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Review Article

Pediatric Osteonecrosis - Diagnosis, Management and Treatment - For (Legg-Calvé-Perthes; Osgood Schlatter; Sever; and Kohler's Disease) Suppl I: Overview

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Abstract

Osteonecrosis, also known as avascular necrosis (AVN), aseptic necrosis, or ischemic osteonecrosis, is a disease that results in the death of bone cells.

If this process involves the bones near the joint, it often leads to joint surface collapse and then arthritis due to uneven joint surfaces. Although it can occur in any bone, osteonecrosis most often affects the terminal ends (coccyx) of long bones such as the femur. The bones usually involved are the upper part femur (the ball of the hip socket), the lower femur (part of the knee joint), the upper arm (the upper arm bone in relation to the shoulder joint), and the orbital bone shared fish's eyes. The disease can affect only one bone, multiple bones at once, or multiple bones at different times. Orthopedic surgeons usually diagnose the disease using magnetic resonance X-rays (MRI).

The degree of disability from osteonecrosis depends on which part of the bone is affected, how much of the area is involved, how advanced the disease is, and how well the bone heals itself.

Bone rebuilding occurs after an injury as well during normal growth. Normally, bones are constantly broken down and rebuilt - old bone is reabsorbed and replaced with new bone. This process keeps the skeleton strong and helps it maintain a balance of minerals. With osteosarcoma, the healing process is often ineffective and bone tissues are broken down faster than the body can repair them. If left untreated, the disease progresses and the bones can crack, so the bones can be compressed (collapsed) together (similar to compressing a snowball). If this occurs at the end of the bone, it leads to uneven joint surfaces, joint pain, and loss of function of the affected areas.

Keywords: *Pediatric Osteonecrosis; Legg-Calvé-Perthes; Osgood Schlatter; Kohler's Disease; Avascular Necrosis (AVN)*

OVERVIEW OF OSTEONECROSIS

The bones of the human body are made up of living cells that need a blood supply to stay strong. In osteonecrosis, blood flow to part of the bone is interrupted. This leads to the death of the bone tissue and eventually the bone can break down and the joint will collapse. Osteonecrosis is a degenerative bone condition characterized by death of the cellular components of bone secondary to disruption of blood supply to subchondral bone [1]. It is also known as avascular necrosis (AVN), aseptic necrosis, and ischemic osteonecrosis.

It usually affects the growth of long bones at weight-bearing joints. Severe cases can lead to bone destruction under the cartilage or collapse of the entire joint.

Osteonecrosis is also known as: Avascular necrosis, aseptic necrosis, ischemic necrosis of bone.

The most common sites for AVN to occur are the femoral head, knee, hoof, and femur. Overall, the hip is the most common position. AVN is less common than in other bones of the body, such as the carpal tunnel and the jawbone. Therefore, early recognition and treatment of osteonecrosis is essential. This activity discusses the etiology and pathogenesis of the disease. In addition, it covers presentation and treatment options of the most common forms of osteonecrosis.

Osteonecrosis can occur in any bone, but it most often develops at the ends of long bones. Such as: The femur (femur), especially the upper ball in the hip socket. The lower head, part of the knee joint, is also commonly affected. The upper arm bone (humerus), especially the upper part, ball at the shoulder joint.

When the disease involves part of the bone in a joint, it can lead to bone breakdown and arthritis. Less often, the bones of the elbow, ankle, foot, wrist, and hand are affected.

The main symptom of osteonecrosis is pain, and imaging methods such as X-rays or magnetic resonance imaging (MRI) are often used. Most people require surgical treatment to prevent further bone damage, to preserve bone and to improve joint use.

Etiology

It is widely accepted in the literature that decreased subchondral blood supply is the cause of osteonecrosis. However, there are many risk factors and theories for the development of this vascular insufficiency. Shah., *et al*. [2] briefly categorize them into six groups:

- Direct cytotoxicity:
    - Chemotherapy
    - Radiation therapy
    - Heat injury
    - Smoking
- An abnormally broken artery:
    - Hip dislocation
    - Fracture of femoral neck
    - After surgery causing anemia
    - Congenital arterial anomalies
- Abnormal veins:
    - Abnormalities of veins
    - venous stasis

- Peripheral intravascular compression:
    - Hemorrhage
    - Increased bone marrow pressure
    - Fatty infiltration in the bone marrow due to prolonged use of high doses of corticosteroids
    - Cell hypertrophy and marrow infiltration (Gaucher disease)
    - Bone marrow edema
    - Fractures and dislocations
- Unimaginable intravascular embolism:
    - Coagulation disorders such as increased thrombosis and decreased fibrinolysis
    - Sickle cell crisis
- Multi-factor.

In a small percentage of cases, mutations in the COL2A1 gene encoding type 2 collagen production show autosomal dominant patterns of inheritance. However, in many cases the cause cannot be determined and these patients are indicated for treatment of idiopathic osteosarcoma.

Repetitive trauma, like working on a complex line, can lead to AVN over time. Non-traumatic risks for AVN include anything that could affect blood vessel flow to the bone. Radiation can cause bone marrow changes that lead to AVN. Hyperlipidemia causes significant blockage of small blood vessels reducing blood flow that delivers nutrients to the bones. Medical conditions such as sickle cell anemia can also reduce the blood supply to the bones.

Anatomy with low accessory or retrograde vascular system, such as carpal tunnel, has a higher risk of necrosis. The unique anatomical structure also plays an important role in the nail, where a significant portion of its surface area consists of articular cartilage, which also limits the opportunity for blood circulation.

Glucocorticoids used in high doses and for long periods of time can induce bone resorption through osteoclast apoptosis. Apoptosis disrupts the lacrimal gland system.

Other risk factors for AVN: Alcohol abuse, blood dysfunction, and autoimmune diseases like Lupus, etc.

For 25 percent of people with AVN, the cause is blood flow. Interrupted is unspecified. For example, in Kienbock and Preiser disease, the exact cause of AVN is often unexplained.

Epidemiology

Osteonecrosis are most commonly found in the hip, but are also found in the shoulder blades, knees and shoulder blades and are rarely seen in the smaller bones of the wrist such as the fibula. Although the function may be affected, this evaluation chooses to focus on the more common forms presented to orthopedic surgeons.

Ten percent of all hip cases in the United States are caused by AVN and typically affect ages 30 - 65. Men tend to be more affected by ON in general, but autoimmune conditions that affect women like Lupus are also significant [1]. Less common variants, such as Preiser's disease (bone typhoid), tend to affect the dominant hand of middle-aged women. In contrast, Kienbock disease (periosteal lipoma) is more common in middle-aged men in association with manual labor, and there have even been case reports involving children.

The decrease in subchondral blood supply causes hypoxia, leading to loss of membrane integrity and cell necrosis. The pathological appearance of necrosis marked by the presence of neutrophils and macrophages will predominate. Macroscopically, this causes subchondral collapse and subsequent joint degeneration. MRI will demonstrate osteolytic changes secondary to decreased bone resorption due to disrupted osteoclast function. Specifically, T2 signal will be increased and T1 signal decreased due to adipocyte edema/ischemia of bone marrow.

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Histopathology

Osteocytes undergo apoptosis, and phagocytosis cannot occur. Therefore, the bone cells are not replaced.

This process leads to poor bone regeneration and fibrosis.

History and physical

Non-traumatic cases often present with mechanical pain with varying degrees of onset and severity and often difficult to localize.

In the early stages of the disease, the physical examination is often normal and inevitably causes a delay in diagnosis. Focus history should include recent trauma, steroid use, autoimmune disease, sickle cell disease, alcoholism, tobacco use, manual labor, gait changes, connective tissue disorders, onset of dull pain and reduced range of motion.

Hip osteonecrosis, in their early stages, are often asymptomatic. Hip and groin pain are the most common symptoms and are often a sign of advanced disease. Associated symptoms may include buttock and thigh pain. Most patients are pain free with rest. Others include stiffening and altered gait.

Osteonecrosis of the knee most commonly presents as acute-onset knee pain that occurs under load and at night. A history of osteoporosis or osteoporosis and no recent trauma are typical reactions. On physical examination, pain on palpation of the midfemur curve and decreased range of motion is observed.

Osteonecrosis of the shoulder. This granulomatous pharyngitis is often associated with trauma and bone necrosis elsewhere in the body. The pain is characterized by radiation pulses to the elbow and reduced range of motion.

Osteoarthritis is associated with polyarthritis and trauma. Patients will often complain of pain and difficulty recovering during the expected recovery period from the injury.

Lipomas and squamous cell fibrosis most commonly present without a history of trauma. Patients are usually skilled workers and complain of unilateral pain in the dorsal and radial side of the wrist. Reduced range of motion, wrist swelling, and impaired grip are other common findings.

There is general agreement on the histopathology and pathology of osteonecrosis (ON) of the bone, but no such consensus on the possible etiological relationships constituting the risk factors for this disease. The methodological approach to identifying risk factors accounts for much of the uncertainty about the risk factor composition and the strength of that association. Previously, the retrospective case-control approach was used to examine patient populations when ON the presence of comorbidities could be incorporated as risk factors. In general, this approach results in a large number of putative risk factors of low prevalence and no causal relationship between the causative factors and ON. May over-identify and overestimate the prevalence of pathogens constituting risk factors. A more modern approach is to examine subgroups of patients with putative risk factors (e.g. alcohol, corticosteroids, trauma) and consider the possibility of progression ON and estimate the true prevalence.

This review focuses on the structural consequences of skeletal ischemia and suggests a common pathway through the lesional circulation leading to ischemia and consequent marrow necrosis and osteoclasts. Etiology has been established and risk factors for ON are presented.

Pathophysiology

Cell and tissue necrosis

Osteonecrosis is characterized by a typical pattern of cell death and a complex process of bone formation and resorption (Figure 1). The earliest pathological features of ON were subsequent necrosis of hematopoietic and adipocyte interstitial edema (Figure 1a). Osteocyte necrosis occurs after about 2 to 3 hours of hypoxia, but histological signs of osteoclast death do not appear until about 24 to 72 hours after hypoxia. Osteocyte necrosis is reflected initially by narrowing of the nucleus and then by hollow osteoblasts. Capillary occlusion and recirculation occurs to some extent in the necrotic periphery, and with vascular infiltration, the repair process begins to include bone resorption and production. Completely replace dead bone with backbone. The new backbone was laminated onto the dead backbone with partial absorption of the dead bone (Figure 1b). In subchondral trabeculae, bone resorption exceeds formation leading to bone resorption, loss of trabeculae structural integrity, subchondral fractures, and joint dysfunction (Figure 1c). It is not necrosis in itself but the repair process and especially the resistive component leading to loss of structural integrity and subchondral fracture. The finite element model demonstrated that it lost the structural integrity of the basal trabeculae array instead of the subchondral plaque causing subchondral fractures.

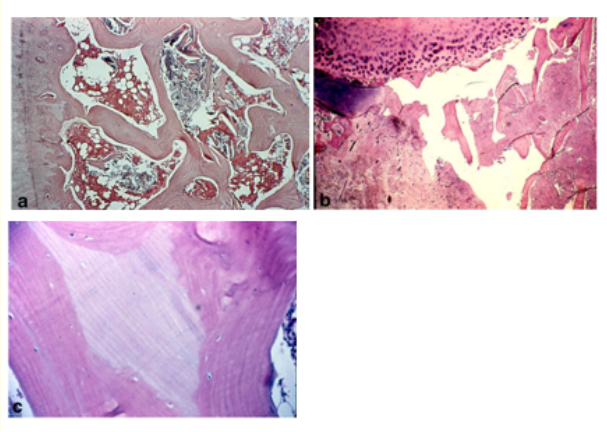

Figure 1: *Histopathological signs of osteonecrosis. a. Necrotic marrow with interstitial edema and hollow cells showing necrotic osteoblasts. b. Partially restored subchondral fracture of the tibia. c. Lesions on the broken bones. Osteocytes present in lacunae backbone but not dead.*

These histopathological changes are reflected on radiographs of the femoral head, giving rise to sclerosis and macular degeneration. Shaded areas reflect bone resorption, while sclerotic areas including vertebrae and dead vertebrae recover (Figure 2).

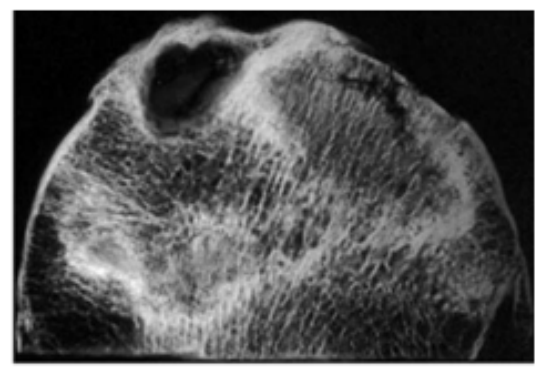

Figure 2: *The slide radiograph shows both sclerosing and luminous areas. The areas of sclerosis represent both dead bone and repair bone; the fields of insight reflect bone resorption. Subchondral fractures are also present.*

Compromised circulation

Understanding of the pathophysiology and risk factors of ON is limited by the availability of longitudinal studies in humans and the lack of a bipedal mammalian model. Thus, pathophysiological descriptions were synthesized from observations of human disease or extrapolated from animal models. However, the best evidence suggests that the usual pathophysiological pathways involved in subchondral microcirculation are compromised. The vascular anatomy of the femoral head and neck has been well described.

Microcirculation examination of the femoral head revealed impaired subchondral blood supply with vascular disruption, internal occlusion, and extravascular compression. The accumulation of perfusion to the retinal vessels gradually leads to decreased circulation of the subchondral bone of the femoral head. Other studies have shown that large areas of ON are accompanied by external involvement and inferior metaphyseal artery. Using direct measurement and computer simulations, a 1.6 decrease in blood flow is expected to reduce the internal pO_2 from 75 to 50 mmHg, assuming a constant rate of oxygen consumption, leading to anemia local clear. A unified concept of the pathogenesis of ON has been emphasized the central role of vascular and ischemic pathology leading to trophoblastic necrosis (Figure 3). Hypovolemia in the femoral head can occur through three pathogenic mechanisms: vascular rupture due to fracture or dislocation, intravascular occlusion due to thrombosis or fat embolism, intravascular compression by adipocytes, or Gaucher hypertrophy. A fourth mechanism, abnormal venous obstruction, has been demonstrated experimentally but may be of clinical significance.

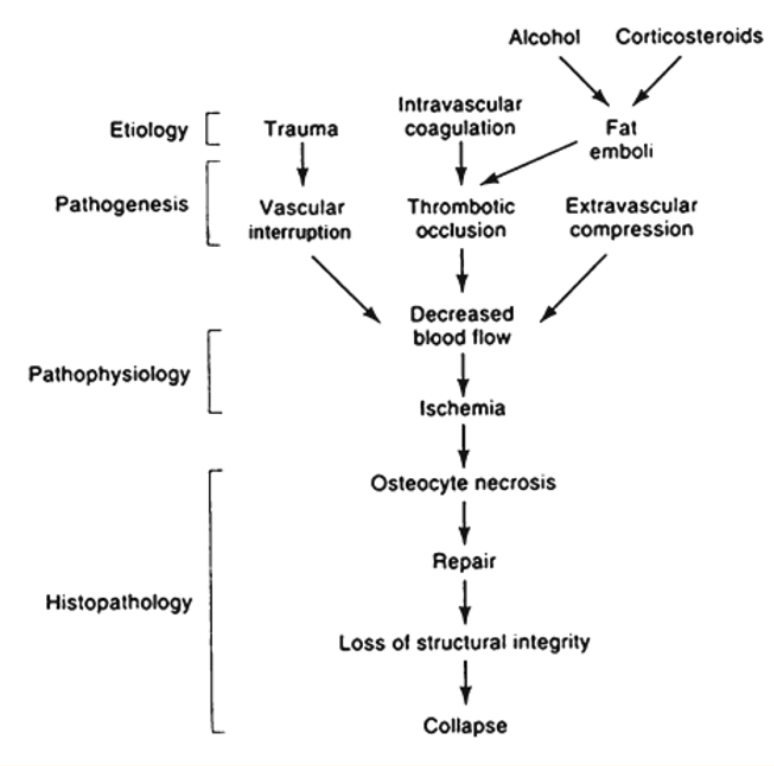

Figure 3: *Unified concept of circulatory pathophysiology. Diverse etiologies contribute to ischemia and necrosis.*

Unreasonable high blood pressure

Attention has been focused on increased pressure in the body as an ON-state pathogenic mechanism and has recently been revisited. Elevated trunk pressure has been measured at the ON femoral head in association with venous outflow obstruction and venous stasis. Normal bone marrow pressure has been reported to be around 15 mmHg with records above 30 mmHg considered abnormal. The infusion of 5 mL saline hydrates the volume of the intraosseous venous system. Infusion of fluid into the femoral head typically causes a transient increase in pressure of about 10 mmHg, which returns to baseline within seconds. In the ON mode, this stress test results

in a continuous increase in intra-oral pressure greater than 30 mmHg. However, other observers did not find increased intra-intestinal pressure reproducible, specific or sensitive measurements. One study suggested that diagnostic sensitivity of the ON trial was low with 17% in the ON mode having an endotracheal pressure less than 30 mmHg. Another study found a pressure lower than 30 mmHg in 32% of people with an ON hip and concluded that this stress test lacked sufficient accuracy as a clinical diagnostic tool. Other observations also cast doubt on the accuracy of inaccurate pressure measurements. Experimentally increasing intraocular pressure to more than 30 mmHg has been observed to increase periosteal, periosteal, and bone proliferation but not ON production. Increased internal pressure can be found in osteoarthritis as well as ON and can also be caused by increased pressure in the joint. These observations lead to the conclusion that Pressure, although commonly observed in ON, is not causally related to the pathogenesis of the clinical syndrome. In view of this, increased endothelial pressure is a nonspecific and secondary factor, but is likely to contribute to the pathogenesis of total ON. Clinical usefulness of blood pressure Measurements appear to vary widely due to varying perceptions of accuracy. It should be noted, however, that tissue that occupies space in the intravascular extravasation space, such as adipocytes or Gaucher cells, may not be consistently detected by intravascular pressure measurement, but still form the root element for ON.

Risk factors

Most reports of risk factors associated with ON are observational studies. Observational studies can start with potential associations and rapidly follow a cohort, determine prevalence of ON (vertical cohort study), measure predisposing factors, and ON at the same time (cross-sectional study) or define a cohort of ON patients and look back in time for putative associations (case-control studies). An example of a cohort study would be to ask what percentage of patients develop a femoral neck fracture? ON, while a case-control study asked the percentage of ON patients with fractures. Similarly, the question about the proportion of patients treated with corticosteroids rose to ON as a cohort study while determining the proportion of IN patients treated with the corticosteroid case study. The strongest methodological observational design is the cohort study; the weakest is case control research. Unfortunately, many of the studies on these ON risk factors are either anecdotal or use case control methods that lead to relationships of putative risk factors to ON where the causal relationship is the problem. In this review, we will highlight relationships mainly derived from longitudinal cohort studies with a causal relationship with ON that can be estimated with the greatest confidence.

Several pathogenic mechanisms can lead to ischemia and ON including vascular disruption, endovascular occlusion, and ventricular extrasystoles.

Disruption of blood vessels

Fractures of the femoral neck may directly damage the subchondral bone supply vessels and a relatively high rate of ON of the femoral head has been reported in these patients. A recent meta-analysis reported an ON prevalence of 14.3% (range 10 to 25%) in this population. Liu., *et al*. [3] shows it by digital angiography minus ON. The incidence following femoral neck fractures is directly related to the number of vessels crossing the fault line. Other studies have attempted to relate error type, accuracy reduction, and reduction time with ON occurrence. A Garden study showed that an X-ray-based deviation of the Endpoint resulted in ON and segment collapse in 65.4% of patients, compared with 6.6% of patients with acceptable alignment after reduce the opening and medial fixation of femoral neck fractures. The acceptable relationship in this study was defined as the angle between the midbrain of the femoral axis and the center of the neck on anterior radiographs and through the center of the femoral and neck axis on internal radiographs from 155 to 180°. In a prospective study, Barnes and Garden reported on a series of 1108 patients with femoral neck fractures, most of whom underwent open reduction surgery and internal fixation. They found segmental femoral head fractures in 16% of patients with stage I non-healing fractures and 27.6% of patients with stage III and IV displacement fractures. Similar to the studies outlined above, the authors found rates of 0 and ON in patients who made a mistake at the time of their surgical intervention. Among them, the results demonstrate that patients with varus-directed fixation have a significantly lower rate of fusion when compared with valgus-directed-fixed patients (50 vs. 71%).

However, people in the valvular region also have the highest risk of femoral head ON. Similarly, Nikolopoulos., *et al*. also demonstrated that nondisplaced femoral neck fractures (Garden classification I, II) resulted in a lower ON rate when compared with displaced femoral neck fractures (Garden III, IV) during fixation screw treatment. In (19.5 vs 39.5%) Tao and associates also found error patterns, as identified by the Garden classification, as well as poor mitigation as significant risk factors. For the femoral head ON in their retrospective review. During the treatment period, a meta-analysis was performed by Papakostidis., *et al*. no relationship was established between the ON ratio and the time interval between injury and complete internal fixation.

Fracture of the femoral neck due to intra-articular compression of the posterior hip has been suggested to theoretically reduce the risk of ON by minimizing excessive compression of the vessels supplying the femoral head. However, the literature lacks strong support for or against this theory. Shrader., *et al*. did not find any association between crown decompression and subsequent progression of femoral head osteonecrosis. However, in a retrospective analysis, Ng., *et al*. found that hip decompression significantly reduced the risk of type II femoral head fractures and type III femoral neck fractures.

Corticosteroid medial fractures distal to the entrance of the femoral arch artery branches have a significantly lower ON rate.

Dislocation of the hip can also disrupt the blood vessel supply to the femoral head. The deep branch of the MFCA can be injured at dislocation after it passes behind the lateral stump and in front of the quadriceps. For posterior dislocations, ON rates have been reported to be between 5 and 60% depending on duration of reduction and severity of fractures and other injuries. Hougaard., *et al*. found ON rates of 4.8 and 52.9% in case-control studies analyzing dislocation patients reduced before and 6h after injury. There are limited data on the long-term outcomes of anterior hip dislocation, but some studies suggest the occurrence of femoral head dislocation in about 10% of patients.

Intravascular occlusion

Disruption of blood flow to the femoral head may be secondary to intravascular obstruction. Many reasons can cause this interference, namely sickle cell aggregation or blood clots or lipid thrombosis.

Sickle cell disease is caused by an inherited mutation in the beta chain of hemoglobin that produces abnormal hemoglobin, which polymerizes under physiological stress. The polymerization of many hemoglobin molecules gives red blood cells the characteristic sickle shape. The prevalence of ON in patients with sickle cell anemia has been reported to be as high as 11 to 37% in prospective and cross-sectional studies. It has been hypothesized that an hypoxic stressful environment would trigger hemoglobin precipitation in these patients leading to sickle cell anemia. Sickle cells are prone to stick together and cause endovascular obstruction, especially in areas of low blood flow, especially the femoral head. Therefore, the ON rate of the femoral head increases with the age of the patient. Presumably, this is due to the repeated vascular lesions that these patients are prone to throughout their lives. Matos., *et al*. reported ON in 11.1% of their series of patients under 21 years of age, and Mukisi-Mukaza., *et al*. found ON in one or both hips in 37.2% of their patients over 18 years of age [4]. In addition, there is a high probability that ON progression is seen in sickle cell patients with radiographic evidence of its presence. Hernigou., *et al*. prospective follow-up of a cohort of 123 patients with sickle cell disease with unilateral ON symptoms and no obvious ON symptoms on that side's imaging. At follow-up, 91% of these patients had asymptomatic pain on the anterior side and 77% had femoral head collapse on that side.

Coagulation factor abnormalities are also associated with ON of the femoral head. Genetic defects leading to thrombolysis or thrombosis can lead to increased thrombus formation and impaired blood flow in the circulatory tubes. Decreased fibrinolysis from secondary to high plasminogen activator inhibitor (PAI) concentrations was observed in 31% of ON patients compared with 3% of controls in a prospective cohort of femoral ON patients. For thrombophlebitis, Zalavras., *et al*. reported in a retrospective case-control study that the proportion of patients with osteonecrosis factor V Leiden had a significantly higher mutation compared with controls (18 vs. 4.6%).

In subjects without known genetic defects, elevated levels of clotting factor have been reported in ON patients using a case-control approach. Jones and associates reported that 82.2% of ON patients had at least one abnormal coagulation factor compared with 30% of unaffected controls; 50% of affected patients had two or more abnormalities compared with 2.5% of controls. Similarly, higher levels of lipoprotein A, von Willebrand factor and lower levels of proteins C and S have been reported in patients with idiopathic and secondary ON compared with healthy controls. Reduced levels of proteins C and S and genetic resistance to activated protein C both downregulate the physiology of prothrombotic factors V and VIII, allowing endovascular injury to occur in the femoral head. Lipoprotein A has been implicated in several studies. It should be noted, however, that there is some controversy regarding the role of the femoral head's hypercoagulability and ON. It is not always observed in the ON of the femoral head and is commonly seen in other disorders affecting the femoral head, namely osteomyelitis and osteomyelitis syndrome. Similarly, abnormalities of protein C and S, antithrombin III, or antiproliferative C protein were not found in two retrospective studies of patients with Perthes disease. Information appearing in longitudinal cohort studies may suggest a lower incidence of coagulopathy in ON.

Massive extravascular compression

The concept of a connection resistor can be used to form this secondary cause ON concept. This resistor consists of a rigid-walled chamber through which the tubes can be compressed. The flow of liquid through these tubes is related to the amount of pressure exerted on them by the external components of the cavity. The femoral head can be conceptualized similarly to a Starling resistor with the oil circuit representing the compression ducts and the intravascular space representing the extraductal space of the chamber (Figure 4). Increased pressure in the extravascular space, even if it cannot be consistently recorded, can reduce blood flow in the small vessels that pass through it.

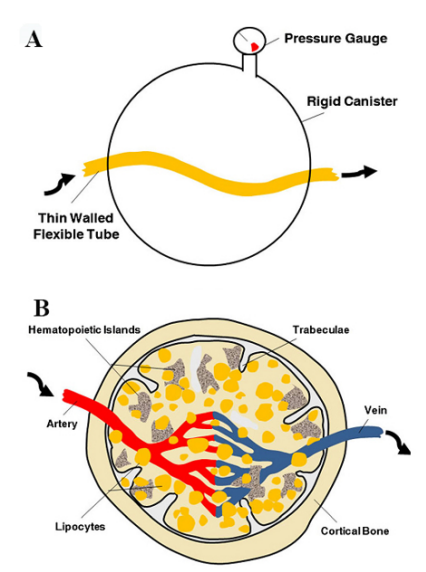

Figure 4: *Concept of the Starling resistor as applied to bone microcirculation. A. Raising the pressure in a rigid-walled chamber can decrease fluid flow in a flexible-walled tube passing through the chamber, B. In the case of bone, the intraosseous extravascular compartment may function like a rigid walled chamber. Intraosseous hypertension or space-occupying tissue may sufficiently restrict microcirculatory blood flow to produce ischemia.*

Therefore, lipid deposition and adipocyte hypertrophy in the medullary cavity are the two main clinical manifestations. Extrasystolic intravascular pressure can reduce circulation. Often combined with corticosteroids or alcohol intake, an increase in extravascular pressure has been thought to produce arterial or venous outflow obstruction leading to medullary and cellular ischemia. Bone in the femoral head. Administration of both alcohol and corticosteroids has been shown to increase adipocyte size, alter lipid metabolism, and shift cells from osteoclasts to adipocytes.

Corticosteroid related osteonecrosis were involved in 10 to 30% of cases in retrospective studies. Corticosteroids are used in many medical conditions including systemic lupus erythematosus, rheumatoid arthritis, asthma, organ transplants, and vasculitis. Although it is difficult to separate the contribution to the development of corticosteroid use ON from the underlying condition, a large meta-analysis of 22 studies found no association between the underlying disease and ON. A considerable effort has been made to determine which components of mean daily dose, cumulative dose or time are involved in the development of ON. Prospective cohort studies have suggested that a mean daily dose of > 20 mg/day is associated with a significant risk of ON. A meta-analysis by Felson., *et al*. determined ON increased 4.6-fold for each increase in the 10 mg/day input oral corticosteroid dose.

Clinical impressions of the relationship between corticosteroid use and ON are largely formed from cross-sectional and retrospective studies that have determined the prevalence of corticosteroid use in ON patients. These studies did not determine the prevalence of ON in patients using corticosteroids and did not determine an etiological risk for corticosteroids, but did report some patients with ON who also used corticosteroids. Studies have been evaluated with prospective cohort studies of ON. Rates in patients receiving corticosteroids have been reported to range from 4 to 7%.

Excessive alcohol use is also associated with ON in the femoral head in 10 to 40% of cases. Matsuo., *et al*. found that people who consumed more than 400 ml of alcohol per week were 9.8 times more likely to be ON than those who did not drink. This risk increased 17.9 times in those who drank more than 1000 ml of alcohol per week.

Gaucher disease is also associated with ON growth of the femoral head due to its role in decreased capillary blood flow, possibly due to increased intracranial pressure in the external intravascular space. Due to beta-glucocerebrosidase deficiency, patients with Gaucher disease accumulate large amounts of glucocerebroside in the lysosomes of their histiocytic cells, appropriately named Gaucher cells. A recent study by Polls., *et al*. reported an ON rate seen on MRI of 46% in these patients.

Other causes

The staff are different Series of controls. Hyperlipidemia, hyperuricemia, inflammation, leukemia or lymphoma, and hypertriglyceridemia are all considered potential causes of femoral head ON. Osteoma has also been reported in pregnant patients, other characters have been associated with ON of the femoral head in reported reports and cases - those undergoing radiotherapy, grafting and those with tumor block. metastatic or diffuse properties. The Dysbaric ON has good features but a great benefit of History due to safe operating pneumatic pressure and established diving decompression.

The other kernel theory is not found in the prefrements and our relative risk has not been established. See also text sources Enter a text source for more translation information.

Many conditions have been linked as bases for ON. However, it is difficult to determine the true base using follow-up or retrospective approaches, with regard to the base of low rates, especially when many studies report ON. Apartments for 10 to 15 years % case. Where possible, we rely on reports to use system functions, longitudinal or analytic, to identify strong associations between risk factors and ON. This does not mean that we exclude other, non-restrictive, possible conditions that may appear ON, but substantial evidence of a causal relationship is needed.

The closely related causal risk factors for ON seem to converge through vascular degradation mechanisms to produce subcutaneous or segmental and marrow ischemia and bone cell death. Subsequent repair often results in subchondral bone loss beyond formation, resulting in structural damage and fracture. Understanding the risk factors and pathophysiology provides therapeutic implications. Several treatment regimens are available to optimize femoral primary circulation, prevent bone resorption, and preserve subchondral bone. In traumatic ON conditions, fracture is acceptable Location and timing, technique and approach to immobilization are important. In the case of non-traumatic ON, a specific prophylactic approach is available to suppress adipocyte proliferation (by limiting alcohol intake and corticosteroid dosages), administering statins, and treating Gaucher disease with replacement therapy enzyme potential. Osteoma associated with the hypercoagulable syndrome has been prevented with warfarin and enoxaparin. Bisphosphonates have been used to rebalance the rate of bone resorption and bone formation under the cartilage with the expectation of maintaining the mechanical integrity of the subchondral bone and minimizing the risk of fractures and unnecessary joints.

DIAGNOSIS, MANAGEMENT AND TREATMENT

1. Legg – Calvé – Perthes Disease

Legg-Calvé-Perthes disease (LCPD) is used by necrosis of the femoral head (FH), unilateral or bilateral. Which affects the range of motion of the hip. In our experience, patients often report pain in the affected joint, which is more intense during and after physical activity. On the other hand, the limp or tendency to walk is used by being the main sign that they come for advice. Incidence rates vary widely, from 0.4/10,000 to 29.0/10,000 children < 15 years old [5].

Although LCPD was first described at the turn of the last century and has been studied for more than 100 years, its etiology remains limited. Remaining bones with changes specifically associated with LCPD have been found in Argentina, Czech Republic, Italy and China, suggesting that the disease has been present from very distant times. From 1909 to 1910, advances in radiology allowed the distinction of LCPD from other conditions such as fractures, rickets, septic arthritis, and tuberculosis arthritis. Therefore, LCPD is described almost simultaneously in different countries; by Arthur Legg, Jacques Calvé, Georg Perthes and Henning Waldenström independently. In 1922, Waldeström proposed a classification of the disease into four stages: the osteonecrosis stage, the fragmentation phase, the regenerative phase, and the healing phase. This classification is still useful today. However, although different diagnostic methods and treatments have been used throughout history, the etiology of LCPD remains largely unknown. However, there are several theories that suggest environmental, metabolic and genetic factors are causative agents of the disease.

Epidemiology

The incidence of LCPD varies widely across countries, cities and races, ranging from 0.4/100,000 to 29.0/100,000 children. LCPD usually appears between the ages of 3 and 12 years, with peak incidence occurring between the ages of 5 and 7 years. Boys are affected 3 to 5 times more often than girls, and the disorder is bilateral in 10 - 24% of patients, with genetic correlation in about 8 - 12% of patients.

Pathogenesis

The pathogenesis of LCPD is complex. From a mechanical point of view, deformation in FH will occur when the force acting on FH is greater than its ability to resist deformation. Animal models have shown that necrosis reduces the mechanical and supportive properties of FH, articular cartilage and bone. It is thought that the mechanical properties of infarcted bone are compromised by different mechanisms at play during different stages of the disease.

First, during the avascular phase, an increase in calcium in the necrotic bone renders the bone vulnerable to microscopic damage, affecting the mechanical properties of FH. Necrosis will lead to the breakdown of osteoclasts, osteoclasts, and osteoblasts, causing

undetected and/or unrepaired micro-cracks. Then, during the revascularization phase, the necrotic bone will be reabsorbed, affecting the mechanical properties. The hip is one of the main bearing joints.

It is important to consider the forces acting on the joint, as they will affect the degree of tension in the FH.

From the radiological point of view, the process of ischemia and subsequent bone remodeling is divided into several stages. Determining the stage is paramount. The duration of each stage varies widely, but in general, the necrosis and fragmentation phase lasts about six months; the period of enjoyment, from 18 months to three years; and the final stage, until the bone is mature. According to other authors, the fragmentation phase lasts about a year, and the recapture phase, from three to five years (Figure 5).

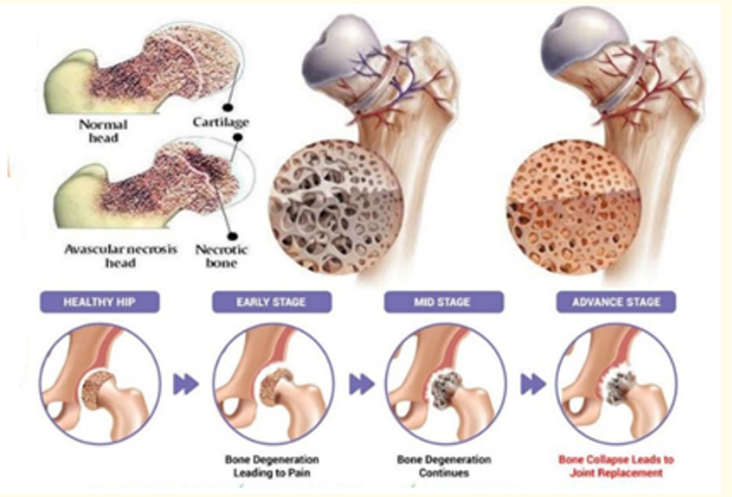

Figure 5: *Pathogenesis of avascular necrosis with LCP.*

Diagnosis

Due to lack of information, LCPD diagnosis can be difficult; however, there are several important diagnostic criteria. The differential diagnoses that must be considered based on radiographic findings include, coxacidosis, Meyer dysplasia, epithelial dysplasia, spinal dysplasia, chondroblastoma, juvenile idiopathic arthritis adolescence, drug-induced head necrosis, Gaucher disease, sickle cell anemia, thandroplassemia (Figure 6).

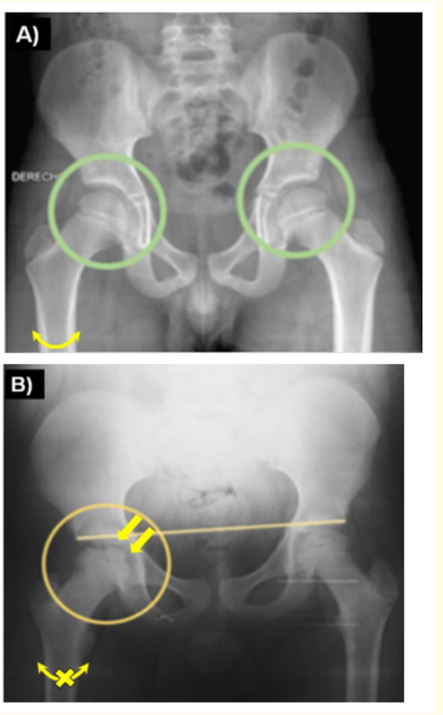

Figure 6: *AP radiography. In the AP X ray the deformity of the hip and femoral head characteristic of LCPD is demonstrable, A healthy control, B LCPD patient. Courtesy of INR LGII genetics laboratory 2017.*

Classification

To predict prognosis and decide on appropriate treatment, there are classifications that primarily consider the affected area and the region.

Catterall, 1971, divided the disease into 4 grades, according to the degree of epithelial damage - Type I: 0 - 25%; Type II: 25 - 50%; Class III: > 50% and Type IV: 100% (Figure 2).

In 1984, Salter and Thompson described a classification of two groups (A and B), defined by the degree of subchondral fracture visible on axial radiographs in the early stages of the disease. The disadvantage of this approach is that not all patients are diagnosed at an early stage (Figure 7) [6].

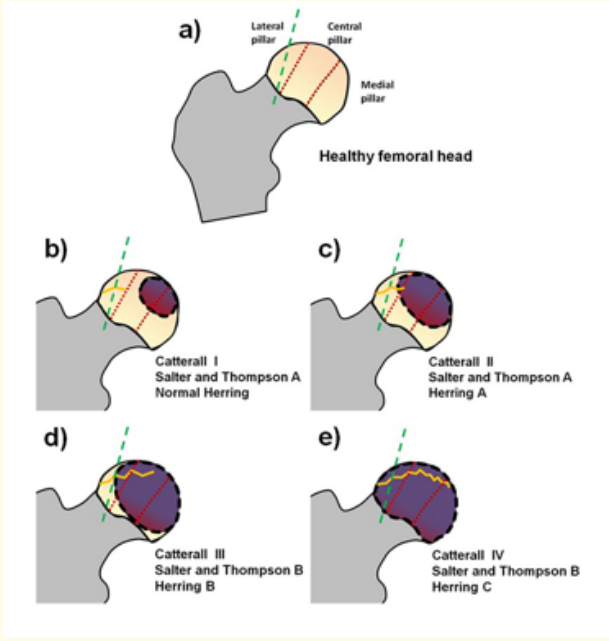

Figure 7: *The dotted lines divide the femoral head into medial, medial, and lateral pillars. The gray dotted line represents the midline of the lateral pillar. Its dotted line is the area of necrosis. The zigzag shows the size of the subchondral fracture (fs). a) Femoral head sound. b) Area lost 25% of total area; its discontinuous edge is an area of necrosis and has an accessory fissure (fs). Compared with ~50% total surface area loss, increased necrotic area, increased fs size, and <50% decrease in lateral column height. c) Loss of >50% of total surface, gain of fs, and loss of height of side stop ~50%. d) Maxillary space loss of almost 100% of the surface, maximal involvement of the lower wall, and >50% involvement of the lateral cavity.*

The most recent classification was proposed by Herring in 1992. It is based on the height of the lateral embryos of epigenetic FH during the fragmentation phase of the disease and is divided into three groups - group A: no involvement of side pillars and its full height is maintained; group B: height reduction <50%; and group C: height reduction > 50%. The predictive value of the Herring classification is higher in the early stages of the disease. Recently, a fourth group has been proposed between groups B and C, in which the lateral abutment is narrow, less rigid, or maintains 50% of its height (Figure 3) [7].

Etiology

The cause of LCPD is unknown. Various causes have been suggested; however, LCPD can be caused by multiple etiological factors that share a common final pathogenesis. A new view suggests that LCPD is a multifactorial disease caused by a combination of environmental, metabolic and genetic factors. However, during the diagnosis, various etiological factors may be considered.

Environmental, metabolic, and genetic factors described in the LCPD In terms of race, LCPD occurs at a higher incidence in Caucasians, with a reduced number of Asian cases and a lower prevalence in Asian populations. Disease is reduced more than blacks. The prevalence of LCPD varies widely in different geographical regions. On the other hand, sex can be considered as another factor, since LCPD mainly infects men and the prevalence of the disease, indicating climate, hours of sun exposure, in a number of other factors can be the cause of LCPD. Other studies have shown that, at lower socioeconomic levels, there is an increased incidence of LCPD, so it can be assumed that the nutritional status of patients may be related to each other to develop disease.

Several studies have shown that there is a correlation between LCPD and exposure to tobacco smoke and wood smoke. It was found that there was a small correlation between LCPD, growth disorders and low birth weight infants. Neal., *et al*. reported that the prevalence of obesity is high in LCPD patients, as it is associated with several risk factors such as poor nutrition, inflammation, and increased mechanical load [8]. Mechanical overload seems to lead to LCPD, as it has been shown that repetitive gymnastics training and technical errors can be important factors contributing to the development of gangrene. Vascularity in the FH, excluding many exercisers with LCPD. Animal models show that, after joint overload, changes in FH similar to those found in LCPD are notable. Another important aspect is that in children with ADHD, who tend to be more active, there is an increased risk of LCPD.

The biochemical changes that cause bone to fully develop are due to several factors: obesity, waist circumference, high-density lipoprotein (HDL), tumor necrosis factor alpha (TNF-α), interleukin (IL-1β), and IL-6), and defects in lipid metabolism. Tese has defects in bone metabolism and is therefore considered a risk factor for osteonecrosis and LCPD. High concentrations of leptin and lipoprotein A, which are highly obese proteins, have been found in the serum of LCPD patients.

The disease is often associated with thrombotic or hypercoagulable changes, such as factor V Leiden, FVIII and overactive prothrombin mutations, altering natural anticoagulants such as protein C and S, decreased lipolysis and increased selectin (E and P); however, data also suggest that infection and endothelium may be important factors in the development of LCPD.

Infection that affects the bone pattern; in fact, it is thought that heterozygotes of the IL-6 G-174C/G-597 mutant are more likely to develop LCPD. Kamiya., *et al*. observed increased IL-6 in the synovial fluid of LCPD patients. The neutrophil/lymphocyte ratio is a marker of subclinical inflammation, which increases as lesions in the FH enlarge; therefore, it can be assumed that inflammation is related to the occurrence of LCPD and its severity [9].

Absence plays an important role in the etiology of LCPD. Risk factors such as hypertension, increased lipoprotein A, structural vascular abnormalities, reduced gill diameter and decreased blood velocity of chickens have been described in LCPD patients, suggesting that the cardiovascular apparatus may be impaired hurt in many ways. Several authors have reported mutations associated with various metamorphic modifications of FH that alter the conformation of type II collagen. Embryonic alterations induce local collapse in the stroma surrounding blood vessels, promoting sterility during development in the presence of early signs of osteonecrosis.

There are studies that describe families with more than one member of the disease, demonstrate genetic mechanisms that may be involved in LCPD, and genetic patterns, ranging from recessive to multi-infection, have been demonstrated propose. However, in families with a high percentage of individuals infected, an autosomal dominant phenotype is often formed. Loder., *et al*. found that the combined incidence of LCPD in first-, second- and third-degree relatives combined was 1:39, and in siblings it was 1:26; i.e. 35 times and 50 times

more than the general population [10]. LCPD is associated with various genetic disorders such as Alagille syndrome, Albright hereditary osteodystrophy, and trichorhinophalangeal syndrome, which are characterized by craniofacial malformations and altered skeletal abnormalities. Epigenetic changes may be involved in the onset of LCPD, as Zheng., *et al*. reported that there is a lower level of methylation in patients with LCPD, affecting bone and cartilage growth in a number of ways.

Because hypercoagulability may be related to the origin of LCPD, there are studies linking mutations in factor V Leiden, polymorphisms in prothrombin (PT), and methylenetetrahydrofolate reductase (MTHFR) with an increased risk of developing the disease. LCPD development. Inflammation is also considered important in the development of LCPD. Azarpira., *et al*. reported that endothelial nitric oxide (eNOS) polymorphisms 894G>T and -786 T>C increased the risk of LCPD and TNF-α-308G polymorphisms. >A and TNF-α-238C>T cannot be directly related to LCPD, but may be involved in the development of osteonecrotic FH. Furthermore, eNOS is involved in many physiological processes, including angiogenesis, thrombus formation, coagulation, and fibrinolysis and recently, the G894T mutation in the eNOS gene has been described as a factor risk in LCPD.

Treatment

The main symptoms of LCPD are lameness and are localized to the hips, spreading to the thighs and knees; However, some cases present with a painless limp. The general limits are abduction and internal rotation, as well as the limit to a temperature of approximately 20 degrees. In some cases, there is shortening of the infected pole. Most of these symptoms were related to the loss of the hip axis (Figure 8).

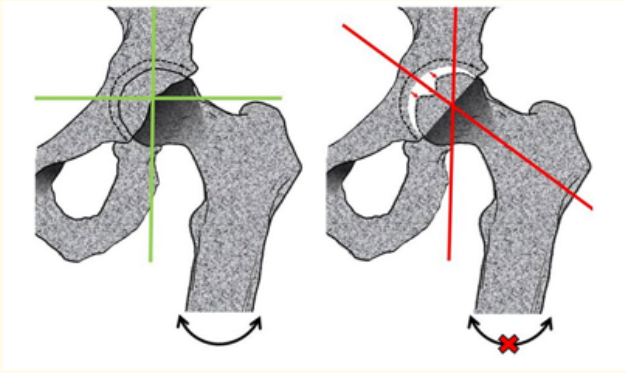

Figure 8: *Loss of hip joint shaft. The deformity of the femoral head, as well as the shortening of the infected limb, results in loss of the hip axis, which, due to mechanical damage, causes the characteristic symptoms of LCPD.*

Since the FH format varies widely among employees, work is determined on a case-by-case basis. Current treatment methods range from observation and observation to technical procedures on the femur and hip. All approaches are aimed at preventing deformity of the FH, any duplication of the infected hip, and the early onset of coxarthrosis.

The Fucos method is performed based on X-ray films of each specific patient. In general, treatment algorithms are not needed in patients with early-stage disease who have adequate hip range of motion and are painless and have little radiological risk associated with FH, with no limitations such as at Catterall I or II and Salter and Thompson's Group A.

Patients with hip pain or tenderness should rest for 5 to 7 days and may be prescribed non-steroidal anti-inflammatory drugs to minimize some symptoms. Patients who did not respond at rest were admitted to the hospital and placed on bilateral skin traction with progressive abduction for a period of 7 to 10 days to immobilize. Joints that do not regain motion will be imaged. With that in mind, if FH is malformed in relation to calcification, a number of different approaches should be considered. Percutaneous abduction quality release can be used for joints that appear stiff during abduction but retain their shape. When maximal motion is achieved, data containment is considered for the first grade of bad radiographs, but the effectiveness of these treatments may be on the case of treated.

Patients with a larger lesion area in the FH may be candidates for treatments, such as spondylectomy or ablation surgery, to maintain the femoral head as appropriate as possible clavicle body. Recommended for use on the shelf for children over 8 years old or Catterall III and IV groups. Patients with an adjustable hip and active disease or those who have had hip rehabilitation but have longitudinal pain may be candidates for hip extension. Jaw resorption can be corrected by resection of the jawbone. Osteotomy is more commonly used than osteotomy; however, a regional hysterectomy is used significantly more commonly in North America, Australia and South America, while a hysterectomy is performed more commonly in Europe, Asia and Asia. Africa. However, our experience with LCPD suggests a different guessing algorithm (Figure 9).

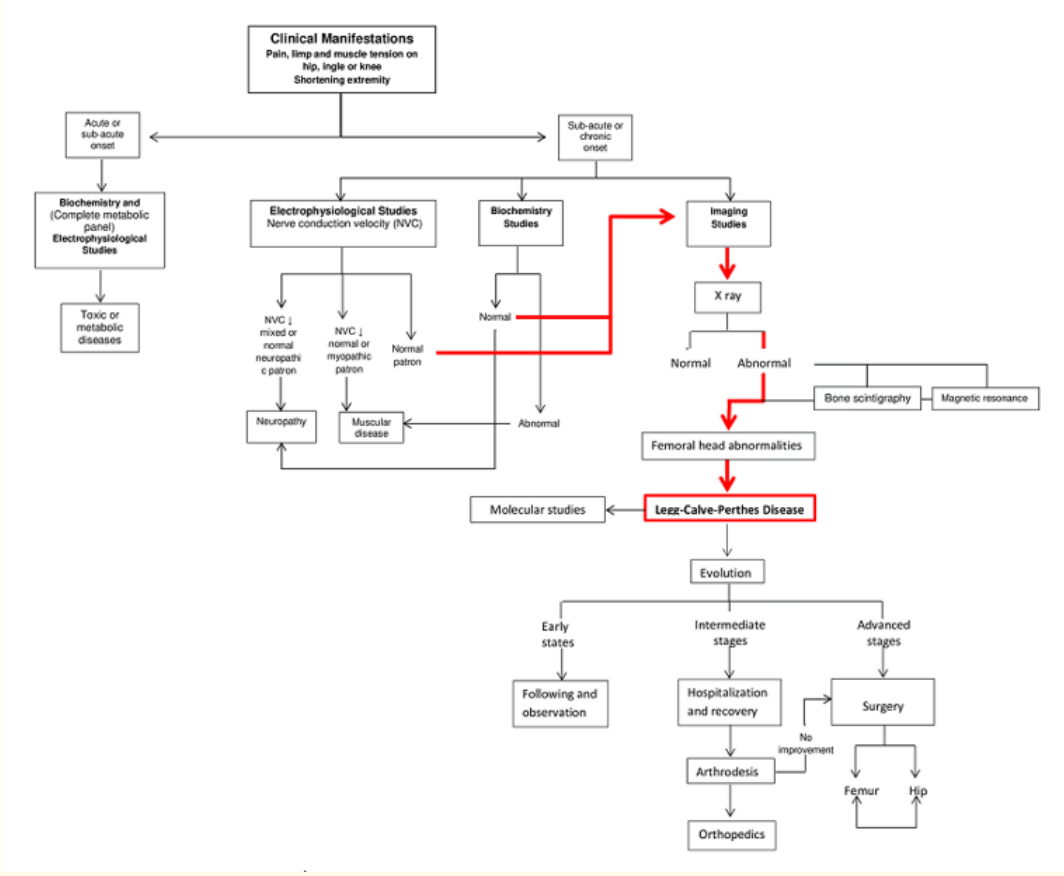

Figure 9: *Study algorithm for patients with Legg-Calvé-Perthes disease.*

Prognosis

The sequelae found in LCPD patients after age 40 are minimal, and the long-term prognosis tends to be good in 60% to 80% of cases. These are multiple prognostic factors in LCPD, such as age of onset and diagnosis, sex, hip range of motion, and classification. While, in general, patients aged 7 to 7 years have a better prognosis than older patients, adolescent patients have a poor prognosis. In the case of women, it is reported that they tend to have a worse prognosis; however, Guille., *et al*. reported that the prognosis may be similar between men and women. Finally, cases of diplopia also have a poor prognosis. The severity of the lesion, the classification of the patient, the size of the lesion, and the treatment method used must be considered.

Discussion

Despite its low incidence, LCPD represents a major global health problem, as it infects a significant portion of the world's population. LCPD is characterized by a limp, pain, and limited range of motion of the hip, all due to avascular necrosis in the FH.

According to the literature, treatment and prognosis are determined according to the characteristics of each patient. For example, the age, sex, type and size of the infected area in FH.

Limited information about the etiology of the disease is an important question in LCPD. In this sense, and because many families have been described in different parts of the world, with more than one member having been infected. As well as the various evidences that have been reviewed, there are genetic factors that play an important role in the occurrence of LCPD.

On the other hand, cloning around FH plays a central role in disease development. Changes related to the vascular system, among which are those that induce the thrombotic state, have been suggested by different authors. The mechanism proposed by Te involves the formation of blood-blocking microthrombi in the FH delivery vessels, leading to clonality. This theory is relevant to different situations, such as the presence of FVL mutations and variable thrombotic changes in populations of patients with LCPD. As well as the relationship to environmental factors, such as the association found between secondhand smoke exposure and the development of LCPD.

On the other hand, inflammation may play a central role in bone destruction and remodeling, leading to the development of LCPD as well as more severe forms of the disease.

It is important to point out that environmental factors, such as malnutrition, obesity, mechanical overload, and others that have been previously exposed, will exacerbate the aforementioned mechanisms and the emergence of LCPD through different pathways.

Conclusion

The pathogenesis of LCPD is so complex that the degree of involvement may vary. Although the etiology is unknown, available information suggests that LCPD has a multifactorial etiology, where multiple environmental, metabolic, and genetic agents may be involved.

2. Osgood - Schlatter Disease

Osteoarthritis of the tibial tubercle was first documented in the early 1900s. Two different physicians reported an experience in which hyperactive adolescents complained of pain centered on the tibial tubercle in the tibia. When participating in activities that involve jumping and running. Both Osgood and Schlatter are credited with identifying the condition and thus associated with its title. This process, they explain, occurs in children who are in a period of rapid growth and in those who place stress on the developing tubercle through force of the stellate tendon. Researchers have differentiated this condition from fracture of the tibia and emphasized that this is caused by the

area being subjected to repetitive loading [11]. Osgood-Schlatter disease (OSD) is a traction abscess of the tibia caused by repetitive stress on the quadriceps muscle of the thigh. The main cause of this condition is stress from the stellate tendon at its insertion point.

Etiology

The pathophysiology of the disease is partial loss of continuity of the tendon-cartilage-bone junction of the tibia. An inflammatory process begins in the region and ends with stellate tendonitis, subacute multiple fractures, and abnormal ossification with the underlying bone. The most accepted theory for this condition is the repetitive knee flexion mechanism. As a result of these contractions, vibration or microstrain occurs in the chondro-fibro-osseous tubes. However, several radiological studies have shown that patients affected by OSD have anatomical differences at the insertion point of the stellate tendon. In addition, histological studies supporting the traumatic etiology showed no inflammation.

Epidemiology

OSD was initially reported to occur more frequently in boys than in girls. With an increasing number of young female athletes, the disease is now being reported at a rate comparable to that in young men. There are a few recent studies showing no significant difference in incidence between men and women OSD is more common between the ages of 8 - 13 years in girls and 12 - 15 years in girls. Boys. OSD affects 21% of athletic adolescents, while it is seen in 4.5% of age-related nonathletic controls. The disease is bilateral in 20 - 30% of patients.

Clinical findings and physical examination

An individual's history and physical examination are usually sufficient to diagnose OSD. The patient complains of activity-related pain centered on the tibial tubercle and distal tibial tendon. Pain, which occurs with activity and subsides with rest, is the presenting symptom. There is a history of trauma behind this condition occurring during athletic activities such as basketball, volleyball, gymnastics, and soccer. Pain during activities such as running and jumping causes the knee to flex, leading to quadriceps contraction [12]. Usually observed on physical examination, pain, swelling, thickening of the stellate tendon, and extension of the tibial canal are common. The patient can walk with an unobtrusive gait. During palpation, a solid mass (abnormal bone) is often observed in a chronic condition. Acute cases may present with extender latency. There were no signs of effusion or instability, and complete passive range of motion in the knee. Frequency of spasticity of the quadriceps and hamstrings is common [12].

The differential diagnosis of OSD includes osteomyelitis, Sinding-Larsen-Johansson syndrome, patella-femoral syndrome, dislocation or dislocation, osteomalacia, tibial fracture, bursitis, and bursitis translate. Pes anserinus outbreaks, tumors and infections. If pain is worse at night or at rest, the differential diagnosis should be considered. They should be supplemented with a detailed history, focused physical examination, and radiograph of the patient.

Radioactive detection

Radiographic evaluation may reveal superficial pus in the stellate tendon, anterior soft tissue swelling of the tibial canal, and thickening of the meniscus (Figure 10). This can be a normal variation in children without symptoms, especially in the preparatory phase. On the other hand, there have been reported cases diagnosed by radiography without any symptoms. A sequelae of OSD such as sphincter discharge, which is rarely observed, may present with acute knee pain and may at first be considered a fracture. A cluster of fragmented abscesses indicates that the patient is in the chronic stage.

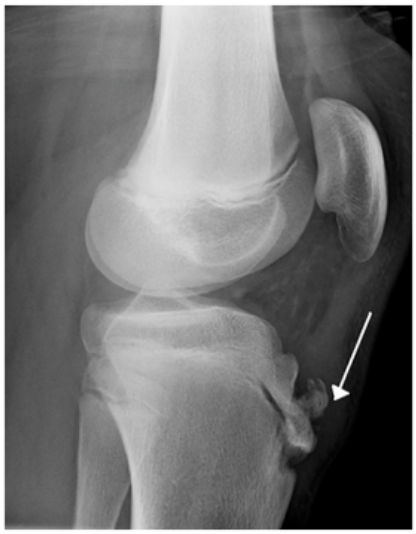

Figure 10: *Bony prominence over the tibial tuberosity at lateral knee X-ray as a sequel of OSD.*

Ultrasound (USA), magnetic resonance imaging (MRI), and computed tomography (CT) are other imaging modalities used to diagnose OSD. USA may show denser stellate veins better than radiographs alone. It can also demonstrate pre-bacterial swelling, fragmentation of the liquefaction center, and excessive fluid accumulation in the fallopian tubes. In the MRI, T2-weighted images, the irregular signal intensity can be observed superior to the epithelial line in the proximal tibia. Alternatively, MRI may be more useful for detecting early and progressive lesions or atypical manifestations of OSD. It may play some future role in staging and predicting clinical course, as the role of MRI in diagnosis, prognosis and management is currently limited [12].

Treatment

Conservative treatment

Treatment of OSD is guided by the severity of symptoms. OSD is a self-limiting disease and usually resolves spontaneously as the skeletal system matures. Improvement can be gradual. This condition can recur for 12 - 18 months before it goes away completely as the bones mature. This correlates with closure of apophysis. Although most patients continue to actively participate in sports, the severity of pain in some individuals leads to changes in sports or posture. Non-reactive activities, including swimming and cycling, can be done to maintain the patient's cardiovascular health. Hamstring and quadriceps flexibility exercises will maintain the knee's range of motion and may speed recovery.

Conservative treatment includes limiting or modifying painful activities and placing appropriate cushioning in the tibial tubercle until symptoms resolve. This may include a brief period of controlled immobilization for people who are unable to carry out their daily activities of living. OSD can cause knee joint disability in the chronic stage.

According to one study, patients with such recurrent symptoms should be followed up regularly with clinical and radiological evaluation during conservative treatment. Complications such as pseudo-convexity, osteogenesis imperfecta, patellar luxation, and periosteal migration/fragmentation can lead to early osteoarthritis. Up to 10% of patients experience persistent symptoms into adulthood, despite conservative measures.

Medicine

For OSD medications, non-steroidal anti-inflammatory drugs are usually used for a short time. They are used to relieve pain and reduce inflammation locally. In particular, ibuprofen, naproxen, flurbiprofen and ketoprofen, which reduce prostaglandin synthesis and have analgesic, antipyretic and anti-inflammatory effects, were selected.

Injections

In the past, some authors recommended injecting corticosteroids into the stellate tendon for symptom relief. However, it is not recommended at present due to its harmful effects. It can cause subcutaneous atrophy and rupture of the patellar tendon. In 2011, a study of hyperosmolar dextrose injections for persistent OSD was performed in adolescent athletes. In the study, the ability of 12.5% dextrose injection versus 1% lidocaine injection versus usual supervised care to reduce athletic variability and sports-related symptoms was examined in core patients. Topol., *et al*. [13] suggest that both the duration of exercise restriction and the duration of sports-related symptoms could be reduced by dextrose injection instead of lidocaine injection or usual care in individuals with persistent OSD.

Surgical treatment

Although conservative treatment is often preferred, for patients with intolerable symptoms, surgical intervention can be successful. In particular, adults with continuing symptoms may need surgical treatment and there have been some studies on it. Surgical procedures include drilling the tube, removing fragments, inserting autologous bone pins through the tube, tibial tubectomy, or surgical excision. Surgical management of OSD can be approached by open resection or arthroscopy or direct arthroscopic surgery.

Open procedure

The two most commonly performed procedures are excision of the pus and anterior excision of the genital warts. Tissue excision is believed to be the best surgical approach to treat OSD. Removing tuber protrusions also gives good results in stubborn cases.

Procedures that promote early fusion of cartilaginous abscesses, such as immobilization of the tubercle to the tibial plateau with autologous bone grafting or flexible tube drilling, are not recommended. Premature fusion of the anterior part of the perineum leading to genu recurrence has been reported.

In 1980, Mital described an untreated Osgood-Schlatter lesion as a condition that does not resolve on its own and responds to ineffective measures. Recommended surgical treatment for unresolved OSD.

In a 2009 review of surgical treatments for unresolved Osgood-Schlatter syndrome, Pihlamajaki., *et al*. it has been concluded that in young people, good to excellent functional outcomes can be improved after surgical treatment. In total, 75% of patients regained their preoperative level of athletic activity. In total, 38% reported the ability to kneel without pain.

In 2010, El Husseini., *et al*. [14] reports a study of surgical outcomes for OSD in adults. In total, 91% of patients were pain free before surgery.

All patients returned to their previous levels of physical activity within 12 weeks of surgery. Their results were all good; the only failure related to inclusion criteria was due to mistake in the lateral radiograph that did not show clear lymphatic separation.

Arthroscopy and endoscopic procedures

Arthroscopy for the surgical treatment of persistent OSD has also been recommended in recent years. This is the minimally invasive surgical modality for most intraocular procedures. It is thought to be more beneficial than the open procedure because the stellate tendon is not violated.

Eun and associates [15] revealed that orchiectomy has favorable outcomes in a select number of young and active patients with persistent symptoms. However, in arthroscopic surgery, the fatty tissue in the joint can be damaged during the removal of the fat sac. Eun and associates suggests that endoscopic approach may be more suitable for unresolved OSD to minimize the violation of excess adipose tissue.

Physiotherapy and rehabilitation

Rehabilitation after surgical procedures involves the placement of a knee brace that is stretched and full weight bearing. Allows the passive knee early range of motion. Lifting weights while stretching is mandatory for the first 3 - 4 weeks if tendon-skeletal rehabilitation is required.

Osgood Schlatter Disease is a self-limiting condition that usually occurs in adolescence. The patient had a history of rapid growth and involvement in high-intensity sports as a child, presenting with pain in the front of the knee during activities. Although conservative treatments are effective in the acute phase, symptoms can persist in severe cases. It can affect a patient's daily activities and impair performance in sports.

There has been a report of successful surgical treatment of patients with unresolved OSD. Surgical procedures include capsular drilling, debridement, insertion of autologous bone pins through the tube, tibial tubectomy, and surgical excision. Cosmetic discomfort, late postoperative recovery, and longer time to return to activity occur after open surgery. Laparoscopy has also been described as an alternative to other procedures, but this technique.

3. Sever Disease

Plantar fasciitis, also known as plantar fasciitis, is a common cause of foot pain in skeletally immature operators due to overuse. Excessive damage to the focal quality of play is attributed to traction abscesses in the leg, which correlates with the location of the Achilles tendon (Figure 11). Thus, the disease state often co-occurs with the onset of pediatric/adolescent patients with rapid growth, or increased honeycomb in active associations. The latter is appreciated in sports that require repetitive running and/or jumping [16].

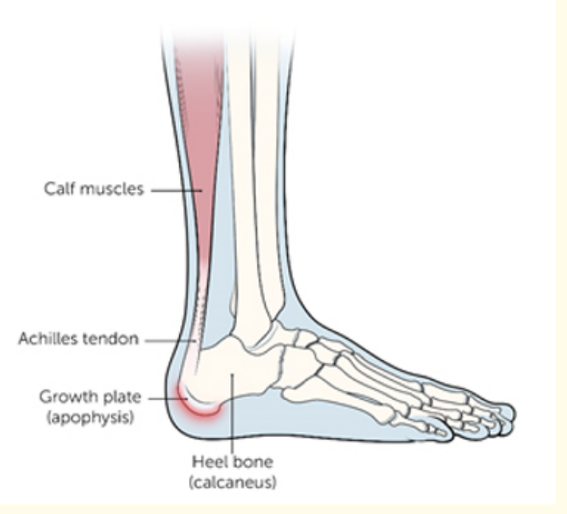

Figure 11: *Illustration shows the area where the Achilles tendon attaches (inserts) into the heel bone.*

Classic findings from a thorough history during clinical evaluation will often include resolution of pain during periods of rest or inactivity. The physical examination is notable for pain on insertion of the Achilles tendon and a positive squeeze test. Diagnosis is clinical and does not require imaging studies. The course of the disease is self-limiting and management involves adjusting relative activity or rest as guided by pain. Symptoms can be controlled with ice, anti-inflammatory medications, cups or heel lifts, and in severe cases, immobilization. A rehabilitation regimen that focuses on stretching and strengthening the heel cord should be incorporated into the care plan to improve symptoms and correct underlying biomechanical factors.

Etiology

Sever's disease is an overuse injury caused by repetitive stress and microtrauma caused by force of the strong Achilles tendon and results in irritation and possible partial loss of a relatively soft bone abscess. Force is increased after periods of rapid development and with increased activity. Rarely, trauma can lead to total body fractures. Contributing factors include increased or excessive athletic activity (especially sports that require repetitive running and jumping), heel laces, weak ankle strain, shoes sports that have poor cushioning or are too worn and run on hard surfaces. Additional biomechanical factors that contribute to poor shock absorption such as genu varum, forelimb varus, pes cavus, or pes planus may predispose to this condition (Figure 12) [17].

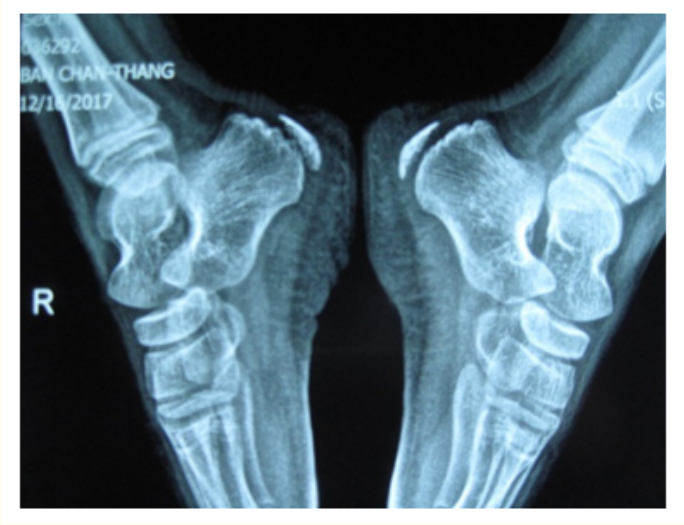

Figure 12: *An x-ray of foot shows the open growth plate of the calcaneus. The x-ray appearance of Sever's disease looks similar to those without symptoms. heel bone.*

Epidemiology

Sever's disease most commonly occurs during the growth spurt in active adolescent patients 9 to 12 years of age and is the most common cause of heel pain in this particular age group. Symptoms may be unilateral, but up to 60% of cases may present with bilateral pain. Fever is more common in men, manifesting most frequently at an average age of 12 years for men and 11 years for women. The sports most commonly encountered in these situations require repetitive running and jumping such as basketball, football, track and field, cross country, and gymnastics. Risk factors for Sever's disease include general risk factors for overuse injuries such as prolonged or year-round activity, ill-fitting or worn-out footwear, or exercise regimens. At least additional biomechanical factors such as inflexible heel spurs, pes cavus, pes planus, genu varum, or forefoot varus may predispose patients to developing this condition [16].

Pathophysiology

Posterior bone develops as a secondary chemosensor that provides attachment for the Achilles tendon. During the early adolescent growth spurt, bone growth exceeds the ability of the tendon-muscle unit to stretch sufficiently to maintain prior flexibility, thereby increasing stress on the unmodified or incomplete osteoma. Apophysis is the weakest point in the muscle-tendon-skeletal connection (as opposed to tendon in adults), and so it is at risk for repetitive stress injury. Excessive and repetitive traction from the strong Achilles tendon leads to micro-trauma and chronic irritation causing thickening and pain in the stratum corneum.

History and physicality

Typical presentation includes active adolescents with unilateral or bilateral heel pain, which is worse during and after activity, especially running and jumping, and often occurs in the setting of recent growth spurts this or start a new sport/training. Usually no prior trauma. Pain improves with rest and is usually absent in the morning. Over time, the pain can progress to the point of limiting activity. Physical examination will be negative for erythema or ecchymosis, but mild pain and swelling may be felt at the Achilles insertion on the heel. Examination may also reveal pain with passive ankle muscle spasm. The pain recurs with compression of the sternocleidomastoid muscle (pressure test) and worsens on tiptoe (Sever's sign). Low heel flexibility or weakness with dorsiflexion may be predisposing factors.

Evaluate

Sever's disease is a clinical diagnosis, and imaging is usually not needed. If presentation is atypical, severe, or persistent, consider simple radiographs for evaluation to rule out infection, cancer, or an occult fracture. Radiographs alone may show fragmentation, sclerosis, or increased density of bone abscesses; however, these changes can also be seen in the normal variant. If radiographs are required, bilateral imaging should be considered to identify ovarian abnormalities versus normal variation in the individual patient [18].

Treatment/Management

Final Sever disease is a self-limiting condition and resolves itself as the apophysis matures and closes.

Method not working

Surgical treatment has no role in controlling Sever's disease.

In general, options that don't work include:

- Rest/time of inactivity (guided by pain)
    - This may also include stopping sports/exercise until symptoms are relieved
- Orthopedic use/casting
    - Specific treatment regimens for each patient should be prescribed by the treating physician when necessary. May need immobilization including duration of infusion or use of CAM initiation depending on symptom severity
    - Heel or heel pad
- Heel tendon strain

- Ice application
    - Before and after sports activities
- NSAIDs

Footwear must be well maintained and up to date. A rehabilitation regimen is needed and should include heel strap stretching along with strengthening of the locomotor muscles. If the pain does not respond to conservative measures, walking boots or a short leg cast can be used for short-term immobilization. Symptoms are usually self-limited with improvement within 6 to 12 months and complete resolution with closure of the apophyseal. There is no role for injection therapy or surgical intervention in the treatment of Sever's disease. There are no long-term complications and the prognosis is good.

What are the treatments for Sever's disease?

Symptoms of Sever's disease often improve with home treatments such as rest and over-the-counter pain relievers. It may take a few months for the symptoms to go away completely. Treatment of Sever's disease includes:

- Rest: Your child will need to take a break from vigorous activities for a few days or weeks. Talk to your healthcare provider about how long your child should rest. Encourage your child to begin activities gradually to prevent the pain from returning.
- Ice and pain relievers: Apply an ice pack to your heel a few times a day for four or five days. Over the counter nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce pain and swelling.
- Supportive shoes: Make sure your child wears shoes with arch support and foot protection. Cushioned heel pads can absorb impact and reduce pressure on your child's heel.
- Stretching exercises: Ask your healthcare provider or physical therapist to perform exercises that help stretch the Achilles tendon and relieve stress on the disc. Stretching and strengthening the heels, calves, and hamstrings strengthen the muscles and are better able to support the foot and heel.
- Immobilization: If your child still has heel pain after a few weeks of rest, your healthcare provider may recommend a cast or brace to protect the growth plate and give it time to heal treatment.
- Physical therapy can be very beneficial for the treatment of Sever's disease. The therapist will establish specific exercises, such as stretching, to help improve symptoms.

Prognosis

Recurrence is relatively common.

Pearls and other matters

Prevention includes general advice to avoid injury from overuse. Patients should be encouraged to stay hydrated, diet and sleep, and avoid increasing activity levels > 10% per week.

Make sure to use proper equipment and technique, encourage stretching to maintain flexibility, and consider early recommendations for early single sport specialization.

The decision to avoid or limit activity should be shared among providers, patients, and parents and includes discussion of short- and long-term goals and priorities driven by pain.

Since patients are often very active in multiple arenas (multiple sports or multiple teams within the same sport) during the same season, consideration should be given to removing a team/sport rather than inactivity completely. It can be difficult to obtain patient consent.

Enhancing healthcare team outcomes

Sever's disease is relatively common in young people but often goes unnoticed because it is self-limiting. Patients may go to the emergency room, primary caregiver, or urgent care clinic. Nurses and doctors need to be familiar with this condition as it is sometimes confused with plantar fasciitis. Sever's disease is managed conservatively with most people experiencing symptom relief after cessation of overactivity [19].

Patients (including parents and family members) should be educated using patient-reported symptoms as guidelines for treatment and possibly return to play. In addition, patients and parents should be informed of the relatively high incidence of symptoms until skeletal maturation and apophysis closure have occurred. The growth plates usually begin to close between the ages of 8 and 14.

4. Kohler's Disease

Kohler's disease is avascular necrosis of the pelvis in the arch of the foot seen only in pediatric patients [20]. X-rays show this bone is initially compressed and then breaks into pieces before healing and hardening back into the bone wall. Kohler's disease occurs most often in children aged 5 to 10 years (Figure 13). Signs and symptoms of Kohler's disease include swelling, redness, and/or pain in the affected foot, which can lead to a limp or abnormal gait (walking pattern). Although the exact underlying cause of Kohler's disease is unknown, some scientists suspect that it may be caused by excessive strain on the pelvis and its associated blood vessels before the bone is completely solidified (hardened). This leads to blood flow abnormalities leading to avascular necrosis.

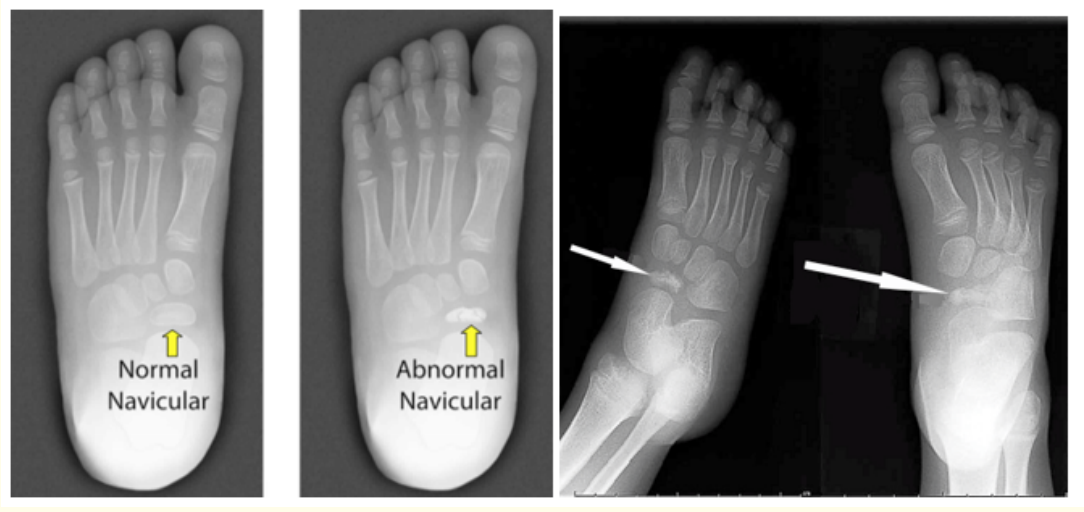

Figure 13: *Radiograph of foot. Arrows point to the navicular bone with avascular necrosis.*

Kohler disease is usually unilateral, although one report in the literature suggests that 25% of Kohler disease is bilateral. Patients typically present with medial lateral leg pain, midfoot swelling, and/or limping. On plain film, the iliac peritoneum will have the standard features of avascular necrosis (AVN), including sclerosis, fragmentation, and flattening. Kohler's disease is a self-limiting condition with a good prognosis. There have been no reported cases of Kohler disease developing persistent clinical or radiological abnormalities.

The incidence of Kohler's disease is not well known, as not all patients with Kohler's disease have symptoms. One publication estimates Kohler disease to be present in 2% of all children. Kohler's disease is five times more likely to affect men than women, and is most common in children between the ages of 4 and 7.

Kohler's disease usually resolves on its own with or without treatment; however, pain medication, rest, avoidance of weight-bearing activities, and/or a cast may be recommended to help control symptoms. Children seem to grow out of the disorder, and the affected bones usually regain their size, density, and structure within three months. Rarely, symptoms may persist for up to two years [21].

Is Kohler's disease hereditary?

The exact underlying cause of Kohler's disease is currently unknown. Although some scientists have suggested that genetic factors may play some role in the development of Kohler's disease, no causative genes have been identified (Figure 14).

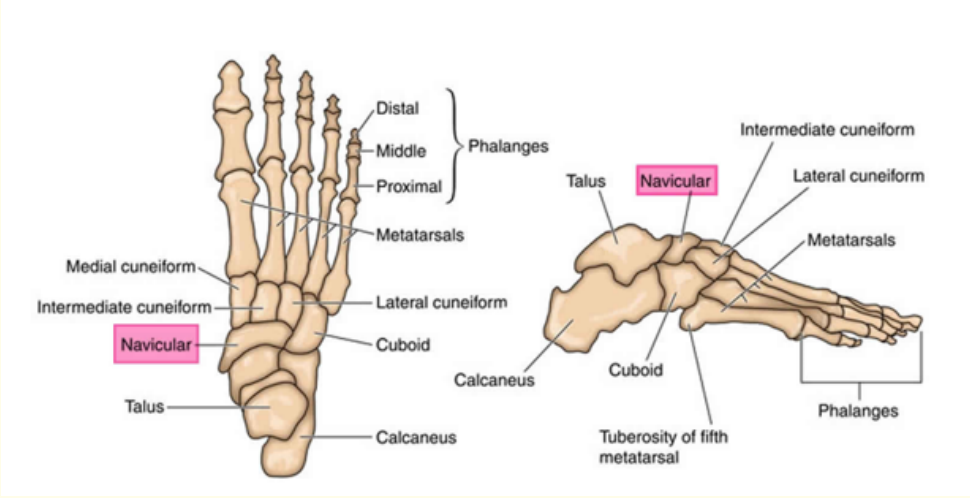

Figure 14: *Navicular bone.*

How common is Kohler's disease?

The incidence of Kohler's disease is not well known, as not all patients with Kohler's disease have symptoms. One publication estimates Kohler disease to be present in 2% of all children. Kohler's disease is five times more likely to affect men than women, and is most common in children between the ages of 4 and 7.

What is osteonecrosis?

Kohler's disease is considered a type of osteonecrosis, which refers to a group of conditions that affect the immature skeletal system. In people affected by bone resorption, a chemical center undergoes degeneration (breakdown) followed by calcification. The ossification center is a point inside the growing bone where bone formation (ossification) begins. Osteosarcoma commonly affects the formation of long bones in children.

What is osteonecrosis?

Osteonecrosis also known as avascular necrosis (AVN) is a medical term that refers to bone death caused by reduced blood flow to bones and joints. This condition can occur in almost any bone in the body; however, the shins, upper arms, knees, shoulders, and ankles are most commonly affected. Although men and women of all ages can develop the condition, it most commonly occurs in people between the ages of thirty and fifty.

Kohler's disease causes

The exact underlying cause of Kohler's disease is currently unknown, but the condition is thought to be caused by compressive stress-related trauma at a critical time of development. Vascular insults, retarded bone age, and genetic decline are also implicated. Although some scientists have suggested that genetic factors may play some role in the development of Kohler's disease, no causative genes have been identified.

The pelvis possesses dual blood supply. A branch of the tibial artery supplies the dorsal surface of the bone, while the vertebral blood supply originates from the medial branch of the posterior tibial artery. Both the back and spine blood supply enters the pelvis and branches to supply the middle and lateral thirds of the bones. This creates an avascular zone in the central third of the bone. Vascular foraminas help supply this avascular area and are found on the dorsal, pelvic, medial, and lateral surfaces of the pelvis. However, in a study of 100 cadavers, 97% of vascular foramina were less than 1 mm in adults. In theory, any compression of these small vessel foraminas could lead to decreased blood flow and put the pelvis at risk for avascular necrosis.

Some orthopedic experts think that Kohler's disease may be related to trauma to the area around the pelvis in the foot and may be the result of slow bone formation (ossification). In children, the pelvis is the last of the tarsal bones to form. In girls, the pelvis forms between 18 and 24 months of age, and in boys between 30 and 36 months of age. This theory indicates that due to the slow ossification of the pelvis, it is weaker than other bones. As the child grows and becomes heavier, the pelvis can become compressed between the hyoid bone and the already frozen wedge. Compression of the non-purulent pelvis leads to compression of perforated vessels in the central cancellous bone, possibly leading to ischemia and avascular necrosis later on.

Kohler's disease symptoms

Kohler's disease may have no symptoms. However, children often present to their pediatrician with concern about mid-back pain. On physical examination, the patient may have a painful spot on the pelvis with or without redness, heat, and swelling. When asked to walk, the child may limp with mismatched legs.

Putting weight on the legs or walking is difficult, causing additional discomfort and limping. Usually, the symptoms are mild and the patient may not seek treatment until the pain and swelling persists for a while.

Signs and symptoms of Kohler's disease vary, but may include [22]:

- Swollen feet
- The affected area is red
- Softness, especially along the length of the arch
- A limp or abnormal gait (walking pattern).

Symptoms can be aggravated if weight is placed on the affected foot, which can make walking painful and difficult.

For reasons that are not well understood, the flow of blood to one of the bones in the foot (the pelvis) is disrupted, leading to progressive degeneration of that bone. However, in a relatively short time, the bone will heal on its own.

Kohler's disease diagnosis

The diagnosis of Kohler's disease is suspected based on the presence of characteristic signs and symptoms. X-rays of the feet may be used to confirm the diagnosis and assess the progression of the condition.

Radiographic imaging alone is the imaging modality of choice in the diagnosis of Kohler disease. The navicular will appear as thin as thin sheets with the collapse of the bone. The bone will appear disjointed with loss of surface shape. There will be patchy sclerosis and increased radiation density. Soft tissue swelling around the affected pelvis may also be seen on plain radiographs. Advanced imaging such as CT and MRI are not necessary for diagnosis, although they may become necessary if a patient's symptoms do not improve with treatment. Although pelvic sclerosis may be consistent with a normal variant in asymptomatic patients, it is important to correlate radiographic findings with clinical suspicions.

Basic laboratory tests, such as complete blood count (CBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) are needed in cases of suspected infection. If any of these are increased, further diagnostic testing is warranted.

Kohler's disease differential diagnosis

Kohler's disease is often misdiagnosed as osteomyelitis in children. However, basic laboratory tests (white blood cell count, CRP, ESR) will help differentiate between the two diagnoses. If a child has an elevated ESR or CRP, a high index of suspicion is needed. Kohler's disease should not have elevated inflammatory markers and pediatric patients should not have elevated inflammatory markers. If infection is suspected, bone aspiration, bone biopsy, or blood culture may be performed.

Kohler's disease treatment

If Kohler disease is suspected, the patient should be referred to a pediatric orthopedic surgeon for further evaluation [23].

Treatment of Kohler's disease is conservative. Nonsteroidal anti-inflammatory drugs (NSAIDs) can be used to relieve symptoms but have not been shown to shorten the duration of symptoms. Short walking cast immobilization for 4 to 6 weeks can be used by patients to shorten the duration of symptoms. The effect of weighted embryos on weightless embryos is unclear and often depends on the surgeon. Several reports of the use of load-reducing orthotics for symptom relief have been reported. However, it does not appear that chiropractic shortens the duration of symptoms. There is no indication for surgery in Kohler's disease. If symptoms do not improve, the doctor should consider an alternative diagnosis. Both symptoms and radiographs should begin to improve in about six months.

Kohler's disease prognosis

The long-term outlook (prognosis) for people with Kohler's disease is usually very good, and to date, there have been no reports of long-term symptoms or disability in children with Kohler's disease. Radiographs should improve in about 6 to 48 months from the start of symptoms. If no cast is present, symptoms usually resolve after 6 to 9 months. In a review of case reports, patients were treated with a painless (non-load-bearing) plaster cast for a median of 3 months. Arch-supported chiropractors have been shown to relieve local pain but found that symptoms lasted an average of 7 months.

Symptoms can last from a few days to two years. However, most cases resolve within a year. People affected by this condition usually recover all function of the affected foot and have no long-term consequences. The progression of the X-ray appearance in Köhler disease is variable. Normal radiographs can be obtained 6-18 months from baseline. In adulthood, the pelvis is expected to be normal. The patient has excellent rehabilitation.

Summary

Osteonecrosis often presents a difficult diagnosis for orthopedic surgeons. There are several known risk factors in the literature, but the exact pathophysiology is still not fully understood. Difficulty in diagnosis often results in a slowly progressive disease presentation, often rendering the joint incurable, and increasing patient morbidity. Although orthopedic surgeons are almost always involved in the care of patients with osteonecrosis, it is important to educate healthcare professionals who meet these patients at the hospital door such as general practitioners, emergency department physicians, nurses, and physiotherapists.

Many conditions are thought to be risk factors for uterine fibroids. However, it is difficult to determine the true etiology using a diagnostic or retrospective approach, regarding the etiology of the low prevalence, especially since many studies report idiopathic osteosarcoma. In 10 to 15% of cases. When possible, we rely on prospective cohort reports, longitudinal or analytic, to identify strong associations between risk factors and osteosarcoma. This does not mean that we exclude other possible conditions as risk factors for osteosarcoma, but significant evidence of a cause and effect relationship is needed.

Some facts about avascular osteonecrosis:

- Vascular necrosis is a disease caused by temporary or permanent loss of blood to the bone. It occurs most commonly at the end of a long bone.
- Vascular necrosis can be the result of trauma, drug or alcohol use.
- Symptoms may include joint pain and limited range of motion.
- Medicines, assistive devices, or surgery may be used to improve function or to prevent further damage to the affected bone or joint.

The closely related causal risk factors for osteonecrosis appear to converge through vascular degenerative mechanisms to produce subcutaneous or segmental ischemia and osteoclast cell death. Subsequent repair often results in loss of subchondral bone beyond formation, resulting in structural damage and fracture. Understanding the risk factors and pathophysiology has implications for treatment. Several treatment regimens are available to optimize primary bone circulation, prevent bone resorption, and preserve subchondral bone. In traumatic conditions, fracture is acceptable Location and timing, technique, and approach to immobilization are important. In the absence of trauma, a specific prophylactic approach is available to suppress adipocyte proliferation (by limiting alcohol intake and corticosteroid dosage), using statins, and treating glaucoma with replacement therapy enzyme potential. Osteoma associated with the hypercoagulable syndrome has been prevented with the use of warfarin and enoxaparin. Bisphosphonates have been used to rebalance

the rate of breakdown and formation of subchondral bone with the expectation of maintaining the mechanical integrity of the subchondral bone and minimizing the risk of fractures and dislocations.

Conclusion

Osteoma-related research explores the causes of osteosarcoma, which may lead to new treatment strategies. Efforts have been made to compare the effectiveness of current and new therapies, which require clinical trials.

The following are examples of other types of research going on:

- Researchers are actively looking for pharmaceutical alternatives to surgical procedures, which are currently the mainstay of treatment. One study is looking at whether low-dose aspirin, which has anticoagulant properties, can increase blood flow to affected bones and slow disease progression.
- The underlying cause of osteonecrosis is unknown, but genetics may play a role. Some studies aim to detect genetic factors that contribute to an increased risk of the disease. If found, these genetic factors could help doctors identify high-risk individuals who need to be monitored closely for signs of the disease.
- Research in degenerative joint disease has shown that stem cells called mesenchymal stem cells are drawn to the knee joint. Scientists are investigating whether these cells aggregate at sites of bone destruction and whether their concentrations correlate with disease severity. If so, doctors can use the level of mesenchymal stem cells to help make decisions about disease staging and treatment.
- Osteoporosis drugs called bisphosphonates tend to build up in the jawbone and in rare cases this can lead to osteonecrosis of the jaw. Investigators have found that certain types of oral bacteria are attracted to these sites of bone necrosis, suggesting that they may play a role in bone destruction. By exploring the relationship between bisphosphonates and these bacteria, the researchers hope to find a way to halt bone death without compromising the therapeutic benefits.
- Scientists are testing different approaches involving bone marrow stem cells to regenerate healthy bones. Several studies are looking at the benefits of inoculating stem cells directly into the channels created by core decompression procedures. Another approach is to focus on testing the effectiveness of biotechnological stem cell-based composites in restoring bone lost to disease.

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