Role of Stem Cells in Treatment of Femoral Head Osteonecrosis

ESSAY

Submitted for partial Fulfillment of M.Sc.Degree in Orthopedic surgery

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2013


بسم الله الرحمن الرحيم
بما يخشى الله من عباده العلماء إن الله عزيز غفور
صدق الله العظيم

سورة فاطر28

Acknowledgement

It is the faith and belief in almighty Allah that gave me the strength all through this work till it is finished.

I would like to thank ***Dr. Ibrahim elganzory*** assistant professor of orthopedic surgery faculty of medicine ,ain shams university who headed this work and for his generous supervision, interest and precious time he offered me through this study .I consider myself very fortunate to work under his supervision

I would like to thank ***Dr .mohammed elgebiely*** lecturer of orthopedic surgery, ain shams university for his continuous support, valuable remarks, his care that I really appreciate it so much.

Words are short of expressing my deepest gratitude to ***my parents and brothers*** for their support and their prayer to allah to help me in my life.

Words are short of expressing my deepest gratitude to ***my wife*** who was very patient with me and gave me much of her time, effort and care.

I would like also to thank all staff members of orthopedic surgery department for their help, deep support and blessings.

Introduction

Osteonecrosis (ON) : (aseptic avascular bone necrosis) is a relatively frequent disorder. When not consequent to trauma, it can be associated with steroid usage, alcoholism, storage disorders, vaso-occlusive episodes such as fat embolism or sickle disease, and some autoimmune disease, but a considerable fraction of osteonecrosis cases are idiopathic. [1]

The common features are increase of bone cell death, and altered intramedullary vascularity, which are potentially all causally related. [1]

Core decompression as a treatment for AVN was described by Arlet and Ficat as early as 1964. The aim of the technique is to improve repair in the osteonecrotic segment at least at earlier stages before mechanical failure of the femoral head has occurred. Reconstruction repair has been observed after core decompression, but usually this repair is incomplete. [2]

New vessels and bone cells from a theoretical point of view arrive in the dead bone along the channel of the core decompression. In the adult, hematopoietic red marrow is normally absent in the femoral head, but red marrow containing stem cells persist in the proximal shaft of the femur. One of the reason for bone remodeling leading to an insufficient creeping substitution after osteonecrosis in the femoral head may be the small number of progenitor cells in the proximal extremity of the femur with osteonecrosis of the femoral head. [2]

While fundamental research and clinical studies have shown that dead bone may be repaired by living bone, the reparative osteonecrotic ential is slight in osteonecrosis because the number of bone progenitor cells in the uninvolved part of the femoral head and in the trochanteric region is less than healthy subjects.[3] Because this lack of progenitor cells, treatment modalities preserve the integrity of the femoral head guide bone remodeling to sufficient creeping substitution to preserve the integrity of the femoral head. [3]

Using progenitor cells or growth factors may be one of the solutions. The treatment of osteonecrosis with bone marrow **autografts** is based on the view, now commonly held, that the osteogenic cells derive from a stem cell in the bone marrow stroma. When red bone marrow is transplanted, the graft will contain osteogenic precursors, which will repopulate the osteonecrotic bone. [3]

Stem cells are a subset of cells that have the unique ability to replenish themselves through self-renewal and the potential to differentiate into different types of mature cells.[4]

The outcome of bone marrow stem cell implantation into the osteonecrotic zone was studied in two prospective trials. This treatment avoided the progression of the disease to the stage of the subchondral fracture (stage III) and reduced the need for total hip replacement. This new therapeutic approach should modify the treatment of early-stage osteonecrosis of the femoral head. .[5]

Aim of work

The aim of this work is to review the current concepts and possible future applications of stem cells in the field of management of femoral head osteonecrosis and there advantage over the traditional methods of treatment of this disease.

Anatomy of the femoral head

The femoral head is the most vulnerable site for development of osteonecrosis. The site of necrosis is usually immediately below the weight bearing articular surface of the bone; the anterolateral aspect of the femoral head. This is the site of greatest mechanical stress. [41]

The blood supply of the femoral head:

The principal sources of blood flow to the femoral head are the lateral epiphyseal vessels (LEVs), branches of the posterior superior retinacular vessels (PSVs), which are branches of the medial femoral circumflex artery, a branch of the profunda femoris artery. The PSVs run along the posterior-superior aspect of the femoral neck under the synovial membrane. They are extra osseous in location and give rise to the LEV; they supply the lateral and central thirds of the femoral head.[41] When patent, the artery of ligamentum teres (ALT) supplies the medial third of the femoral head. Branches of the LEVs and ALT anastomose in the junction of the central and medial third of the femoral head. [41]

The head of the femur is entirely intracapsular, and therefore the blood supply of the head is of surgical importance. [42]The arterial supply to the femoral head is principally provided by 3 sources: (Fig 23, 24).

[1] An extracapsular arterial ring at the base of the femoral neck,

[2] Ascending branches of the arterial ring on the femoral neck surface,

[3] Arteries of the round ligament. This arterial supply is well affixed to

the femoral neck and is easily damaged with any femoral neck fracture . Furthermore, nutrient vessels to the femoral head terminate in small arterioles that are easily occluded with small embolic matter (e.g., lipids).[43]

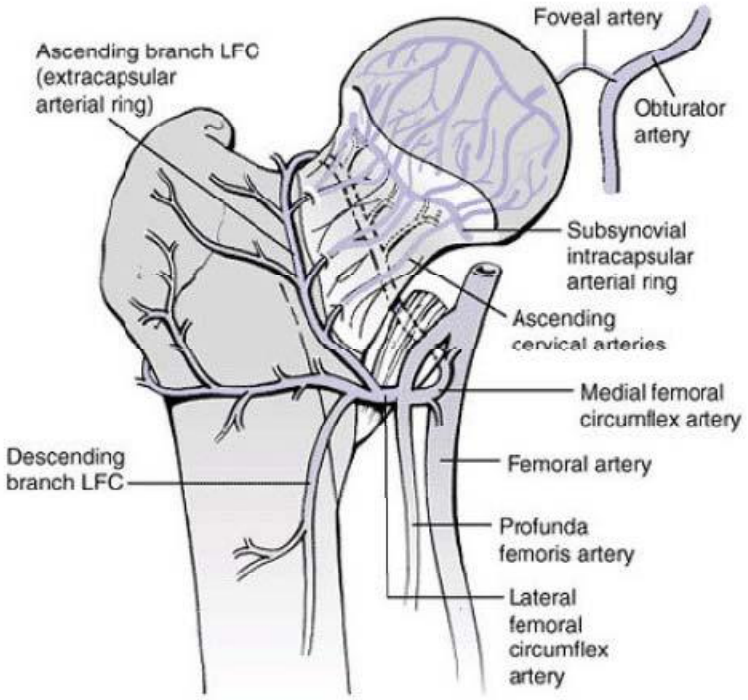
Applied anatomy:

Anat

The majority of the femoral head's vascular supply originates from the Medial and lateral femoral circumflex arteries, which form an extra capsular ring about the femoral neck. Ascending cervical branches pass the femoral neck proximally and enter the capsule at its insertion. [44]

Fractures of the femoral neck may disrupt the vascularity of the femoral head. However, displaced fractures of the femoral head can occur without disruption of the medial femoral circumflex or lateral epiphyseal systems. Therefore, it is important to perform urgent anatomic reduction and internal fixation of displaced femoral neck fractures to restore blood flow in vessels that may be kinked by the displaced fragments. Rarely, collateral circulation can maintain the viability of the femoral head when the primary vessels are disrupted.[44]

The bony anatomy of the upper end of the femur is also extremely important, because it determines where internal fixation devices should be implanted for maximum purchase in the femoral head. The strength of the proximal femur decreases with increasing age as the cortex of the femoral neck thins and cancellous trabeculae are resorbed.[44]



(Fig 23). Vascular anatomy of the femoral head and neck. Anterior view. [43]

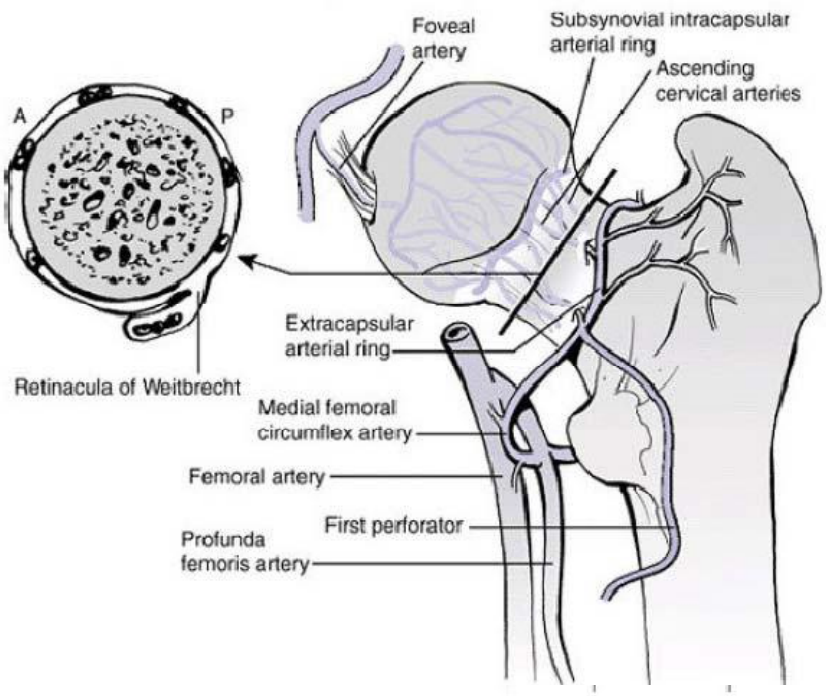


Fig. (24). Vascular anatomy of the femoral head and neck. Posterior view. [43]

Etiology:

A variety of traumatic and non traumatic factors contribute to the etiology of osteonecrosis (Table 1). A definitive etiologic role has been established for some of these factors, but the majority of them are probable relationships. Glucocorticoid use and excessive alcohol intake and sickle cell disease are reported to account for more than 90 percent of cases.[45]

table1:etiology of osteonecrosis.[45]

Traumatic
Femoral neck fracture
Dislocation or fracture-dislocation
Minor trauma
Non traumatic
Corticosteroid administration, rarely hyper secretion of cortisol
Alcohol use
Sickle cell hemoglobinopathies
Caisson (dysbarism) disease
Systemic lupus erythematosus
Gaucher's disease
Chronic renal failure or hemodialysis
Pancreatitis
Pregnancy
Hyperlipidemia
Radiation
Organ transplantation
Intravascular coagulation
Thrombophlebitis
Cigarette smoking
Hyperuricemia/gout
Human immunodeficiency virus infection
Idiopathic

Pathology:

A- Gross pathology:

Osteonecrosis is characterized by areas of dead trabecular bone and marrow extending to involve the subchondral plate. The anterolateral aspect of the femoral head, the principal weight bearing region (the site of greatest mechanical stress), typically is involved, but no region of the femoral head is necessarily spared. [46]

Breaks in the smooth contour of the femoral head become visible, most often at the superior margin of the fovea and beneath the acetabular lip. After collapse of the femoral head, progressive destruction of the articular cartilage and underlying bone occurs, loose bodies appear, and marginal osteophytes develop, heralding the development of degenerative joint disease . [46]

In order to investigate the mechanism of collapse in osteonecrosis of the femoral head,it has been examined which part of the femoral head was the key point of a collapse and whether a collapsed region was associated with the size of necrotic lesion.Using 30 consecutive surgically removed femoral heads it is retrospectively analysed whole serial cut sections,specimen photograghs, specimen radiographs and histological sections. In all of the femoral heads,collapse consistently involved a- fractures at lateral boundary of the necrotic lesion.histologically ,the

fractures occurred at the junction between the thickened trabeculae of the reparative zone and the necrotic bone trabeculae .When the medial boundary of the necrotic lesion was located lateral to fovea of the femoral head ,18 of 19 femoral heads collapsed in the subchondral region.By contrast ,when the medial boundary was located medial to fovea ,collapse in subchondral region was observed in four of 11 femoral heads .It was found that collapse began at the lateral boundary of necrotic lesion and that the size of the necrotic lesion seemed to contribute to its distribution . [47]

B- Histopathology:

Osteonecrosis can be divided into a phase of cell necrosis followed by the repair of cancellous bone. (Fig 25)

1- Cell necrosis:

Hematopoietic elements are the first to undergo death (within 6-12h of the insult), followed by the death of bone cells, e.g., osteocytes, osteoclasts and osteoblasts (12-48h) and, subsequently, by marrow fat cells (48h to 5d). Bone infarcts can be divided into 4 zones, i.e., a central zone of cell death surrounded by successive zones of ischemia, hyperemia, and normal tissue, death of marrow cells is reflected by loss of nuclei and disruption of clusters of fat cells (forming lipid cysts). [46]

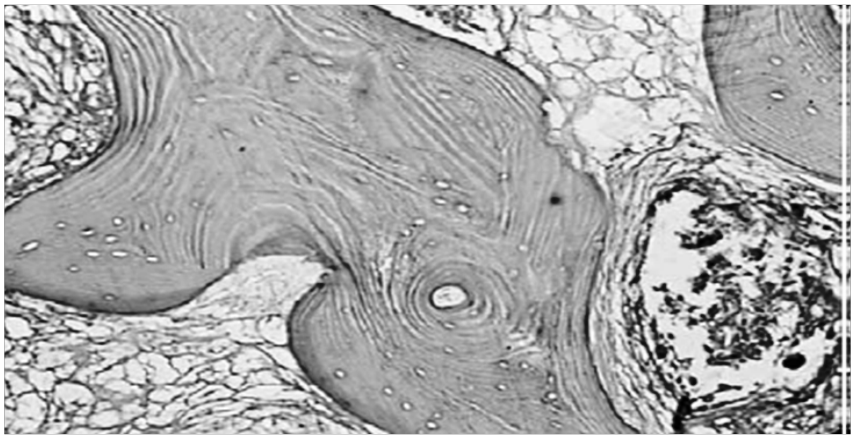


Fig 25: Histopathology of avascular necrosis. Histologic section of the subchondral bone exhibiting dead trabeculae with empty osteocyte lacunae and hemorrhagic marrow with necrosis. [47]

2- Repair:

Bone resorption occurs first, followed by new bone formation. Repair begins along the outer perimeter at the junction between the dead area and the viable area containing an intact circulation (i.e., hyperemic zone). [46]

New bone formation fails to keep pace with bone resorption, resulting in significant loss of bone in the subchondral plate. Further weight bearing causes subchondral bone plate fracture and focal articular cartilage collapse, Fragmentation and impaction of subchondral bone debris leads to the development of a subchondral lucent area along the fracture line, which is the crescent sign seen on plain radiographs (Fig. 26). [47]

Excess osteoclast activity over osteoblast activity may decrease mechanical strength of the repair region and lead to collapse of the

femoral head. Collapse may be prevented if bone resorptive activity is inhibited or delayed by therapeutic procedures. [48]

3- Late complications:

Osteonecrosis of femoral head is generally seen between age of 20 and 60.It often leads to destruction of the hip after collapse of femoral head,when the necrotic lesion is in the weight-bearing area of the femoral head ,it often collapse ,causes secondary osteoarthritis with severe pain and dysfunction. [49]

Continued weight bearing results in flattening of the articular cartilage, Capillary invasion results in articular cartilage resorption. Such a loss predisposes patients to ostearthritis. [50]

In some cases of sever deformity,end-stage osteoarthritis can occur in the second or third decade of life .To ensure a good long-outcome,development of the femoral head deformity must be prevented or minimized during the early stage of disease . [51]