

Chemotherapy-induced femoral head avascular necrosis in patient with highly malignant non-Hodgkin's lymphoma

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Abstract

Introduction: Femoral head avascular necrosis (FHAN) in late arthritis stage leads to hip arthroplasty. Identification of at-risk patients, especially young haematological patients, and timely involvement of the orthopaedic surgeon are crucial. This is the first time in our clinical practice arthroplasty of both hips was performed on such a young patient with chemotherapy-induced FHAN.

Case Report: A clinical case of a 21-year-old male with bilateral femoral head osteonecrosis is presented, caused by the treatment of highly malignant, stage IIIB T cell non-Hodgkin's lymphoma. Due to the underlying disease, the patient completed six courses of chemotherapy according to the VACPE and CHOP regimens that resulted in the development of FHAN; arthroplasty of both hips was indicated.

Conclusion: A closer collaboration between the therapists of the Clinic of Chemotherapy and Hematology and orthopedic surgeons should be encouraged to avoid treatment of severe osteonecrosis with arthroplasty in young patients.

Keywords: Osteonecrosis; Hip arthroplasty; Non-Hodgkin's lymphoma

Introduction

Non-Hodgkin's lymphoma (NHL) is the most common hematologic malignancy in the world [1]. The lymphoma primarily occurs with non-specific symptoms, such as increased lymph nodes, or a general feeling of being unwell; patients refer to a doctor late, after testing for another disease. Once the diagnosis is made and the level of malignancy is determined, chemotherapy is applied to achieve a stable remission. Increased survival of patients with leukemia is reflected in musculoskeletal complications like osteonecrosis of weight-bearing joints [2]. Osteonecrosis is a degenerative bone condition characterized by the death of the cellular components of bone secondary to an interruption of the subchondral blood supply [3]. Non-traumatic avascular necrosis of the femoral head usually affects adults of young or middle age and occurs bilaterally. An increasing incidence of idiopathic cases has been reported, but steroid and immuno-suppression therapy, alcohol misuse and chemotherapy remain important causes [4]. In clinical practice, to determine

FHAN changes and stages of development of hip osteoarthritis, the Ficat and Arlet classification is widely applied that combines patient complaints with X-ray changes and Magnetic Resonance Imaging (MRI) examinations [5] (Table 1). Hip osteoarthritis that develops due to untreated osteonecrosis leads to hip arthroplasty in 5–18% of cases where the primary diagnosis was FHAN [6,7].

The case of a 21-year-old male patient with T cell non-Hodgkin's lymphoma and bilateral FHAN is presented. Taking into consideration the high-malignancy and stage (III B) of NHL, a decision was made to treat the patient with chemotherapy. Early after six chemotherapy courses, the patient developed bilateral FHAN. The follow-up CT scans showed initial signs of osteonecrosis, but they had no correlation with the patient's complaints of pain and stiffness in the hip. The patient referred late to an orthopedic surgeon with severe arthritic changes in the joints, and became suitable for total hip arthroplasty (THA). Currently, the patient's condition is assessed as stable, with no complaints of pain, and the lymphoma in remission.

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Figure 1: X ray showing severe changes in both hips. Left hip: subchondral lucency with cortical collapse; right hip: sclerosis with subchondral cysts



Figure 2: Pelvic CT scan showing normal hip anatomy

Case Report

In December 2015, a 21-year-old male patient presented to our hospital with severe bilateral pain in the groin region, greater on his left side, and minor range of motion of the hips (Fig. 1 a, b, c).

Anamnesis data: The patient primarily complained of an increased lymph node in his neck, which had appeared in recent weeks. Due to suspicion of lymphoproliferative disease, the patient underwent biopsy of the formation. The pathological-histological finding in July 2013 showed that the morphological and immuno-histochemical picture most closely corresponded to the mixed cell variant of a classical Hodgkin's lymphoma; the patient was enrolled in the Clinic of Chemotherapy and Hematology in August 2013. Thoracic and abdominal Computed Tomography (CT) findings in August 2013 showed increased lymph nodes in both axillary pits, splenomegaly, minor ascite, and abdominal lymphadenopathy (Fig. 2).

The patient was assigned four courses of chemotherapy according to the VACPE (Vincristine, Adriamycin, Cyclophosphamide, Prednisone, Etoposide) regimen in November 2013, and January, February and March 2014. To determine the metabolic activity of NHL, Positron Emission Tomography scan (PET) was performed in April 2014 – the activity of the metabolite of the disease was not detected. Due to this, two courses of chemotherapy according to the CHOP (Cyclophosphamide,

Doxorubicin, Vincristine, Prednisone) regimen were prescribed: in May and June 2014. Thoracic and abdominal CT findings in July 2014 showed minor lymphadenopathy in the mediastinum, abdominal cavity, and splenomegaly. These CT scans are very important for detecting the initial signs of FHAN, even if the patient is still asymptomatic (Fig. 3).

The follow-up on the CT scans and patient complaints was facilitated by fact that the patient consistently entrusted all scans and subsequent NHL treatment to one hospital. Notably, all CT scans were performed on the NHL patient for dynamic lymphoma monitoring, and insufficient attention was paid to the body-bearing joints or pseudo-negative CT scans (Table 2).

After the end of chemotherapy courses and after consulting with an orthopedic surgeon, due to severe FHAN with signs of hip osteoarthritis, more pronounced on the left, the patient was prepared for both hip arthroplasty (Fig. 4).

Both postoperative periods passed without complications; post-arthroplasty protocols of the hip joint did not differ from those of patients without oncological arthroplasty (antibacterial and thrombotic prophylaxis, volume of postoperative physiotherapy). The patient is currently in the clinical remission phase, fully regaining movement independence (Fig. 5).

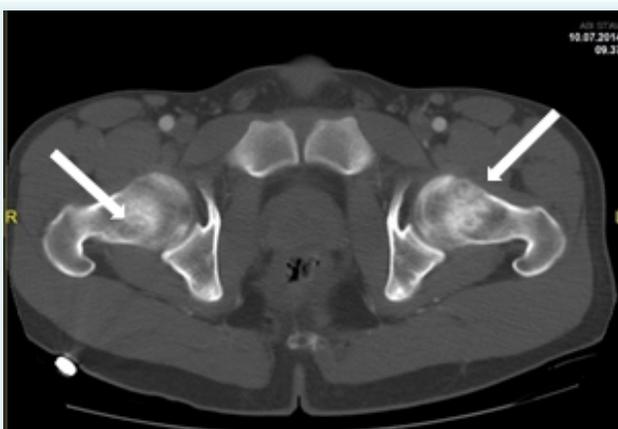


Figure 3: Pelvic CT scan showing osteopenia of both hip bones, greater on the left side



Figure 4: Pelvic CT scan showing end-stage FHAN with secondary degenerative changes in the both hip joints



Figure 5: X ray showing both hip arthroplasty with cementless prosthesis

Table 1: The Ficat and Arlet staging of avascular necrosis of the femoral head

Stage of FHAN	Patient Complaints	X-ray	MRI
0	nil	normal	normal
1	pain in the groin	normal or minor osteopenia	oedema
2	pain and stiffness	maxed osteopenia and/or sclerosis and/or subchondral cysts, without any subchondral lucency	geographic defect
3	pain and stiffness +/- radiation to knee and limb	subchondral lucency and eventual cortical collapse	subchondral lucency and eventual cortical collapse
4	pain and limp	end-stage with evidence of secondary degenerative change	end-stage with evidence of secondary degenerative change

Discussion

Upon reviewing this NHL patient's course of treatment and analyzing his examinations, it becomes clear how comprehensive the treatment of an oncohematological patient should be. Of course, the main specialists in the treatment of lymphoma are the hematologist, chemotherapist, radiologist-therapist and oncologist, but orthopedic surgeons have a place in the treatment of these patients. The amount of information collected (Table 2) allows to put forward the theory: after the first course of chemotherapy, when there is no evidence of osteonecrosis, MRI should serve as a gold standard for the diagnosis of FHAN. An early diagnosis of FHAN is essential to allow for joint-preserving surgical management attempts [4]. Surgical treatment of a precollapsed stage FHAN involves hip-preserving procedures like core decompression, nonvascularized or vascularized bone-grafting, curved intertrochanteric varus osteotomy; for a collapsed and arthritic hip – hip arthroplasty. Core decompression is the most commonly performed surgical procedure for the treatment of early FHAN. It decreases the intraosseous pressure in the femoral head and increases the blood flow to the necrotic area, thus discouraging osteonecrosis formation. Core decompression is an effective and safe method of treating FHAN. The combined use of autologous bone or bone marrow can increase the success rate [8,9,10,11,12]. Nonvascularized (nVFG) and vascularized fibular grafting (VFG) are unusual surgical methods for FHAN management. Both methods do not show significant radiological differences in early follow-ups, but VFG is significantly better at late follow-ups for patients with FHAN [13,14]. VFG in patients with lymphoma has shown favourable outcomes on radiographical changes, the

Table2: Relation between patient complaints, CT data and FHAN stages

Date d/m/y	Patient complaints*	CT data**	FHAN stage** (by Ficat and Arlet)	Hip arthroplasty date
21.08.2013	nil	nil	nil	-
19.09.2013	nil	nil	nil	-
28.11.2013	nil	nil	nil	-
13.02.2014	nil	nit	nil	-
10.07.2014	nil	nil	2 stage	-
15.05.2015	pain and stiffness with radiation to knee and limb	nil	2nd stage in right hip /3rd stage in left hip	-
05.02.2016		nil	3rd stage	-
21.02.2017		end-stage with evidence of secondary degenerative change	4th stage	
04.04.2017		Left hip arthroplasty		
11.12.2018		end-stage with evidence of secondary degenerative change	4th stage in right hip	
23.05.2019		Right hip arthroplasty		

* the first visit to an orthopedic surgeon with complaints of pain and stiffness was on December 17, 2015

**radiologist's conclusion of FHAN findings based on CT data

***evaluation of the same CT examinations, 0–1 stages by the Ficat and Arlet classification are omitted because bone oedema cannot be detected by CT data

4 courses of chemotherapy according to VACPE

2 courses of chemotherapy according to CHOP

Harris Hip Score and the Visual Analogue Scale, because it can enhance revascularisation of the bone tissue and arrest the progression of FHAN [15]. Curved intertrochanteric varus osteotomy (CVO) allows diverting the osteonecrosis region of the head and placing the intact region in a weight-bearing position. CVO produces good clinical results in the treatment of FHAN and delays total hip arthroplasty (THA). However, the postoperative shortening of the leg by an average of 10–13 mm can cause imbalance, especially with bilateral FHAN [16,17,19]. THA is not the first-choice method for the treatment of young patients with early FHAN and is often associated with complications that lead to revision arthroplasty [20,21].

Conclusion

A closer collaboration between the therapists of the Clinic of Chemotherapy and Hematology and orthopedic surgeons should be encouraged to avoid treatment of severe osteonecrosis with arthroplasty in young patients. The orthopedic surgeon should always consider the benefits of each surgical method and discuss them with the patient.

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