]. Mild brain injury, such as headache or behavioral changes, has been reported in children with HSP. However, severe brain injury manifesting with seizures, cerebral hemorrhage and hemiplegia, has been rare [4]. We report three cases of HSP with encephalopathy seen in our hospital over a five-year period.

CASE REPORTS

Case 1

A 6-year-old Chinese girl was brought to us with acute onset of a rash on her lower extremities, paroxysmal abdominal pain and bloody stool. She had proteinuria and macroscopic hematuria. After receiving methylprednisolone, a somatostatin analog and other supportive therapy, her abdominal pain and hematochezia improved. However, at day 7th of admission, she developed nephrotic range proteinuria, and renal biopsy revealed ISKDC grade IIIb [5]. According to the classification criteria for HSP by EULAR/PReSh [6], she was diagnosed as HSP because she presented with palpable purpura, diffused abdominal pain, renal involvement, and predominant IgA deposit in mesangial area by renal biopsy.

On day 12, during treatment with methylprednisolone and cyclophosphamide, she developed nausea, vomiting, headache, dizziness and convulsions. She had a clonic seizure in her hands for 20-30 seconds, developed incontinence and agitation, and gradually developed unconsciousness. She did not have any improvement after symptomatic treatment, and as per her guardian's request, the patient was discharged and transferred to another hospital for further treatment (no details available). Neuroimaging findings are described in ***Table* I**. Convulsions, intellectual disability and inability to function independently were present 6.5 years after disease onset.

Case 2

A 10-year-old Chinese girl presented with history of petechiae for more than one month, and abdominal pain, bloody stool and gross hematuria for 6 days. The patient had seizures on the second day of admission. Neuroimaging findings are described in ***Table* I**. On the 39th day after admission, a kidney biopsy revealed ISKDC grade IIb changes. According to the classification criteria for HSP by EULAR/PReS [6], this patient was also diagnosed as HSP because she presented with palpable purpura, diffused abdominal pain, gross hematuria, and predominant IgA deposit in mesangial area in renal biopsy. She was treated with cyclophosphamide and anti-hypertensive drugs.

The blood abnormalities and elevated creatinine (up to 175.6 ìmol/L) normalized after 22 days. Urine protein became negative after 3 months; however, microscopic hematuria remained present for a year and then resolved.

TABLE I LABORATORY FEATURES IN THREE PATIENTS WITH HENOCH-SCHÖNLEIN PURPURA-ASSOCIATED ENCEPHALOPATHY

	Case 1	*Case 2*	*Case 3*
CSF examination	protein+	Normal	Normal
Brain CT	Obscure boundary between gray and white matter, and cerebral atrophy	A clear boundary between gray and white matter, multiple patchy, low-density areas in the bilateral parietal lobe near the midline, cerebral atrophy, and cerebral sulci widening	Not done
Brain MRI	Not done	Bilateral cerebral hemispheres with scattered heterogeneous patchy areas of high T1 and T2 signal, blurred edges, mainly involving the cortex, limited cortex swelling and wide and deep sulci	Left temporal and bilateral frontal, parietal and occipital lobes scattered with multiple patchy areas of high T1 and T2 signal, mainly in the white matter lesions with clear borders
Repeat brain MRI	Not done	After 35 days, wide and deep sulci, swelling disappeared, lesions resolved. T1WI phase showed bilateral parietal cortices with patchy areas of low T1 signal, indicating focal infarction.	Improvement after 14 days and back to normal after 8 months.

Case 3

A 10-year-and-8-month-old Chinese boy had recurrent abdominal pain and vomiting for 10 days. One day before admission, he had a generalized seizure. On the 2nd day, there was blood in the stool and a dark red rash scattered throughout his lower extremities. Gastroscopy revealed features of HSP with gastrointestinal involvement and *Helicobacter pylori* (Hp) infection. According to the classification criteria for HSP by EULAR/PReS [7], this patient was diagnosed as HSP. He received multiple doses of intravenous methylprednisolone. During course of stay in hospital, he developed sudden-onset slurred speech and upper right extremity numbness, while maintaining consciousness. The results of craniocerebral MRI are described in ***Table* I**. On the 18th day, the child could walk steadily, and he was discharged. On follow-up, he did not develop any pain, seizures or any other neurological sequelae.

DISCUSSION

HSP-associated encephalopathy, including cerebral infarction, cerebral hemorrhage and degenerative white matter brain disease, is rare. To be diagnosed with HSP-associated encephalopathy, the patient should present with a typical palpable rash and clinical manifestations of CNS damage, while excluding systemic lupus erythematosus, and other connective tissue diseases, metabolic diseases and neurological diseases, such as intracranial infections. Cerebral MRI/CT scanning, particularly MRI, would be useful for detecting abnormal images in the brain [7].

The pathogenesis of HSP-associated encephalopathy is not fully understood. As vasculitides affects small blood vessels in the brain, damage to the endothelial cells and micro-thrombosis may occur. Hypoxic-ischemic brain injury induces cytotoxic cerebral edema, and the same time vasculitides increases vascular permeability, leading to cerebral hemorrhage. Murakam, *et al.* [8] reported brain biopsy finding from a fatal case of HSP, and demonstrated leukocytoclastic vasculitides on light microscopy. A perivascular inflammatory cell infiltrate was evident in the small vessels, and there were IgA deposits in the vessel wall. Few cases of posterior reversible encephalopathy syndrome (PRES) have also been described in HSP.

HSP is usually self-limited in children, and treatment remains controversial. With evidence of more complicated course and irreversible sequelae that can result from encephalopathy, aggressive treatment may be indicated. Currently, pulse methylprednisolone therapy is most commonly used for HSP encephalopathy [9]. Plasmapheresis has been recommended for patients not responding to methylprednisolone.

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