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CASE REPORT

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Cyclosporin-induced cortical blindness in a patient with dermatomyositis

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Abstract Cyclosporin A (CsA) has various adverse effects including neurotoxicity. We report the case of a 49-year-old Japanese woman with dermatomyositis who showed CsA-induced cortical blindness. The patient demonstrated cortical blindness despite having a normal blood concentration of CsA. The risk factors of CsA-induced cortical blindness include the use of corticosteroids and vascular injury, which are frequently observed in patients with systemic autoimmune diseases. Clinicians should consider CsA neurotoxicity when using CsA for patients with systemic autoimmune diseases.

Key words Cortical blindness · Cyclosporin A (CsA) · Dermatomyositis (DM)

Introduction

Cyclosporin A (CsA) is an immunosuppressive agent that is now applied to the treatment of various systemic autoimmune diseases.[1] However, it has some diverse adverse effects, such as nephrotoxicity, hepatotoxicity, and neurotoxicity.[1–10] One of the neurotoxic side effects is posterior reversible encephalopathy syndrome (PRES).[4–10] Patients with CsA-associated PRES often show cortical blindness, which is caused by the dysfunction of the visual cortex. The risk factors for CsA-induced cortical blindness include the administration of corticosteroids and vascular damage.[2–6] Patients with systemic autoimmune diseases frequently have these risk factors, but there are no reports of the occurrence of cortical blindness in a patient with a systemic autoimmune disease. We describe a case of cortical blindness associated with the use of CsA for a patient with dermatomyositis, who also showed severe vasculitic manifestations.

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Case report

A 49-year-old Japanese woman was admitted to our hospital with polyarthralgia, myalgia, muscular weakness, and skin erythemas in April 2000. On admission, the patient presented fever, facial erythemas, multiple livedoes on the extremities, and muscular weakness and atrophy, which were predominant in the proximal muscles. A hematological examination showed mild leukocytopenia (3200/μl). Her serum creatine kinase level was 571 IU/l, aspartate aminotransferase was 288 IU/l, lactate dehydrogenase was 876 IU/l, aldolase was 7.6 IU/l, and myoglobin was 270 ng/ml. An immunological study showed 0.43 mg/dl C-reactive protein, 26 U/ml 50% hemolytic unit of complement, 20 mg/dl complement component 3, and 23 mg/dl complement component 4. The patient's serum was negative for rheumatoid factor, antinuclear antibody, and anti-Jo-1 antibody. Electromyography showed a myogenic pattern, and a muscle biopsy showed diffuse nuclear proliferation and single fiber atrophy. The patient was diagnosed with dermatomyositis (DM) and treated with prednisolone (PSL), which was administered at 60 mg/day (1 mg/kg/day). Soon after the initiation of the treatment, most of her symptoms were resolved. However, the multiple livedoes on the extremities worsened and eventually formed ulcers. Considered along with the finding that the patient had hypocomplementemia, we believed that the patient had severe vasculitis. In August, when PSL was tapered to 30 mg, the patient presented with interstitial pneumonia, which is a frequent complication of DM. Since a pulse of methylprednisolone (mPSL) was ineffective, CsA was introduced from September 30. After starting the treatment, the interstitial pneumonia resolved gradually, and the skin ulcers also im-

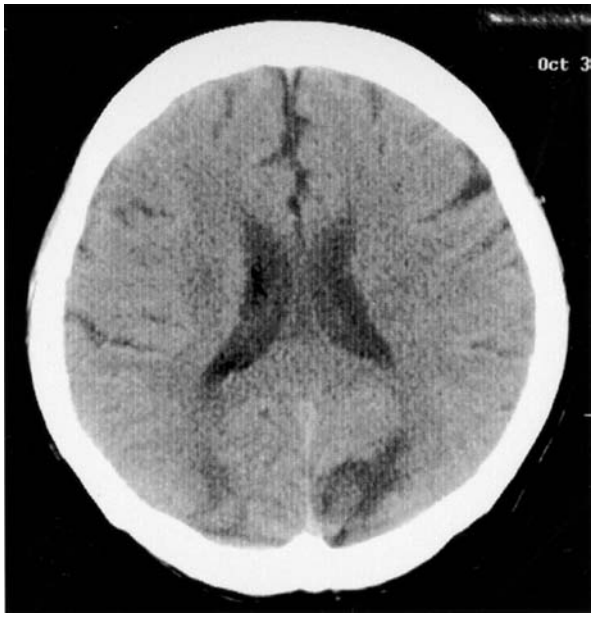

Fig. 1. A head CT scan on October 31, 2000. Low-density areas were observed in bilateral occipital lobes, predominantly on the left-hand side

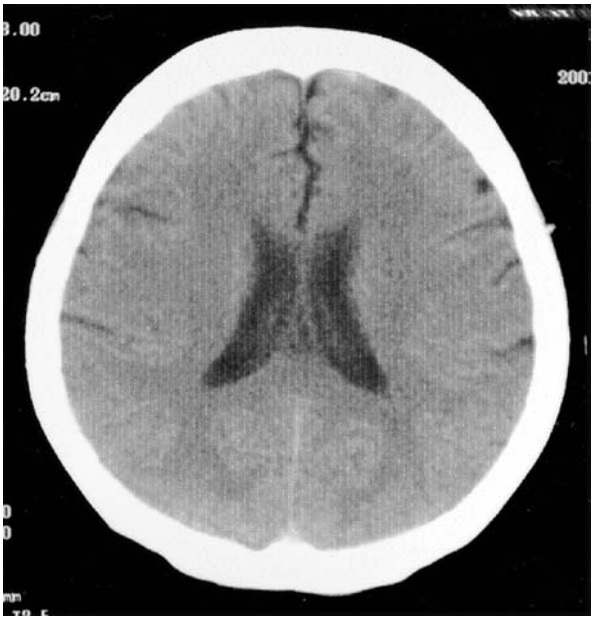

Fig. 2. A head CT scan on November 19, 2001. The low-density areas that had been seen before have disappeared

proved. However, on October 31, when the patient was receiving 125 mg CsA and 32 mg mPSL, the patient complained of a sudden onset of full blindness. She did not have a headache or nausea. The pupils were round and isocoric, light reflexes of the bilateral eyes were prompt, and the patient showed neither paralysis nor sensation abnormality. An emergency head computed tomography (CT) scan revealed low-density areas in the bilateral occipital lobes, predominantly on the left-hand side (Fig. 1). Cerebral infarction was suspected, but full visual recovery was achieved in 1 h. Based on these findings, a diagnosis of CsA-induced cortical blindness was made. However, the trough level of CsA was not in the toxic range on that day (195 ng/ml). Moreover, when the patient developed cortical blindness, she did not present fever, liver dysfunction, hypocholesterolemia, or hypomagnesemia, which are the risk factors of CsA-induced neurotoxicity. The dosage of CsA was reduced, and the patient did not suffer from cortical blindness again. A subsequent head CT scan on November 19, 2001, showed no aberration (Fig. 2). Hence, we concluded that the cortical blindness was caused by PRES associated with the use of CsA.

Discussion

CsA induces various neurotoxic side effects such as headache, generalized seizures, and cortical blindness.[1–10] Some of these effects, including cortical blindness, are caused by PRES.[4–10] The risk factors of CsA neurotoxicity are fever, hypertension, liver dysfunction, hypocholesterolemia, hypomagnesemia, an elevated CsA blood level, the use of corticosteroids, and vascular injury.[2–6] Patients who received CsA for the treatment of a systemic autoimmune disease frequently have some of these risk factors. They are often febrile and are usually administered high-dose corticosteroids, because CsA is generally given to patients who show resistance to treatment with corticosteroids alone in cases of systemic autoimmune diseases. Moreover, they often present vasculitic manifestations, including cerebral vascular accidents. As CsA is believed to induce PRES by injuring the endothelial cells,[5,11–15] it is likely that vasculitis is a high risk factor of cortical blindness, especially when it occurs in the cerebral vessels. Thus, it is probable that patients with systemic autoimmune diseases show CsA neurotoxicity even if the blood concentration of CsA is within normal limits. Indeed, our patient, who had demonstrated treatment-resistant skin ulcers due to vasculitis and had received a high dose of mPSL, showed cortical blindness under the therapeutic concentration of CsA.

CsA neurotoxicity is generally considered to be reversible, but a recent report suggests that it can be irreversible if it is not properly treated.[7] Therefore, it is very important to diagnose CsA intoxication as soon as it develops. When using CsA for patients with systemic autoimmune diseases, clinicians should carefully observe all neurological and psychiatric symptoms in order to detect CsA intoxication promptly.

References

1. Singer NG, McCune WJ. Update on immunosuppressive therapy. Curr Opin Rheumatol 1998;10:169–73.

2. Trullemans F, Grignard F, Van Camp B, Schots R. Clinical findings and magnetic resonance imaging in severe cyclosporin-related neurotoxicity after allogeneic bone marrow transplantation. Eur J Haematol 2001;67:94–9.
3. Bechstein WO. Neurotoxicity of calcineurin inhibitors: impact and clinical management. Transpl Int 2000;13:313–26.
4. Gijtenbeek JM, van den Bent MJ, Vecht CJ. Cyclosporine neurotoxicity: a review. J Neurol 1999;246:339–46.
5. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996;334:494–500.
6. Hauben M. Cyclosporine neurotoxicity. Pharmacotherapy. 1996; 16:576–83.
7. Antunes NL, Small TN, George D, Boulad F, Lis E. Posterior leukoencephalopathy syndrome may not be reversible. Pediatr Neurol 1999;20:241–3.
8. Utsumi K, Amemiya S, Iizuka M, Iino Y, Katayama Y. Acute posterior leukoencephalopathy in a patient with nephrotic syndrome. Clin Exp Nephrol 2003;7:63–6.
9. Cosottini M, Lazzarotti G, Ceravolo R, Michelassi MC, Canapicchi R, Murri L. Cyclosporine-related posterior reversible encephalopathy syndrome (PRES) in non-transplant patient: a case report and literature review. Eur J Neurol 2003;10:461–2.
10. Teive HA, Brandi IV, Camargo CH, Bittencourt MA, Bonfim CM, Friedrich ML, et al. Reversible posterior leucoencephalopathy syndrome associated with bone marrow transplantation. Arq Neuropsiquiatr 2001;59:784–9.
11. Wilasrusmee C, Da Silva M, Singh B, Kittur S, Siddiqui J, Bruch D, et al. A new in vitro model to study endothelial injury. J Surg Res 2002;104:131–6.
12. Nitta K, Uchida K, Tsutsui T, Horita S, Hayashi T, Ozu H, et al. Cyclosporin A induces glomerular endothelial cell injury in vitro. Acta Pathol Jpn 1993;43:367–71.
13. Benigni A, Morigi M, Perico N, Zoja C, Amuchastegui CS, Piccinelli A, et al. The acute effect of FK506 and cyclosporine on endothelial cell function and renal vascular resistance. Transplantation 1992;54:775–80.
14. Bunchman TE, Brookshire CA. Cyclosporine-induced synthesis of endothelin by cultured human endothelial cells. J Clin Invest 1991;88:310–4.
15. Zoja C, Furci L, Ghilardi F, Zilio P, Benigni A, Remuzzi G. Cyclosporin-induced endothelial cell injury. Lab Invest 1986;55: 455–62.