Osteonecrosis of the Femoral Head in a Patient with Henoch-Schönlein Purpura and Drug-induced Hypersensitivity Syndrome Treated with Corticosteroids

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Accepted May 8, 2012.

Osteonecrosis of the femoral head (OFH) is a progressive, debilitating disease that commonly leads to destruction of the hip joint. Most patients with OFH require surgery within a few years of onset (1). It has been shown that a variety of collagen diseases, such as systemic lupus erythematosus (SLE) and systemic vasculitis, are involved in the occurrence of non-traumatic OFH (2–5). Numerous reports have documented OFH after oral corticosteroid treatment. However, it is uncertain if corticosteroid treatment alone or in combination with other factors leads to the occurrence of OFH. Drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms (DIHS/DRESS) is a severe drug reaction with multiple organ involvement (6, 7). Oral corticosteroid is the first-line treatment for DIHS/DRESS. Recurrence is frequently observed during the course of the disease and may require long-term administration of oral corticosteroids (7–9). We report here a case of OFH after prolonged oral corticosteroid therapy for dapsone-induced DIHS/DRESS in a young adult with Henoch-Schönlein purpura.

CASE REPORT

A 26-year-old man presented with a 3-year history of recurrent purpuric lesions on the legs. On examination, palpable purpuric lesions were observed on both legs. Histological findings revealed lymphocytes, neutrophils with nuclear debris and red blood cells around the vessels in the upper dermis, which were compatible with a histological diagnosis of leukocytoclastic vasculitis. Direct immunofluorescence demonstrated IgA deposition on the capillaries in the upper dermis. Anti-nuclear antibody was negative. A diagnosis of Henoch-Schönlein purpura (HSP) was made and dapsone at 75 mg daily was initiated, resulting in resolution of the purpuric lesions. Twenty-six days after the initiation of dapsone, the patient developed a fever, generalized erythematous skin rashes and lymphadenopathy. Laboratory findings showed leukocytosis with eosinophilia and liver dysfunction. Anti-human herpesvirus 6 (HHV-6) IgG antibody titres increased from 10-fold to 320-fold in fluorescent antibody tests. The result of lymphocyte transformation test (LTT) for dapsone was positive. Based on these findings, a diagnosis of DIHS/DRESS due to dapsone was made and oral prednisolone at 40 mg daily was started. This regimen was continued for a total of 21 days, as the erythematous skin rashes on the trunk and liver dysfunction recurred on the 14th day of treatment, followed by 30 mg daily for 3 weeks and 25 mg daily for 2 weeks, culminating in a total of 5 months of corticosteroid use. The erythematous skin rashes appeared during the tapering stage of oral prednisolone. New purpuric lesions were observed on the legs 4 months after the cessation of corticosteroid, which resolved with leg rest alone. Ten months after the withdrawal of corticosteroid, the patient experienced bilateral hip joint pain in the absence of trauma (Fig. 1). An X-ray revealed necrosis of the femoral heads (Fig. 2). In order to receive a surgical operation near his family home, the patient was transferred to another hospital. Magnetic resonance imaging (MRI) of the femoral heads revealed non-traumatic OFH.

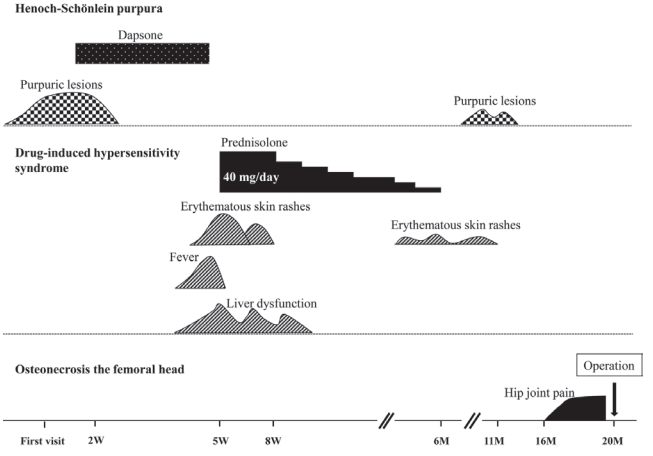

Fig. 1. Clinical course of the patient's conditions. W: weeks after the first visit; M: months after the first visit.

DISCUSSION

Although the pathomechanism of OFH remains unclear, a segment of bone tissue death resulting from the interruption of blood supply to the bone is considered to be responsible for the occurrence of OFH (10). Unlike

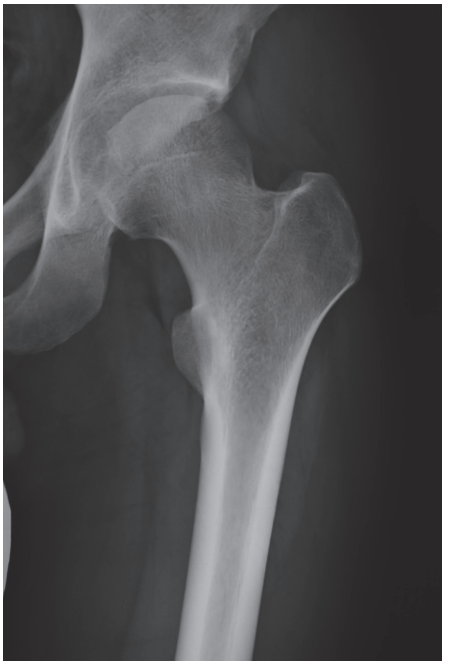

Fig. 2. Osteonecrosis presenting as rough surface of the femoral head.

other adverse effects of corticosteroids, osteonecrosis is irreversible and can be extensive. As the condition most commonly affects male adults in the third and fourth decades of life, the establishment of preventive strategies is required (11). A variety of systemic diseases and conditions are associated with non-traumatic OFH, including collagen diseases such as SLE, antiphospholipid syndrome and systemic vasculitis, in addition to alcoholism, pregnancy, renal transplantation and corticosteroid treatment (1–5).

HSP is a systemic leukocytoclastic vasculitis characterized by cutaneous, articular, gastrointestinal and renal involvement. HSP is generally benign and self-limiting in most cases; however, adult HSP may lead to sequelae, such as myocardial ischaemia and infarction, and bowel ischaemia (12, 13). As OFH has been observed in patients with systemic vasculitis (4), it is likely that the underlying vasculitis in our patient contributed to the development of OFH. The relapse of purpuric lesions on the legs prior to the occurrence of OFH in this patient supports this notion and suggests that regional vasculitis may be a causative factor for bone destruction. The risk of OFH may increase in patients with HSP treated with corticosteroids.

DIHS/DRESS is a severe systemic hypersensitivity reaction caused by specific drugs such as anticonvulsants, allopurinol and dapsone, and involves the reactivation of HHV-6 (6–9). The association between DIHS/DRESS and osteonecrosis has not been reported. In addition, HHV-6 reactivations have not been linked to osteonecrosis.

Oral corticosteroid is the mainstay of treatment for DIHS/DRESS (7–9), and can result in rapid resolution of symptoms within a week after commencement. However, symptom recurrence commonly occurs, thus requiring a longer course of oral corticosteroids, as was noted in our case during the course of the disease.

Studies indicate that corticosteroid therapy is the most common non-traumatic cause of OFH although no data can establish a direct relationship (10). Among OFH patients < 40 years, corticosteroid use is the most prominent potential causative agent. The timing of the occurrence of corticosteroid-induced OFH is commonly within several months after corticosteroid administration. Nagasawa et al. (8) have documented that high-dose corticosteroids, > 40 mg daily, and pulse therapy could be significant risk factors for OFH in patients with SLE. Inoue et al. (9) have reported that a mean daily dose > 25 mg was responsible for the subsequent development of OFH in patients after transplantation. In our patient, the cumulative dose of corticosteroid was 3,446 mg at the end of the 5-month period and the mean daily dose was 21.3 mg.

ACKNOWLEDGEMENTS

This study was partly supported by grants from the Ministry of Education, Sports, Science and Culture of Japan (Y. K. and T. S.), and by Health and Labour Science Research Grants (Research on Intractable Diseases) from the Ministry of Health, Labour and Welfare of Japan (T. S.).

The authors declare no conflicts of interest.

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