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CASE REPORT

Avascular necrosis of the femoral head in multiple sclerosis: report of five patients

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Abstract Osteonecrosis of the femoral head is a severe complication of corticosteroids, which may lead to more disability in multiple sclerosis (MS) patients because of delayed diagnosis. The exact dose and risk period of steroids which cause the necrosis are not clearly known. The aim of the study was to enhance the attention of clinicians to leg pain in MS patients with regard to steroid therapies. We report five MS patients with femoral head necrosis who had relapsing remitting MS and received different doses of methyl prednisolone. Our young cases consist of three females and two males. The duration of disease varied between 1 and 3 years. The least interval between the last pulse of prednisolone and diagnosis of avascular necrosis was 6 months. Two of them received one pulse of 5 g of methyl prednisolone. All five patients had delayed diagnosis because the signs and symptoms were attributed to MS, which indicate the necessity of further focusing attention to early evaluations.

Keywords Avascular necrosis · Femoral head necrosis · Multiple sclerosis · Steroid therapy

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Introduction

Osteonecrosis is a severe condition characterized by the death of the trabecular bone, which is more frequently seen in the femoral head. The majority of cases are due to trauma [1]. Of the non-traumatic avascular necrosis (AVN) cases, 35% are due to long-term corticosteroid treatment [2]. The incidence usually reported for patients receiving high-dose steroids is 3–20% [3], However, the exact dosage and risk period of corticosteroids which cause AVN are not clearly known [2, 4]. In the literature, AVN of the femoral head was more associated with autoimmune disorders, which led to the impairment of medullary blood flow through various pathways, but this complication was rarely noted in multiple sclerosis (MS). Here, we report five patients with MS who developed femoral head necrosis following methyl prednisolone pulse therapy.

Case 1

The patient was a 25-year-old female who presented with ascending paresthesia in both lower limbs. She had history of hemiparesis on the left side with spontaneous recovery 1 year prior to admission. Brain MRI was characteristic of MS according to revised McDonald criteria and a survey of other autoimmune diseases was negative. She was admitted to our hospital on 27 July 2007, and methyl prednisolone (1 g/day for 5 days) was started for her followed by oral prednisolone (1 mg/kg) tapered and discontinued in 10 days. Then, she received once weekly interferon beta1-a (Cinnovex). Fifteen months later, she had pain in both legs. First, she was treated with the impression of MS-related pain and 3 months later she developed limping, but she could walk and was ambulatory for daily activity. Hip MRI

revealed bilateral AVN of the femoral heads (Fig. 1a), and hip joints surgery was performed for her.

Case 2

A 22-year-old man noted two episodes of neurologic deficits on March and May 2007. The first was right hemiparesthesia and fumbling in speech with spontaneous improvement and the second one was weakness of the lower limbs after 2 months. MRI revealed white matter lesions characteristic of MS. He had a history of smoking for 2 years. After excluding other immune-related disorders, he was treated with methyl prednisolone (1 g/day for 5 days) and then received interferon beta-1a (Rebif). He experienced lower limb weakness and transient right hemisensory loss in 2008 and pulse therapy was repeated. Three months later, a pain developed over his right leg. Gabapentin was started with the impression of MS-related pain, and when we visited him 4 months later he had difficulty in walking due to pelvic pain but was still ambulatory. Pelvic MRI demonstrated AVN of both femoral heads (Fig. 1b) and was referred for surgery.

Case 3

The patient is a known case of MS since 3 years prior to her visit with a history of right and left optic neuritis and right hemiparesis. She had received intravenous methyl prednisolone (1 g/day for 5 days) and then once weekly interferon beta1-a (Avonex).One year after the last pulse therapy, she developed right pelvic pain. MRI demonstrated low grade AVN of the right femoral head and the orthopedist recommended conservative management.

Fig. 1 Bilateral femoral head necrosis in case 1(**a**), case 2 (**b**) and case 5 before (**c**) and after (**d**) surgery

Case 4

A 36-year-old male noted ataxia in January 2009. He had the same history 8 months before this attack. Brain MRI revealed periventricular and subcortical lesions compatible with MS. Spinal cord MRI did not show any abnormal signal. For each attack, he received methyl prednisolone (1 g/day for 5 days) with a short course of oral prednisone. Four months later, he developed right leg pain. Pelvic MRI revealed bilateral femoral head necrosis which needed surgery.

Case 5

The patient was a 22-year-old female who presented with optic neuritis in 2006. One year later, she developed imbalance, hemiparesis, impaired deep sensation and sphincter disturbances. She received methyl prednisolone pulse therapy and continued with a short course of oral steroid. Interferon beta-1b (Betaferon) was started for her as a disease modifying therapy. Six months later, she complained of progressive pain and weakness in the pelvic area. Pelvic X-ray demonstrated bilateral femoral head necrosis (Fig. 1c, d).

Discussion

Osteonecrosis of the femoral head is one of the most severe complications of corticosteroid therapy [5]. We report five MS patients with this complication. A summary of their characteristics and steroid dose has been demonstrated in Table 1. It should be noted that none of our patients had a history of alcoholism, or any other autoimmune or metabolic diseases and they did not have any familial relationship with each other. All of the cases were ambulatory at the time of AVN diagnosis. Our patients were non-smokers, except the second case.

The effect of high-dose intravenous pulse steroid treatment on AVN development is still controversial [2, 6].

Steroid treatment may increase adipogenesis and the fat content within the femoral head, causing increased intracortical pressure, sinusoidal collapse and osteonecrosis [3].The number of osteonecrotic lesions was directly related to the dosage of steroids [7]. Previous studies considered cumulative dose of prednisolone as a risk for AVN, but high-dose intravenous corticosteroids including steroid pulse therapy at the beginning of the treatment, not total dose or duration, is also associated with the development of symptomatic AVN [2, 5].

Patients with MS are at risk of developing AVN, because of frequent steroid therapy during their life. In a series of 24 patients, treated for atraumatic osteonecrosis of the talus, one patient had multiple sclerosis [8]**.** In another study, a rate of 15.5% of AVN was reported among MS patients who received pulse steroid therapy at least of 10 or 15 g during the course of the disease [2]. Our first and fifth patients received only a total dose of 5 g, so AVN may occur in lower doses than inthe previous studies and the incidence of this complication in MS may be much higher.

The interval between starting steroid therapy and the onset of symptoms is frequently within 6 or 8 months. It may rarely occur in less than 6 months or take more than 3 years [9].

MS is not an independent risk factor for AVN [2]. To the best of our knowledge, AVN has not been reported as a complication of beta interferons. Whether the interferons have a role in developing AVN should be considered in future studies; although distinction of the possible role of interferons may be difficult, because MS patients on beta interferons may receive steroid pulse therapy for their relapses.

Immobility itself can contribute to development of AVN, a point which should be considered in evaluating the risk of AVN in MS patients, but all of our cases were active and ambulatory.

Early detection of femoral head AVN is important because prognosis depends on the stage and location of the lesion [1]. Early detection allows conservative management including joint rest, nonsteroidal anti-inflammatory drugs, range of motion exercises, strengthening of the muscle surrounding the affected bone, limitation of weight-bearing across the affected joint and mobility training. Delayed diagnosis may lead to progression of the necrosis, to subchondral bone collapse and destruction, and to the

Table 1 Summary of patients' characteristics and steroid dose

	Age (year)	Form of MS	Duration of disease (year)	Pulse number	Accumulative dose of prednisolone (grams)	Interval of the last pulse and AVN diagnosis (month)
Case1	25	RR	2	1	5	15
Case2	22	RR	1	2	10	3
Case3	25	RR	3	3	15	12
Case4	36	RR	1	2	10	4
Case5	22	RR	3	1	5	6

need for total knee or hip replacement, also associated with high rates of failure [4, 10].

Unfortunately, most of our young patients had delayed diagnosis of AVN, which needed surgical intervention. This emphasizes that AVN should be considered in patients with MS who have received steroid therapy. Pain and limping may be attributed to MS, as it happened in three of our cases, and this may lead to delayed diagnosis and treatment. The pain has a gradual onset, usually localized to the hips, but may be referred to the legs and aggravated with motion. In later stages, pain, limping and muscle spasms are the main complaints of patients. In suspected cases, MRI is the most sensitive diagnostic method for early detection of AVN.

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