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Macroscopic and microscopic findings in avascular necrosis of the femoral head

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Abstract

The avascular necrosis of the femoral head is an illness induced by the cutoff of blood flow to the femoral head and it affects mostly young adults between the ages of 30 and 50 years, raising therapeutic and diagnostic issues. Many risk factors are incriminated in the development of avascular necrosis of the femoral head like: trauma, chronic alcohol consumption, smoking, administration of corticosteroid drugs, most of the cases are considered to be idiopathic. The main goal of our paper is to describe the macroscopic and microscopic variations of the bone structure, which occur in patients with avascular necrosis of the femoral head. *Materials and Methods*: The biological material needed for our study was obtained following hip arthroplasty surgery in 26 patients between the ages of 29 and 59 years, which previously were diagnosed with avascular necrosis of the femoral head and admitted in the Orthopedics Department of the Emergency County Hospital of Craiova (Romania) between 2010 and 2011. From a macroscopic point of view, we found well defined areas of necrosis, most of which were neatly demarcated of the adjacent viable tissue by hyperemic areas, loss of shape and contour of the femoral head and transformations of the articular cartilage above the area of necrosis. When examined under the microscope, we found vast areas of fibrosis, narrow bone trabeculae, obstructed blood vessels or blood vessels with clots inside, hypertrophic fat cells, bone sequestration but also small cells and pyknotic nuclei. The microscopic and macroscopic findings on the femoral head sections varied with the patients and the stage of the disease.

***Keywords*:** avascular necrosis, femoral head, macroscopic, microscopic.

Introduction

The avascular necrosis of the femoral head is a disease, which is caused by partial or total disruption of the blood flow to the femoral head. The lack of blood flow at this level results in the death of the bone marrow and bone cells followed by the collapse of the bone structure, events which finally lead to the destruction of the bone tissue, local pain and loss of functionality of the hip joint [1, 2].

Avascular necrosis of the femoral head is an illness, which affects mostly young adults, in their 3rd or 5th decade [3, 4]. It is considered that this disease affects men four times more frequent than women [3, 5]. The severity of this disease resides in the fact that it affects mostly young adults, socially and professionally active and with a great life span [4], which are initially asymptomatic but will eventually need hip arthroplasty surgery until their 5th decade [3].

Nowadays, there are more than 16 different classification systems used to classify and describe avascular necrosis of the femoral head, from which the classification system introduced by Ficat is the most commonly used. The Ficat classification system consists of five stages (0 to IV): the first three describe the events that occur before the collapse of the femoral head and the last two stages describe the post-collapse changes [6].

Avascular necrosis of the femoral head can be either primary (idiopathic) or secondary (traumatic or non-traumatic). Trauma, alcohol consumption, smoking and corticotherapy are frequently incriminated in the development of this disease, as secondary causes [1, 2, 7–9].

Materials and Methods

The study group included 26 patients diagnosed with avascular necrosis of the femoral head and who were admitted in the Orthopedics Department of the Emergency County Hospital of Craiova, between November 2010 and October 2011, and underwent hip arthroplasty.

Data regarding age, sex, risk factors, debut of the illness, stage of disease was obtained from patient charts for statistical purposes. Data processing was achieved using Microsoft Excel (Microsoft Corp, Redmond, WA, USA) together with XLSTAT suite for MS Excel (Addinsoft SARL, Paris, France).

The biological material was obtained during hip

arthroplasty, which was performed on all 26 patients included in our study.

Fragments of bone tissue represented the material from the femoral head and neck. The head and neck fragments of the femur were sawn using a small saw with a smooth blade, into longitudinal sections of 2–5 mm.

These sections were then photographed using a Canon EOS 450D DSLR camera with an 18–55 lens mounted, and for a more detailed view a 50 mm lens was used.

The resulting biological material was instilled in a fixing neutral 10% formaldehyde solution for two weeks. After fixating the biological material, we washed using running tap water for 24 hours to remove any trace of the formaldehyde from the tissue.

The bone fragments underwent a decalcifying process that stretched over six months. The fragments were decalcified using trichloroacetic acid in increasingly higher concentration (2% for two months, 5% for two months, and 10% for two months). In order to test the degree of decalcification, we used ammonium oxalate with a concentration of 2.5%.

After the completion of the decalcification process, we ended up with optimally decalcified bone pieces that were elastic and flexible without losing shape or contour. To facilitate paraffin inclusion, these resulting pieces were sliced into smaller fragments, approximately 1 cm^2, using a scalpel blade.

The bone fragments were subjected to another 24 hours cycle of running tap water rinsing in order to stop the decalcification and to remove any trace of the trichloroacetic acid.

The biological material was then ready to be processed using classical histological technique for paraffin inclusion, and the result was a series of 4–5µm sections, which could be colored and studied using the optical microscope.

The histological samples were stained using Hematoxylin–Eosin and trichromic (Goldner–Szekely) stains.

The samples containing the decalcified bone tissue were inspected using a Nikon Eclipse (Nikon, Apidrag, Romania) optical-electronic microscope and significant aspects were picked up using the integrated 5-megapixel CCD camera on the microscope.

Results

The study included 26 patients, diagnosed with avascular necrosis of the femoral head stage III and IV, with ages between 29 and 58-year-old, with an average age of 46-year-old and a standard deviation of 9 years.

The group was composed of 20 men and six women with a male to female ratio of 3:1. 61.54% of the patients came from an urban habitat and 38.46% from rural surroundings.

The anamnesis revealed that the main risk factors were: trauma (14.92%), chronic alcohol consumption (30.77%), smoking (15.38%), corticosteroid therapy (18.21%), cancer (9.18%), radiotherapy (3.85%), and chemotherapy (7.69%).

The macroscopic findings varied with the stage of the disease and with every patient group. In patients with stage III, avascular necrosis of the femoral head we noticed that the shape and contour of the femoral head was maintained and also the necrosis area was neatly defined (Figure 1).

In some patients, the viable tissue was separated by a hyperemic area lying between normal tissue and the necrotized area. In stage IV patients, the loss of shape and contour of the femoral head was common to all the cases, the structural abnormalities leading to the flattening and collapsing of the femoral head. These patients also manifested modifications in the integrity of the articular cartilage above the area of necrosis.

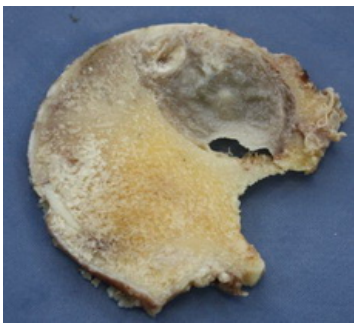

Figure 1 – ***30-year-old patient, diagnosed with avascular necrosis of the femoral head stage III (5 mm section through the femoral head). We can observe an area of necrosis clearly delimited by the viable tissue.***

The microscopic aspects varied from one patient to another and also there were different findings in the same patient, dependent on the studied area of the femoral head.

In all patients included in the study, there were highly diminished bone trabeculae in the area of necrosis, occupying a very small surface compared to the trabeculae found in samples containing viable tissue from the same patient (Figure 2). Their morphology varied with the level of calcium salts remnant at this level. We also found bone trabeculae, which were very much narrowed, losing their integrity within the area of necrosis.

Some samples presented with collagen fibers arranged in the shape of bone trabeculae or totally chaotic arrangements. Another noteworthy aspect was the presence of osteoblasts surrounding islands of viable bone tissue inside the area of necrosis (Figure 3).

Most patients presented a limpid separation line between the necrotic bone tissue and the adjacent viable tissue (Figure 4).

Inside the area of necrosis, we found extensive areas of fibrous tissue, which substituted almost all the bone tissue (Figure 5). The fibrous tissue was also highlighted inside the Havers canal. Less and less islands of viable tissue were found within the area of necrosis, along with areas of bone sequestration with a magma-like appearance. The bone marrow also suffered alterations in the sense that the hematopoietic tissue was subject to destruction or was found in small areas, surrounded by necrotic tissue. Another transformation at this level was represented by hypertrophied fat cells. Most of the blood vessels inside the area of necrosis were occluded, in some of them blood clots were highlighted (Figure 6).

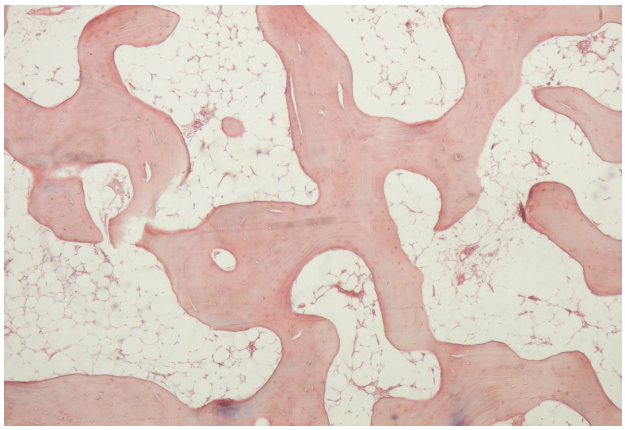

Figure 2 – ***Narrow bone trabeculae of various sizes within the area of necrosis, totally chaotic arrangement, with enlarged areolar cavities that contain fat cells and poor vascularization (HE stain, ×40).***

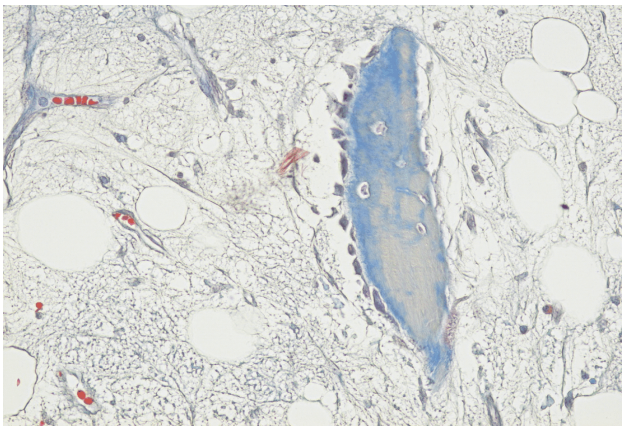

Figure 3 – ***Island of bone tissue, in an extensive necrotized area, surrounded by hypertrophied osteoblasts (trichromic GS stain, ×200).***

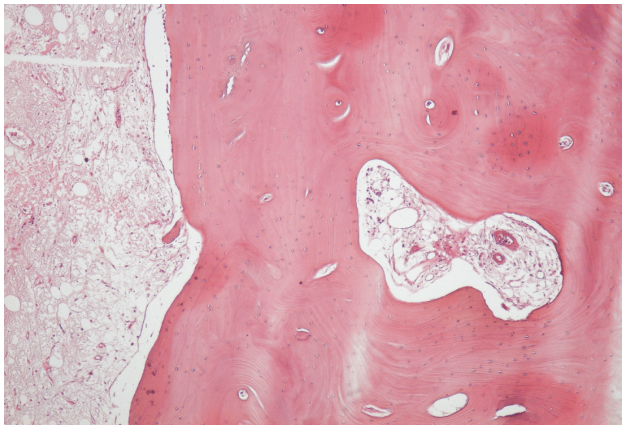

Figure 4 – ***Overview of the boundary between normal tissue and the necrotic area. We can observe the osteocondensation of the perilesional tissue, and the lack of bone cells within the necrotic area (trichromic GS stain, ×200).***

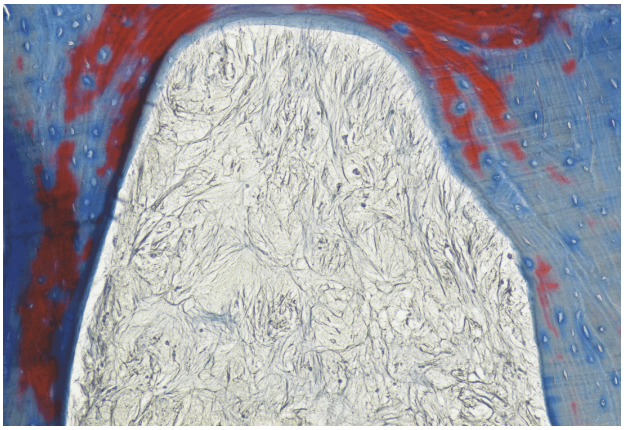

Figure 5 – ***Extensive area of fibrosis in the areolar cavity that has a similar aspect to the tissue observed in the necrotized area (trichromic GS stain, ×100).***

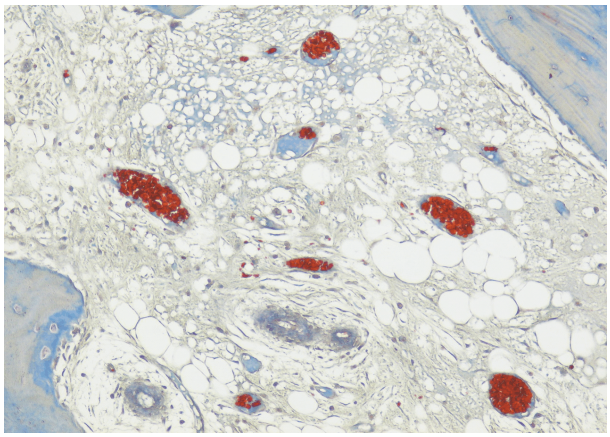

Figure 6 – ***Blood vessels diminished in size, within the necrotic area, some vessels appear congested, some have thickened walls and present lumenal obstruction (trichromic GS stain, ×200).***

Discussion

Nowadays, avascular necrosis of the femoral head is frequent cause of physical disabilities, in young adults, raising diagnostic and therapeutic issues [3]. The non-traumatic causes of secondary avascular necrosis of the femoral head are the following: chronic alcohol consumption, corticosteroid therapy, organ transplant, hematologic disease (anemia, polycythemia, hemophilia, thalassemia), clotting diseases (hypercoagulopathy, IDC), connective tissue disease (systemic lupus erythematous, vasculites, rheumatoid arthritis), infiltrating diseases (Gaucher disease, infection, cancer), endocrine diseases (Cushing disease, hyperparathyroidism), metabolic diseases (gout, hyperuricemia, high cholesterol), congenital diseases (congenital sprain hip joint, Legg–Calvé–Perthes disease), Fabry disease, Caisson disease, pancreatitis, chronic renal failure, hemodialysis, chronic liver disease, HIV infection, pregnancy, chemo- and radiotherapy, thrombophlebitis [2, 4, 10–13].

During our study, we found that some environmental factors were more present than others and we organized them accordingly: trauma (14.92%), chronic alcohol consumption (30.77%), smoking (15.38%), corticosteroid therapy (18.21%), cancer (9.18%), radiotherapy (3.85%) and chemotherapy (7.69%).

The relative frequency of the most common causes of avascular necrosis of the femoral head at a global level is: alcoholism (20–40%), corticosteroid therapy (35–40%) and idiopathic causes (20–40%) [3]. In the last 20 years, the incidence of this disease has signifi-

cantly increased on one hand because of the increasingly high number of chronic alcohol consumers and on the other because of the high number of patients whom have been treated with corticosteroids (alcohol and corticosteroid therapy being well-known risk factors). The advancements in science made organ transplants widely available and the new imaging techniques in radiology are also responsible for the augmented number of cases in recent years.

Regarding our study there is no data available about the prevalence of avascular necrosis of the femoral head in Romania, and the region our patients came from, but, in the United States, there are between 10 000 and 20 000 new cases diagnosed every year [2, 13]. It is considered that between 5 and 18%, out of a total of 500 000 arthroplasty surgeries done every year, are performed on patients diagnosed with avascular necrosis of the femoral head. The estimated cost for these surgeries is approximately 1.6 billion dollars a year [2, 3, 13, 14]. Other studies show that 10% of the patients that underwent arthroplasty surgery were diagnosed with the disease [1].

In our study, there were 26 patients included, diagnosed with avascular necrosis of the femoral head, stages III and IV. The stage of the disease was determined using Ficat staging, based on clinical examination, symptoms and the result of the X-ray and MRI examinations [15]. The Ficat classification system consists of five stages (0 to IV), the last two stages (III and IV) describe the changes that occur after the femoral head collapse [6].

The age of the patients was between 29 and 58-year-old, with a mean age of 46 and a standard deviation of 9 years. Out of all the patients, 38.4% underwent surgery for this disease before the age of 50 years. Avascular necrosis of the femoral head affects especially young adults in their 3rd and 5th decade [1, 3–5, 17]. It is considered that the mean age of the patients diagnosed with avascular necrosis of the femoral head that have arthroplasty surgery is 38 years [2, 4]. Only 20% of the patients diagnosed with this disease have surgery after the age of 50 years [16]. Our group comprised 20 men and six women with a male to female ratio of 3:1. It is considered that avascular necrosis of the femoral head affects men four times more than women [3, 5, 17]. Some authors consider a sex ration of 8:1, with the exception of the cases were this disease is linked this systemic erithematous lupus [1].

The femoral head is the most vulnerable location of the whole skeleton where avascular necrosis can develop. The most common affected region is the anterior-lateral area of the femoral head because it is the most stressed area of the skeleton having to deal with great mechanic stress and support heavy loads [3].

The etiology of avascular necrosis of the femoral head is multi-factorial, many theories about the pathogenesis have been forwarded, most of them in agreement that the final moment, which marks the debut of the illness is the occlusion of the capillaries in the femoral head [7, 18].

Multiple theories have emerged trying to explain the pathogenesis of avascular necrosis of the femoral head but the causes and mechanisms that are responsible for the disease are still unknown. Regardless of the mechanism, one thing is certain: the fact that the vascular network feeding the femoral head is that of a terminal type, with few collaterals that cannot sustain blood flow in case of an obstruction, is a favoring factor for developing avascular necrosis of the femoral head [3, 19].

On samples from some of the patients, we could observe obstructed blood vessels, some of them having blood clots in the lumen. Most authors consider that the mechanism involved in the development of avascular necrosis of the femoral head is related to thrombosis or small artery embolization in the femoral head blood network.

The blood flow can be affected by fat emboli (hyperlipidemia associated with alcohol consumption or secondary to steroid therapy, pancreatitis) [20], abnormal red blood cells (falciform anemia), nitrogen bubbles. In case of anemia or nitrogen bubbles, in addition to the arterial flow, the venous return can be modified. The cutoff of blood flow to the femoral head is considered the initial event that triggers the necrosis or the Legg–Calvé–Perthes disease, the mechanism which produces that event remains unknown [3, 21].

The blood flow cutoff to the arteries can occur directly after a traumatic event at this level, accumulated liquid inside the joint (hematoma, infections, arthritis) increasing the intracapsular pressure [7]. The degrading of the blood vessel wall was found during our study in samples from many patients.

Some authors have concluded that the trigger event of the disease is the decaying structure of the blood vessel wall, similar to what happens in Raynaud syndrome, radiation necrosis and Gaucher disease [3, 5, 22]. On many samples from some of the patients, we found many hypertrophic adipocytes inside the marrow. We also found particular aspects of the marrow infarction like the presence of fat cysts resulted from the destruction of the fat cell links.

Obstructing the venous circulation can present itself when the pressure inside the marrow increases because of adipocyte hypertrophy or the hypertrophy of bone cells at this level. The pressure of the blood flow inside the bone is inversely proportional to the pressure inside the marrow, any alteration in the medullar pressure results in a decrease of blood flow to the bone. This leads to ischemia and necrosis throughout the area that was affected by the diminished blood flow [1, 21, 22]. Another trigger phenomenon is intravascular clotting. This can happen in many illnesses like rejecting organ transplant, cancer, pancreatitis and even pregnancy [7].

On some of the samples, we observed aspects particular to apoptotic cells like a decrease in cell size, pyknotic nuclei. However, this hypothesis was nearly impossible to prove using regular colorations. The most recent hypothesis regarding the physiopathological mechanisms involved in avascular necrosis of the femoral head refer to apoptosis. It has been stated that the metabolism of nitric oxide is disturbed in cells affected by osteonecrosis [22].

Conclusions

The microscopic aspects described in literature as

being particular to some pathogenic theories have been found on samples of bone tissue from our group of patients. More so, on samples from the same patient we described multiple histopathology aspects characteristic to more than one pathogenic theory involved in avascular necrosis of the femoral head. Regardless of etiology and mechanisms involved in the development of avascular necrosis of the femoral head, the management of this disease must have as a goal the pursuit of stopping bone destruction and preventing the collapse of the femoral head.

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