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Original Research

Histological fibrosis may predict the failure of core decompression in the treatment of osteonecrosis of the femoral head

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HIGHLIGHTS

- The extension of reactive fibrosis on specimens from biopsies in ONFH is a predictor of the outcome of the CD.
- There is no relation between ONFH risk factors and the necrosis, fibrosis and trabecular modeling on biopsy specimens.
- In our series, the CD survival rate was 46% at 2-years follow-up, 37% at 3-years and at more than 5 years.
- Histological fibrosis should be a point of reference for further studies investigating the variability in results after CD.

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ABSTRACT

Purpose: Osteonecrosis of femoral head (ONFH) is histopathologically characterized by necrotic areas associated with reactive fibrosis, trabecular bone remodeling and thickening zones. Our double goal was to evaluate if: 1) main ONFH risk factors were related to specific histological specimen patterns 2) different histological patterns were related to the final outcome after a core decompression (CD) procedure.

Methods: This observational longitudinal cohort study respected the STROBE statement. We described a series of 41 ONFH (Ficat stage I and II) treated by CD. Specimens from core biopsies were scored according to the extension of necrosis, fibrosis, trabecular bone remodeling and thickening, and were correlated (multivariate analysis) to clinical, biological and radiological factors (age, delay between symptoms onset and surgery, alcohol, steroids, smoking, related disease, cholesterol, triglycerides, x-ray and MRI findings). Prospectively, differences in survivorship among different histological patterns were assessed (log-rank test on Kaplan–Meier curves). Minimum follow-up was 3 years.

Results: Risk factors did not correlate with the histological pattern. The CD survival rate was progressively decreased at 36 months after surgery, thereafter, remained relatively constant (59% at 1 year, 46% at 2 years, 37% at 3 and 5 years). A survival sub-analysis showed a higher CD survivorship in patients with lower extension of fibrosis on core biopsies than patients with high fibrosis levels (log rank $p = 0.019$).

Conclusions: The extension of fibrosis on specimens from biopsies in ONFH is a predictor of the outcome of the CD, therefore it may be considered a prognostic variable. However, it did not correlate with any risk factor. Different ONFH risk factors background did not correlate with specific histological patterns.

1. Introduction

Osteonecrosis of femoral head (ONFH) affects mainly males in the fifth decade, leading to osteochondral collapse and premature hip osteoarthritis [1]. On microscopic assessment, a necrotic femoral head is characterized by necrotic areas (empty osteocytic

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lacunae) associated with different degrees of reactive fibrosis, trabecular bone remodeling and thickening [2]. Interestingly not many papers evaluated the histological aspect of ONFH and the possibility to detect different pathological 'patterns' irrespective of the similar clinical presentations. Perhaps, the characterization of different 'histological patterns' have rarely been discussed, particularly in terms of correlation with main risk factors and surgical treatment results. The majority of studies concerning the histology of the ONFH was lead on femoral neck fractures [2–4]. Main histopathological classifications of ONFH were edited in 1973 (Arlet and Durroux) [5] and in 1989 (Humphreys) [6]. In 1992, vascular features of ONFH were underlined by Saito et al. who investigated arteriopathy and bone marrow hemorrhages on core biopsies from ONFH [7]. To the best of our knowledge, the first real attempt to correlate pathologic findings on specimens from core biopsies in ONFH and risk factors was done in 1999 by Chernetsky et al., mainly focusing the impact of corticosteroid therapy [8]. A further histological analysis was conducted in 2004 on acetabular and femoral biopsies from total hip arthroplasties in patients affected by ONFH, to understand the reasons for prostheses loosening in ONFH patients [9]. Recently, Traistaru et al. lead a retrospective study on the correlation between imaging and histopatological aspects in ONFH patients, concluding that histopathological aspect have a key role in precise staging of patients [10]. The aim of this observational longitudinal cohort study was to investigate the role of different histological patterns in patients affected by ONFH who underwent core decompression (CD) as salvage procedure. A double analysis was conducted: 1) histological data was correlated to the known ONFH risk factors; 2) the relationship between histopathology and outcomes of CD, reported as being the most commonly offered joint-preserving technique for precollapse osteonecrosis [11], was prospectively evaluated.

2. Methods

This observational longitudinal cohort study lead according to the STROBE statement [12] investigated the correlation between ONFH risk factors and different histological patterns. Additionally, patients were followed up and prospectively evaluated to investigate the correlation between the survival of CD and histological patterns. Our study was conducted on a series of 35 patients (41 hips) aged 18 to 75. Inclusion criteria were: a diagnosis of ONFH stage I and II (Arlet-Ficat), treated with surgical CD of the femoral head, after 5 days of maximum delay between clinical examination and ONFH diagnosis. Exclusion criteria were: Patients with stage III and IV disease. Patients provided a written informed consent after having received explanations about the study. Core Decompression was performed by a skilled senior surgeon using the same technique on all patients.

2.1. The surgical technique

The patient is placed in supine decubitus under general or locoregional anesthesia, with the hip draped. Under fluoroscopic guidance, a 2–3 cm lateral incision is performed at approximately 3–4 cm under the greater trochanter in order to introduce a 2 mm K-wire in the middle of the femoral neck along its main axis, directed in the capital necrotic area. Before introducing the K-wire, blunt dissection is performed up to the lateral cortical bone. After the introduction, an anteroposterior and axial fluoroscopic check of its position is performed. Once the K-wire has reached the necrotic zone, a 6 mm and a 11 mm cannulated drill bits are sequentially introduced along it, stopping at around 4–5 cm from its tip. After the 11 mm drill bit removal, a 10 mm cannulated trephine is manually introduced (along the K-wire as well) in the necrotic area, thereafter it is withdrawn together with the rod and with a cylindrical core trabecular bone specimen inside, that we usually define "bony carrot". About 60 mL of a 0.9% saline solution are introduced in the decompression channel under manual pressure (by means of a syringe), in order to evacuate the bony fragments mixed with blood, thereafter the skin is sutured. At the end of surgery, each carrot is classified according to two macroscopic criteria, namely the apparent blood content and the consistency, being the carrot 'bleeding and hard', 'dry and hard' or 'dry and fragile'. Cancellous bone biopsies are systematically sent to histopathology.

2.2. Histological assessment

All bone specimens were formalin-fixed and embedded in paraffin. Serial macrosections, 5 μm thick, were cut from each paraffin block and stained with H&E for morphological evaluation, bone necrosis assessment (BN), reactive fibrosis (RF), trabecular bone thickening (TT) and remodeling (TR) using semiquantitative scores of 0 (none), 1 (mild), 2 (moderate), 3 (marked) and 4 (extremely marked). All specimens were thoroughly investigated by two skilled physicians at different places and times. Final score was assessed for each variable through discussion and consensus.

2.3. Data collection

All variables investigated are listed in Table 1. Histological ones (BN, RF, TT and TR) were considered as independent variables. All other variables (considered as dependent variables) belong to one of the following fields: (1) Anamnestic profile: the age of patients at the time of diagnosis (A); the delay between the onset of symptoms and the intervention of CD (DSI); smoking (S) and alcohol intake (AI), both evaluated through patient's self declaration on use; corticosteroid intake (CC), considered as positive according to the criteria, as already listed in the literature (assumption was ascertained by medical records); (2) Biological values: cholesterol (CH) and triglycerides (TRI) blood levels at the time of diagnosis (taken out from pre-operative laboratory analysis); ONFH related diseases (ORD) (reported in medical records); (3) Imaging data: pre-operative imaging based on anteroposterior (RXAP) and frog-leg lateral (RXLL) views on x-rays through the Keboul method [13] (AP angle, LL angle and a the sum of them as a global angle or RXGL) and MRI findings through the Beltran indexes [14], calculated on frontal (MRIFR) and axial (MRIAX) images; (4) Surgical outcome: the need of total hip arthroplasty (THA) (required in case of radiographic failure, as progression to stage III or true collapse, associated to clinical worsening in terms of pain and to hip functionality impairment).

Patients were evaluated at 6 weeks, 3 and 6 months, 1 year and then annually for a minimum of 36 months for clinical improvement in pain, hip function and radiographic control. Inadequate pain relief, hip function impairement and radiographic progression was adopted as criteria to define CD failure leading to THA.

2.4. Statistical analysis

To perform a statistical analysis, scores given to each independent histological variable (BN, RF, TT and TR) were pooled in two different main groups: Group 1 with a low extension (pooling scores from 0 to 2) and Group 2 with a high extension (pooling scores of 3 and 4). An independent *t*-test was performed to test the relationship between histological data and dependent variables examined (A, DSI, S, CH, TR, RXAP, RXLL, RXGL, MRIFR and MRIAX). A *p*-value of less than 0.05 was considered statistically significant. A Satterthwaite approximation was performed when the variances were not equal (Levene's F test). The lack of quantitative data did