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CASE REPORT

Cerebral vasculitis in a child with Henoch–Schönlein purpura and familial Mediterranean fever

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Abstract In this case report, a 10-year-old girl with Henoch–Schönlein purpura (HSP) with severe central nervous system involvement and also having familial Mediterranean fever (FMF) is presented.

Keywords Cerebral vasculitis · Children · Familial Mediterranean fever · Henoch–Schönlein purpura

Introduction

Henoch–Schönlein purpura (HSP) is a systemic small vessel vasculitis involving the skin, kidney, joints, and gastrointestinal tract. Although HSP is presumed to be an IgA-related immune complex disease, the pathogenesis has not been well-defined, and several theories concerning the pathogenesis have been proposed [1–6]. Severe neurologic complications such as seizures, focal neurologic deficits, intracerebral hematoma, mononeuropathies, and polyradiculoneuropathies are rare complications of HSP [7–12]. It has been reported that certain vasculitides such as HSP and polyarteritis nodosa (PAN) are more frequent among familial Mediterranean fever (FMF) patients [13–18]. In a few patients, HSP was reported to precede the diagnosis of FMF [13].

Here, we present a severe neurologic involvement in a 10-year-old girl with HSP in whom the diagnosis of FMF was made after the onset of HSP.

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Case report

A 10-year-old girl was referred to our hospital with a 2-week history of intermittent periumbilical abdominal pain associated with nausea and vomiting. She had developed sudden onset of palpable purpuric rash on her extensor surfaces of the lower extremities 1 day before admission. There was no history of recent drug exposure, immunization, or upper respiratory tract infection. The patient denied recurrent attacks of abdominal pain and fever. Family history for FMF was negative. She did not have fever, arthralgia, hematochesia, diarrhea, or hematemesis. Physical examination showed a temperature of 36.6°C, respiratory rate of 28/min, pulse rate of 100/min, blood pressure of 120/80 mmHg. In auscultation, lungs were clear and the heart sounds were normal. Abdominal palpation was painful with defense but without rebound tenderness. Digital rectal examination was normal. There were symmetric palpable purpuric rash on her lower extremities.

Laboratory examination disclosed the following results: hemoglobin, 11.2 g/dl; hematocrit, 33%; white blood cell count (WBC), 11.800/mm^3; platelet count, 450.000/mm^3; erythrocyte sedimentation rate, 74 mm/h; C-reactive protein, 130 mg/l; blood urea nitrogen, 12 mg/dl; serum creatinine, 0.2 mg/dl; albumin, 4.2 g/dl, total cholesterol, 159 mg/dl; triglycerides, 79 mg/dl; calcium, 9.5 mg/dl; sodium, 140 mEq/l; potassium, 3.5 mEq/l; chloride, 103 mEq/l; alanine aminotransferase, 19 U/l; and aspartate aminotransferase, 11 U/l. Serum complement and immunoglobulin levels were normal. Urinalysis revealed hematuria and proteinuria with a 24-h urinary protein excretion of 76 mg/m^2/h. The anti-streptolysin-O titer was 120 Todd unit and throat culture was negative for group A β-hemolytic streptococcus. Antinuclear antibody and antineutrophil cytoplasmic antibody were negative.

Based on these clinical findings, the patient was diagnosed as having HSP with renal, skin, and probable gastrointestinal system involvement. A skin biopsy showed a leukocytoclastic vasculitis. On the third day of hospitalization, she developed persistent colicky periumblical and left lower quadrant abdominal pain with nausea. The abdomen was diffusely tender but without signs of peritoneal irritation or organ enlargement. Stool was negative for occult blood. Abdominal X-ray and abdominal ultrasound were normal. Mesenteric magnetic resonance imaging (MRI) angiography to rule out PAN revealed normal results. A diagnosis of FMF was suspected because of the absence of occult blood in the stool and normal mesenteric MRI angiography. Colchicine was started (1.5 mg/day). An excellent clinical response to colchicine was observed, with complete resolution of abdominal pain. In renal biopsy, diffuse mesangial proliferation with narrowing of the Bowman space and granular vacuolar degeneration in tubular epithelial cells were seen. Immunofluorescence staining showed mesangial granular deposition of IgA, IgG, and C3. No crescent formation or necrotic lesions were seen. Congo-Red staining was negative. Oral prednisolone was started at a dose of 2 mg/kg/day for renal findings. Clinical findings of renal involvement resolved in the follow-up of the patient.

On the fourth day of hospitalization, she had behavioral changes: headache, nausea and emotional irritability with a state like confusion. She developed sudden tonic–clonic convulsions. Examination of the cranial nerves and fundus was normal. Muscular tonus, deep tendon reflexes, cerebellar functions, and sensory testing were normal. The first convulsion responded to midazolam but two additional generalized seizures developed within 1 day. She was treated with phenytoin. The girl remained irritable and apathetic. But seizures did not recur. Her blood pressure was 120/80 mmHg and serum electrolyte levels were normal. Initial brain magnetic resonance imaging (MRI) performed immediately after the onset of the first seizure demonstrated areas of increased signal in bilateral frontoparietal and especially parietooccipital regions (Fig. 1). EEG was normal. Intravenous pulse methylprednisolone

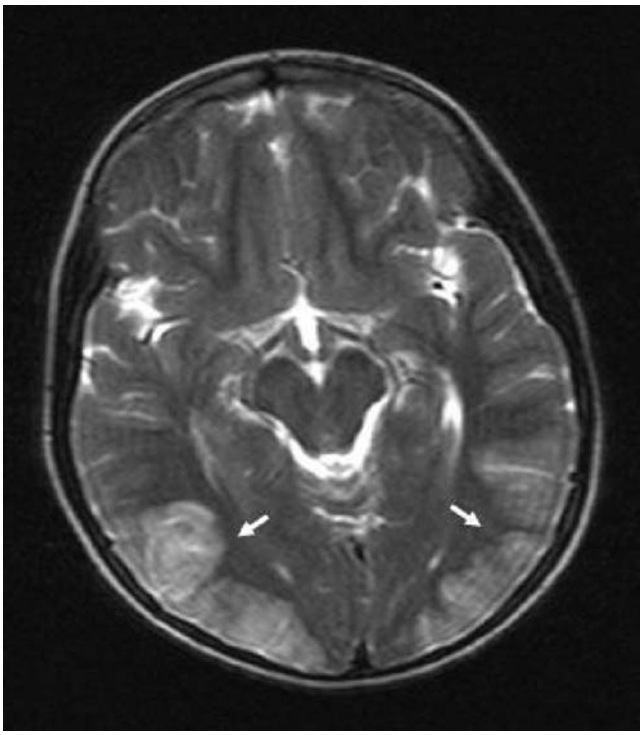

Fig. 1 Areas of increased signal in bilateral frontoparietal and especially parietooccipital regions

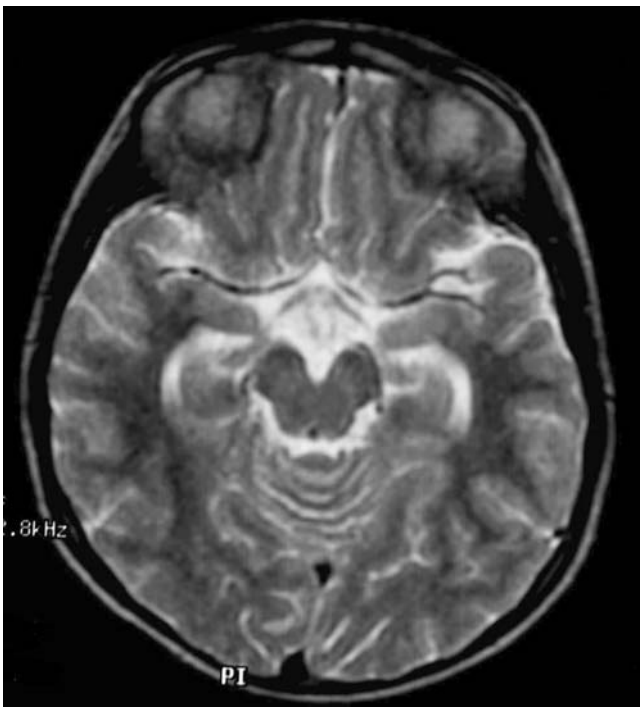

Fig. 2 Completely resolved cerebral lesions

was given (30 mg/kg, three consecutive days), followed by oral prednisolone and cyclophosphamide (2 mg/kg/day) for cerebral vasculitis. Clinical symptoms resolved without recurrent seizures and neurological sequela. The follow-up MRI, performed 10 days later, demonstrated sequential improvement of cerebral lesions. The last MRI on the 30th day showed complete resolution of the cerebral lesions (Fig. 2).

Discussion

Severe neurological complications are rarely encountered during the course of HSP. Belman et al. [7] reported that headache and mental status changes were the most frequent neurologic complications, followed by seizures, focal neurologic deficits, mononeuropathies, and polyradiculoneuropathies. In a prospective study, Ostergaard et al. [8] showed that headache and behavioral changes were leading neurologic complications. The authors reported no cases of seizures, ataxia, or cerebellar hemorrhage. In our patient, central nervous system involvement was manifested by headache, behavioral changes (irritability and apathy), and seizure. Although the exact mechanism is not known, it has been assumed that IgA immune complex deposition initiates arteriolar inflammation in the cerebral vasculature and in the systemic vessels [7, 8]. It has been reported that concomitant occurrence of hypertension, uremia, metabolic abnormalities, and corticosteroid treatment might contribute to the neurologic manifestations [7, 19]. Brain MRI of our patient demonstrated increased signal intensity in bilateral parieto-occipital area. These MRI findings are compatible with radiologic pattern of vasculitis and posterior leukoencephalopathy syndrome which is mainly due to the hypertensive encephalopathy. Posterior leukoencephalopathy syndrome is frequently characterized by symmetrical white matter lesions with or without cortical involvement, mostly in the posterior parietal–temporal–occipital regions of the brain [20, 21]. Our patient developed acute generalized seizure when her blood pressure and serum chemistry were normal. Therefore, we could rule out the possibility of uremic and hypertensive encephalopathy.

There have been several reports of vasculitic diseases such as HSP and PAN associated with FMF [13–15, 18, 22]. The overall incidence of vasculitis in FMF patients is 1% of PAN and 5% of HSP, and it is significantly higher in FMF patients than in normal population [13–15, 18]. The appearance of vasculitis can preclude or follow typical FMF attacks. The pathogenetic relationship of HSP and FMF is not clear. Ozdoğan et al. [13] analyzed 207 patients with FMF and reported that 15 (7%) had HSP, two had definite PAN, and one had probable PAN. The diagnosis of FMF was made after the onset of HSP in nine patients. Occult blood was positive in the first stool specimens obtained after an attack in 17 of the 36 (47%) patients with FMF. The authors proposed considering vasculitis as an integral part of FMF because of the presence of occult blood in stool. The absence of occult blood in repeated stool samples of our patient despite colicky abdominal pain and abdominal tenderness and corticosteroid treatment aroused the suspicion of FMF in our patient. Clinical improvement following colchicine treatment and the detection of homozygous Met694V mutation confirmed the diagnosis.

In conclusion, cerebral vasculitis should be suspected in all cases of HSP with neurologic manifestations. MRI is the modality of choice for diagnosis and follow-up evaluation of neurologic complications of HSP. FMF should be considered in the evaluation of children with HSP, even in the absence of typical attacks or positive family history.

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