



Early diagnosis and treatment of steroid-induced osteonecrosis of the femoral head

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Received: 16 May 2018 / Accepted: 28 May 2018 / Published online: 6 June 2018
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Abstract

Objective This study aims to investigate the early diagnosis and treatment of steroid-induced osteonecrosis of the femoral head. **Patients and methods** From January 2010 to January 2014, a total of 350 patients, who required the use of large amounts of hormones, were enrolled into the study. These patients were followed up every three months after starting the hormone therapy. A total of 62 cases were screened, among which nine cases were asymptomatic. Furthermore, 38 patients were diagnosed as stage I and were given low-molecular weight heparin (LMWH) and vasodilator drugs. Moreover, 22 cases were diagnosed as stage IIa/b and underwent core decompression. In addition, two cases were diagnosed as stage IIc and underwent pedicled bone transplantation. During the follow-up period, ARCO staging was used for radiological evaluation, the HHS score was applied to evaluate for clinical efficacy, and SPSS 22.0 statistical software was used for the data analysis.

Results A total of 60 patients were followed up for 24 months. Among these patients, 38 patients were diagnosed with ARCO stage I and underwent systematic therapy. No progress was found in 29 cases (76.3%). Furthermore, three cases progressed to stage IIb (7.8%), four cases progressed to stage IIc (10.5%), two cases progressed to stage III and IV, respectively (2.6%), and 16 cases (80%) did not progress after core decompression. In the 16 cases at stage IIa and four cases at stage IIb, and four cases (20%) progressed in stage III. The HHS score of stage I was 80.42 ± 3.25 before follow-up, while the HHS score was 86.46 ± 8.54 after follow-up, and the difference was statistically significant ($P < 0.05$). Furthermore, the HHS score of patients with stage IIa/b was 70.38 ± 4.62 before follow-up, while the HHS score was 80.28 ± 6.72 after follow-up, and the difference was statistically significant ($P < 0.01$).

Conclusion MRI remains as the most effective method for the non-invasive diagnosis of osteonecrosis, at present. Enhanced MRI may be able to detect early osteonecrosis, but further research is needed. Drug treatment and core decompression can achieve satisfactory results at the early stage.

Keywords Steroid-induced osteonecrosis of the femoral head · Diagnosis · Treatment

Introduction

Osteonecrosis of the femoral head (ONFH) is a common, but refractory, disease in the field of orthopedics. ONFH can be divided into two categories: traumatic and non-traumatic. The former is mainly caused by hip trauma (femoral neck fracture, joint dislocation, etc.), while the latter is mainly caused by the application of corticosteroids, heavy drinking, and decompression sickness. Hormonal osteonecrosis of the femoral

head (SONFH) refers to the pathological process that results from the death of femoral head active ingredients (osteocytes, myeloid haematopoietic cells, and adipocytes) caused by high doses of hormones. SONFH accounts for the top incidences of non-invasive necrosis [1].

ONFH is a progressive disease that progresses to collapse within one to three years in 80% of patients without effective treatment [2]. Once the collapse of the femoral head appears (subchondral fracture and positive crescent sign), the course of the disease is difficult to reverse. Within a few years, the majority of patients will develop severe osteoarthritis and will require artificial joint replacement. SONFH mainly occurs in middle-aged and young individuals [3], but the long-term effect of artificial joint replacement remains difficult to predict. Therefore, it is particularly important to search for effective

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treatments for keeping one's own joints. The premise of good treatment is to obtain early diagnosis and intervention. With the gradual deepening of the understanding of the disease, in recent years, our hospital targeted to strengthen the early diagnosis and intervention of SONFH.

Patients and methods

Patient screening, diagnosis, and treatment

A total of 350 patients were screened from January 2010 to January 2014 in Zhongshan Hospital affiliated to Dalian University. These patients need to use a large number of hormones due to certain diseases. Among these patients, 190 patients had autoimmune diseases, 40 patients had respiratory diseases, and 120 patients had haematological diseases. All patients provided a signed informed consent prior to screening. Furthermore, all patients used hormones for more than two weeks, with a daily measurement of more than 32 mg, and the cumulative application of methylprednisolone was performed at > 800 mg [4]. MRI examination was used to observe the situation of the femoral head every three months. Patients were followed up for two years. If no osteonecrosis of the femoral head was found, the follow-up was stopped. A total of 62 patients with SONFH were screened according to the clinical guidelines of ONFH [5]. These patients included 26 male and 36 female patients, and the age of these patients ranged within 18–45 years old, with an average age of 35.3 years old. Among these patients, nine patients were asymptomatic, and according to the ARCO staging criteria, 38 patients were at stage I, 18 patients were at stage IIa, four patients were at stage IIb, and two patients were at stage IIc.

Low-molecular-weight heparin (LMWH) (5000LXU subcutaneously, once daily, for 2 weeks) was given to

patients diagnosed as stage I, and these patients needed to use a crutch and skin traction with limited weight bearing. Vasodilator drugs (once a day, intravenous injection, continuous application for 2 weeks) were given, and the course of treatment was every six months.

A total of 24 patients were diagnosed as stage II, and these patients underwent digital subtraction angiography (DSA) radiography to observe the situation of the blood supply in the femoral head.

Efficacy evaluation and statistical analysis

ARCO staging was used for all patients during the radiological evaluation, and the HHS score [6] was used for clinical functional evaluation. SPSS 22.0 statistical software was used for data analysis, and all data were presented as mean \pm standard deviation. $P < 0.05$ was considered statistically significant.

Results

Among the 62 patients, 60 patients were followed up. Two patients at stage IIa were discontinued due to personal reasons. All patients were followed up for 24 months from the onset of the osteonecrosis. The DSA examination revealed intrahepatic femoral venous stasis in patients with stage IIa/b, and all underwent core decompression. Two patients were at stage IIc. These patients presented with artery ischaemia in the femoral head and underwent pedicled bone transplantation (Figs. 1 and 2).

Radiographic evaluation

A total of 38 patients with ARCO stage I underwent systematic therapy. No progress was found in 29 patients (76.3%).

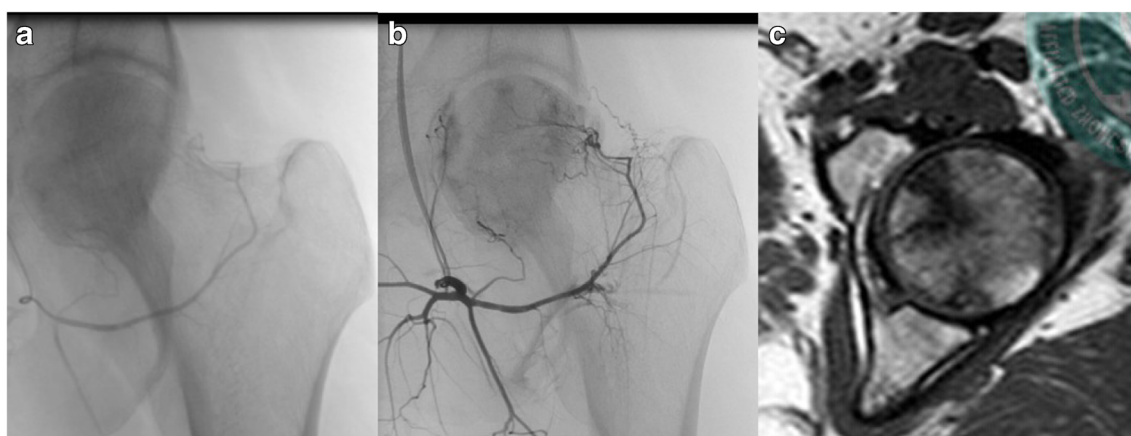


Fig. 1 The DSA shows that the feeding arteries of the femoral head, which were good, and the contrast medium stasis in the femoral head (a and b). The MRI shows that the zone of the necrosis is smaller (c)

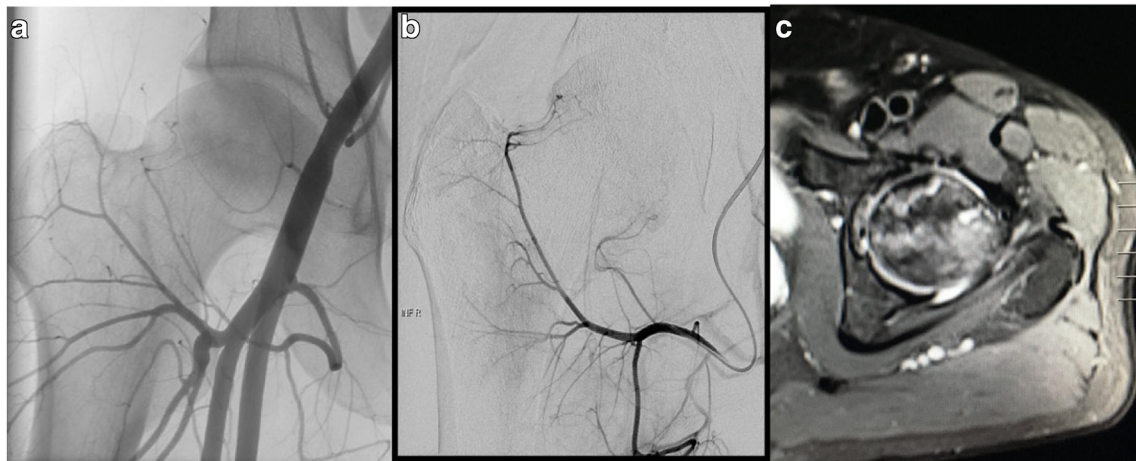


Fig. 2 The DSA shows the arterial ischemia, in which the feeding arteries of the femoral head were interrupted (a and b). The MRI shows that the boundaries of the bone necrosis were clear, and that the zone of the necrosis was larger (c)

Three patients progressed to stage IIb (7.8%), while four patients progressed to stage IIc (10.5%). Two patients progressed to stage III and IV, respectively (2.6%, Fig. 3). A total of 16 patients (80%) did not progress after core decompression in the 16 patients at stage IIa and four patients at stage IIb (Fig. 3). Furthermore, four patients (20%) progressed to stage III. Two patients at IIc had no progress after pedicled bone transplantation treatment.

Function evaluation

The HHS score at stage I was 80.42 ± 3.25 before follow-up, while the HHS score was 86.46 ± 8.54 after follow-up, and the difference was statistically significant ($P < 0.05$). The HHS score of patients at stage IIa/b was 70.38 ± 4.62 before follow-up, while the HHS score was 80.28 ± 6.72 after follow-up, and the difference was statistically significant ($P < 0.01$).

Discussion

Early diagnosis of SONFH

In recent years, with the wide application of glucocorticoids in clinic, SONFH has gradually gained the attention of medical professionals. In particular, the massive use of hormones during the 2003 SARS virus epidemic in China led to the substantial increase in incidence of SONFH.

Li Zirong et al. [7] considered that high-dose hormones and long-term impact are associated with ONFH through a follow-up study. However, the short-term use of small doses of hormones had no significant correlation with osteonecrosis. Hence, hormone has presently become the second leading cause of ONFH following trauma. Therefore, early detection and treatment are effective ways to prevent the eventual disability of such patients.

In general, most of SONFH incidences occur within two years after hormone treatment, and this will most likely occur

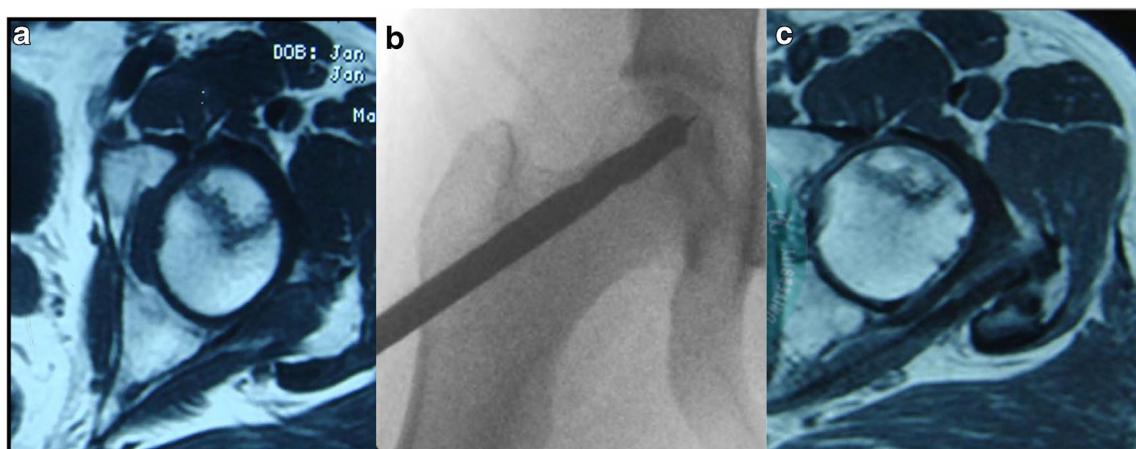


Fig. 3 A 35-year-old male with bilateral osteonecrosis of the femoral head underwent core compression on the right side in 2012. Pelvic MRI at pre-operation (a), during the operation (b), and at 24 months post-operation (c)

within six months. Therefore, after the high dose or long-term use of hormones, the periodicity follow-up observation may be of great significance for the early detection of osteonecrosis. In clinic, various cases without clinical symptoms are often encountered, and these patients are occasionally diagnosed as osteonecrosis due to other examinations. If the patient has clinical symptoms such as hip pain, there is a need to guard against the occurrence of ONFH. X-ray often reveals a negative result in the early stage of osteonecrosis. However, MRI plays an important role in the early diagnosis and evaluation of osteonecrosis [8].

The “line-like sign” is often the early specific performance of ONFH (only bone marrow abnormalities without significant changes in the bone). MRI shows low signals in the femoral head weight area for T1WI, and the signal in this area is stronger than the normal femoral head for T2WI. In recent years, enhanced MRI has been attempted to be used for detecting early osteonecrosis. Enhanced MRI examinations have higher detection rates for patients at stages I–II for bone marrow oedema, line-like signs, single cystic and trabecular structural obstruction, and other pathological features [9]. Enhanced MRI may be a better approach to detect early osteonecrosis in a high-risk population.

Although early diagnosis is possible, the treatment of SONFH remains as a relatively intractable problem, and the efficacy of many methods remains unclear. For stage I, the investigators attempted to use drug-assisted therapy in addition to the usual skin traction and limiting weight.

Early treatment of SONFH

There are many theories in modern medicine for SONFH, such as the theory of fat embolism, increased intraosseous pressure theory, and hypercoagulability state theory. Although the pathogenesis of SONFH has different doctrines, all approaches ultimately lead to the destruction of the femoral head blood circulation, resulting in cell death [10]. Some early osteonecrosis cases have clinical symptoms, while others are asymptomatic. It remains controversial for early asymptomatic ONFH to determine whether or not to take early surgical intervention [11]. The investigators chose medicine treatment and closely observed the patient. Our team in the animal experiment and clinical work explored the method of using non-surgical treatment for early osteonecrosis for several years. Caofang et al. [12] studied the application of enoxaparin and *Ginkgo biloba* extract on the treatment of SONFH in rabbits and confirmed its role in promoting the healing of osteonecrosis.

DSA has been used in clinical practice for many years. It can clearly display the femoral head feeding artery, which can provide guidance in the clinical treatment. The main feeding artery supplying the femoral head is the supporting artery on the femoral neck that originates from the medial

femoral artery (or from the inferior gluteal artery). The DSA technique can clearly reveal the blood supply of the circumflex femoral head artery and the artery of the supporting artery after ONFH [13]. The IIa/b stage is the venous stasis period. DSA revealed the prolonged intravenous phase and intravenous perfusion, and that no stenosis or occlusion was present in the input artery. The stasis can lead to increased intravenous pressure, while for the pathological changes in the femoral head in osteonecrosis, increased intraosseous pressure is one of the main causes of osteonecrosis [14]. Ficat et al. [15] measured a large amount of intramedullary pressure and found that the upper limit of normal femoral head pressure was 4.01 kPa, which was considered as an early indication of ONFH. Core decompression surgery is a simple, less traumatic surgery. Its efficiency is approximately 60–65% for five to ten years. Even if the long-term poor effect does not increase the difficulty of joint replacement, most scholars consider that core decompression has a certain effect in relieving hip pain, which can delay total hip arthroplasty. The effective rate in the present treatment at ARCO stage IIa/b was 80%, with core decompression, which was higher than that in the literature. This was probably because the investigators strictly complied with the surgical indications. In addition, the short follow-up time and small number of cases may be one of the reasons, and the IIc stage is the artery ischemia period. The DSA revealed the prolonged average perfusion time, arterial slender, and the prolonged microvascular phase and venous phase, with no significant delayed drainage. It was found that the core decompression effect of this period was poor. Hence, surgery of the pedicle bone graft was chosen, which has advantages with the independent arteriovenous system, without microscopic anastomosis and blood vessels around the lesion, allowing it to establish contact with the reconstruction in blood in the femoral head. Due to good disease education and timely treatment, most of the patients did not develop to the IIc period. The follow-up result was good for two cases of bone graft. However, due to the sample size, the present study did not conduct an analysis.

Through the present research and clinical practice, a systematic method for the treatment of osteonecrosis was explored. Early diagnosis and treatment can reduce the suffering of patients and reduce social costs. Chinese medicine treatment for osteonecrosis has been continuously performed for many years. The investigators are presently exploring the effectiveness of traditional Chinese medicine in the treatment of osteonecrosis, with the expectation that treating at the early stages of osteonecrosis can reverse the disease. Simple core decompression surgical intervention for stage IIa/b is important for delaying the progression of the disease. Pedicled bone transplantation for IIc and IIIa is a worthwhile approach [16], while IV may have to be performed, in order to improve the quality of life for joint replacement surgery.

In conclusion, MRI remains as the most effective method for the non-invasive diagnosis of osteonecrosis, at present. Enhanced MRI can detect earlier osteonecrosis, but is not widely used in clinical practice. In order to achieve better clinical results, the various stages of treatment need to be further studied. We should also do our best to search for the better treatments for all stages of osteonecrosis.

Compliance with ethical standards

All patients provided a signed informed consent prior to screening.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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