Case report

Henoch-Schönlein purpura nephritis complicated by reversible posterior leukoencephalopathy syndrome

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Abstract

We report a young female patient with Henoch-Schönlein purpura (HSP) nephritis complicated by reversible posterior leukoencephalopathy syndrome (RPLS). The patient suddenly showed generalized seizures and cortical blindness with severe hypertension due to renal insufficiency approximately one year after cessation of corticosteroid treatment for HSP nephritis. Magnetic resonance imaging (MRI) demonstrated bilateral abnormal signals mainly in the cerebellum and white matter of the occipital lobe. Clinical symptoms quickly improved in conjunction with disappearance of abnormal signals on brain MRI after starting control of hypertension and continuous hemodiafiltration with steroid pulse therapy and plasmapheresis. RPLS may be caused by vasculitis but also by hemodynamic change due to severe hypertension in HSP, particularly in patients with nephropathy, and in such cases intensive treatment should be performed as soon as possible in order to avoid neurological sequellae.

Key words: continuous hemodiafiltration, Henoch-Schönlein purpura, hypertension, renal insufficiency, reversible posterior leukoencephalopathy syndrome

Introduction

Henoch-Schönlein purpura (HSP) is an autoimmune disorder characterized clinically by punctate hemorrhages with arthralgia and gastrointestinal symptoms preferentially in children, and histopathologically by systemic necrotizing vasculitis in small vessels. In this disease glomerulonephritis frequently occurs as a major complication affecting the prognosis [1], while involvement of the central nervous system (CNS) is uncommon [2]. Encephalopathy associated with HSP has been described in only a small number of case reports [3-9]. Here, we report a young female patient with HSP nephritis who suddenly showed generalized seizures and cortical blindness with severe hypertension ascribable to renal insufficiency approximately one year after cessation of corticosteroid treatment. Clinical symptoms improved with disappearance of abnormal signals in the cerebellum and white matter of the occipital lobe on magnetic resonance imaging (MRI) soon after starting intensive control of hypertension and continuous hemodiafiltration (CHDF) with steroid pulse therapy and plasmapheresis. These clinical findings are almost compatible with reversible posterior leukoencephalopathy syndrome (RPLS) [10], and we postulate that hemodynamic change due to severe hypertension may be the main factor in the pathogenesis of the CNS lesions in our patient.

Case report

A 13-year-old girl developed abdominal pain and multiple punctate hemorrhages in both lower extremities with no obvious precipitating cause. Although these symptoms soon improved without any treatment, renal function gradually decreased with persistent proteinuria. At age 15 she was diagnosed as having grade V of HSP nephritis at our hospital according to the established classification criteria [11], on the basis of the histological findings of biopsied renal tissue. Anticoagulants and oral prednisolone were given to the patient for two months, but the treatment was discontinued at her request.

At age 16 she suddenly noticed headache and difficulty in watching the left side, and these symptoms gradually worsened. Three days later she was admitted to our hospital by ambulance because generalized seizures lasting a few minutes occurred repeatedly.

On admission her blood pressure was 180/120 mmHg. Physical examination showed semicoma and bilateral mydriasis with papilledema, but no convulsion or signs of meningeal irritation. No abnormal findings were seen in the chest, abdomen or extremities. Routine laboratory tests demonstrated severe renal dysfunction (blood urea nitrogen, BUN, 62.0 mg/dl, normal 9-22 mg/dl; creatinine, 8.62 mg/dl, normal 0.4-0.8 mg/dl; uric acid 23.9 mg/dl, normal 2.7-6.1 mg/dl) with proteinuria, a remarkable increase in creatine kinase (CK, 22610 U/l, normal 30-165 U/l), and slightly positive inflammatory reactions (C reactive protein, 1.6 mg/dl, normal<0.1 mg/dl). Electrolytes, IgA, complements and immune complexes in serum were within normal limits, and autoantibodies such as anti-nuclear and anti-DNA antibodies were all negative. Radiological examination demonstrated abnormal signals bilaterally in the cerebellum, white matter of the occipital lobe and basal ganglia with deformity of the fourth ventricle ascribable to brain edema (Figs. 1A, B and C).

CHDF and intensive control of hypertension were started immediately after admission in addition to methylprednisolone pulse therapy at a dose of 1000 mg/day for three days and plasmapheresis. To avoid worsening of brain edema, intravenous administration of glycerol was also performed every day. Consciousness disturbance quickly improved in parallel with a decrease in the blood pressure and normalization of CK and renal indices, including BUN and creatinine in serum. CHDF and intravenous glycerol were discontinued five and ten days after admission, respectively, but the patient showed no generalized seizures or exacerbation of consciousness disturbance with just oral anti-hypertensive drugs. The abnormal signals previously seen in the brain disappeared on MRI (Figs. 1D and E), and edema ameliorated on computed tomography (CT) two weeks after admission (Fig. 1F). The patient did not complain of either

headache or difficulty in watching the left side after recovery from consciousness disturbance. Three weeks after admission she was transferred to the department of nephrology in order to precisely assess renal function and to formulate a plan of treatment.

Discussion

Our patient suddenly developed generalized seizures following headache and visual impairment while receiving no treatment for HSP nephritis. Brain MRI and CT temporarily demonstrated abnormal lesions with edema mainly in the cerebellum and white matter of the occipital lobe at the onset of neurological symptoms, leading to the clinicoradiological diagnosis of RPLS [10]. Visual impairment in our patient was considered as cortical blindness ascribable to damage to the occipital lobe. RPLS lesions are usually localized to parieto-occipital lobes, but several recent reports have demonstrated that other parts of the brain, including basal ganglia, are sometimes involved in this disease as seen in our patient [12, 13]. The frequent attacks of generalized seizure may have modified the distribution of RPLS lesions in our patient, resulting in the involvement of basal ganglia, which are vulnerable to hypoxia [14]. CNS damage sometimes becomes irreversible even in RPLS if treatment is delayed [15], but our patient was adequately treated soon after admission, and recovered with no neurological sequellae.

The pathogenesis of the RPLS in our patient is not exactly clear, but there are two possible mechanisms worth consideration. One is hemodynamic change ascribable to severe hypertension and renal insufficiency. Since the vertebrobasilar and posterior cerebral arteries are sparsely innervated by sympathetic nerves [10], severe hypertension can easily impair autoregulation of the blood pressure in their perfusion areas, sometimes causing RPLS characterized by vascular edema due to damage to the blood-brain barrier [10, 16]. Despite the renal biopsy clearly showing an advanced stage

of HSP nephritis approximately one year before admission, our patient did not continue corticosteroid treatment. The HSP nephritis gradually worsened, and resulted in renal insufficiency complicated by severe hypertension at admission to our hospital. Considering that the neurological symptoms completely recovered in conjunction with the disappearance of abnormal signals on brain MRI soon after starting CHDF and control of blood pressure, hemodynamic change may have played an important role in the pathogenesis of RPLS in our patient.

The other possible mechanism is CNS vasculitis. According to several case reports, encephalopathy can develop in HSP even without severe hypertension and renal insufficiency, and in these cases CNS vasculitis is suspected as the likely pathogenetic mechanism, although this hypothesis remains unproven by histopathology of the brain [3-8]. CNS vasculitis can probably also produce RPLS in HSP on the basis of indirect evidence such as pleocytosis in the cerebrospinal fluid (CSF) and leukocytoclastic vasculitis in skin biopsy [4, 5]. Since our patient manifested RPLS with a slight increase in inflammatory reactions in serum without corticosteroid treatment, methylprednisolone pulse therapy and plasmapheresis were performed at the onset in order to prevent further worsening of neurological symptoms. Considering that RPLS developed without systemic symptoms such as punctate hemorrhages and arthralgia, however, there was no objective evidence suggesting an exacerbation of vasculitis due to HSP in our patient. CSF may have provided us with important information concerning CNS vasculitis, but this study could not be performed in our patient because intracranial hypertension was strongly suspected at the onset.

In conclusion, the RPLS in our patient is attributable to hemodynamic change due to severe hypertension and renal insufficiency rather than CNS vasculitis. When patients with HSP manifest clinical symptoms or signs suggestive of associated CNS lesions, including RPLS, adequate treatment should be intensively performed as soon as possible after assessment of the pathogenetic mechanism in each case, in order to avoid

neurological sequellae.

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Figure legends

Figure 1: T2-weighted images of magnetic resonance imaging (MRI) demonstrate high intensity signals bilaterally in the cerebellum, white matter of the occipital lobe, and basal ganglia (arrows) at admission to our hospital (A, B). Deformity of the fourth ventricle ascribable to brain edema is simultaneously seen on computed tomography (CT) (C). Approximately two weeks after admission abnormal signals are no longer seen on MRI (D, E), and the brain edema has obviously improved on CT (F).