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(REVIEW ARTICLE)

Anukta vyadhi femoral head avascular necrosis from Ayurveda perspective

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Abstract

Ayurveda, the science of life deals not only with the health of individual but also with disease state. Most of the diseases mentioned in Samhita are the diseases that occurred at that period of time. Lifestyle changes and infections are the unavoidable causes for the newly emerging diseases. Such diseases can be categorized as "*Anukta vyadhi*". *Anukta* literally means unspecified or unstated. These diseases cannot be identified in Classical texts but can be understood with the eternal principles mentioned in Ayurveda texts.

These Principles not only help in understanding the pathophysiology of diseases mentioned in Ayurveda but also prove to be useful to understand newly emerging disease pathology in terms of Ayurveda perspective.

Avascular necrosis (AVN) is considered one amongst such *Anukta vyadhi*. There is increase in the incidence of AVN after COVID pandemic situation due to excess use of steroids to treat moderate to severe cases of Covid-19 infection. So, an attempt is made to understand etiopathology of femoral head avascular necrosis from Ayurveda Principles.

Keywords: *Anukta vyadhi*; *Asthimajjagata vata*; Avascular necrosis; *Raktadushti*; *Shatkriyakala*

1 Introduction

Ayurveda is the science of life which deals with health of healthy individuals and treatment of diseased ones.[1] The classical texts of Ayurveda include the disease often present at that era of time. As time progressed, there has been change in lifestyle of people along with eating habits, daily regimen, medicine etc. These unavoidable and unfavorable changes in lifestyle lead to manifestation of new diseases. The clinical presentation of these diseases is not precisely similar to the diseases mentioned in the classical Ayurveda texts.

Diseases like Sickle cell anemia, Dengue, Rheumatoid arthritis, Hypothyroidism, Hyperthyroidism, Cancer, Swine flu, Avascular necrosis, AIDS, Covid etc. are not mentioned in classical Ayurveda texts. But to deal with such newly rising clinical conditions Acharyas have given certain guidelines and concepts like *Anukta vyadhi sankalpana, Shatkriyakala* etc.

Since all disorders cannot be given standard names, one should not be ashamed of it, as commented by Acharya Charak. There are innumerable diseases, as the same vitiated *Dosha* causes various disorders according to variations in etiology and location. Hence, one should initiate the treatment only after acquiring complete knowledge about nature of the disease as well as its pathogenesis, location and etiological factors. [2] The concept of *Anukta* is useful to understand the Ayurvedic aspect of various disease etiopathology as well to understand and integrate new emerging disease pathology.

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Avascular Necrosis (AVN) is also called as Osteonecrosis or Bone infarction. It is the death of bone tissue due to interruption of the blood supply. Avascular Necrosis of the femoral head is now recognized as a major musculoskeletal problem, mostly affecting the young generation in their productive years of life. [3]

Disruption of the blood supply can result from trauma (femoral neck fracture or hip dislocation), Sickle cell anemia, abnormalities of fat metabolism (associated with alcoholism, lipid storage disease and corticosteroids), and can also be idiopathic.[4] Avascular Necrosis may be asymptomatic and gradually joint pain may develop which may limit the ability to move. In Ayurveda, there is no any direct reference found about disease resembling to Avascular Necrosis. In Avascular Necrosis of femoral head, *Vankshan Sandhishool* is one of the major symptoms.

Considering AVN as an *Anukta vyadhi*, an effort is made to understand the possible pathogenesis of Femoral head avascular necrosis in terms of factors like *Hetu, Dosha, Dushya*, *Sthana* etc. which will be useful to initiate a proper line of treatment for the disease.

Aim and objectives

- To study Avascular Necrosis (AVN) as an *Anukta vyadhi* in terms of Ayurveda.
- To understand the etiological factors and pathogenesis of Femoral head avascular necrosis through Ayurveda perspective.

2 Material and Methodology

As it is a review article, references of AVN were studied from modern medical text books and relevant articles from internet.

The Pathogenesis of Femoral head Avascular Necrosis is formulated according to Ayurveda principles.

3 Avascular necrosis disease review

Avascular Necrosis is a degenerative bone condition. It is characterized by the death of cellular components of the bone secondary to an interruption of the subchondral blood supply. [5] It typically affects the epiphysis of long bones at weight-bearing joints. In advanced stage of disease, it may result in subchondral collapse which threatens the viability of the joint involved.

AVN is also called osteonecrosis, aseptic necrosis, bone infraction and ischemic bone necrosis. [6] In general, bone infarct refers to lesions occurring in the metaphysis and diaphysis of bone. Lesions in the epiphysis are called avascular necrosis. [7]

Osteonecrosis is most common in the hip, [8] but also seen in the humerus, knee, and talus and more rarely seen in the smaller bones of the wrist such as the lunate or scaphoid.

3.1 History

Osteonecrosis of the femoral head was first described in 1738 by Munro. In 1835, Cruveilhier depicted femoral head morphologic changes secondary to interruption of blood flow. In 1962, Mankin described 27 cases of AVN, and the number of reported AVN cases has been increasing steadily thereafter. [9]

3.2 Causes and risk factor [10]

Femoral head avascular necrosis can be caused by trauma or non-traumatic events.

3.2.1 Joint or Bone trauma

- An injury, such as a dislocated joint, might damage nearby blood vessels.
- A fracture in a bone e.g. femoral head.
- Cancer treatments involving radiation also can weaken the bone and harm blood vessels. Neck fracture or dislocation of the femoral head is most common traumatic causes of Femoral AVN.

3.2.2 Non-traumatic

- Excessive alcohol consumption and steroid abuse have been identified as major risk factors.
- Person who drinks more than 400 ml of alcohol per week for long term are at higher risk for developing the disease. [11]
- Glucocorticoid intake was found to have a stronger association with the disease than alcohol use.
- Cigarette smoking: - Due to changes in nitric oxide bioavailability, there is an increased oxidative stress level and endothelial dysfunction
- Obesity: - Osteonecrosis is positively associated with BMI. Overweight and obesity, just like steroid and alcohol use are often associated with hyperlipidemia.
- A medical condition, such as Sickle cell anemia or Systemic Lupus Erythematosus.
- Less common, but clinically important causes, one of which is Legg-Calve-Perthes.
- Vascular disease secondary to diabetes, also direct damage from cytotoxic agents have been implicated in the development of femoral head osteonecrosis. [12]
- Studies show that there is a higher prevalence among males, this could be attributed to higher levels of smoking and alcohol use. Greater fluctuations in climatic temperatures may also contribute to higher rates of non-traumatic osteonecrosis. [13]

3.3 Pathophysiology

The hematopoietic cells are most sensitive to low oxygen and are the first to die after reduction or removal of the blood supply, usually within 12 hours. Experimental evidence suggests that bone cells (osteocytes, osteoclasts, osteoblasts etc.) die within 12–48 hours, and that bone marrow fat cells die within 5 days. [14]

Upon reperfusion, repair of bone occurs in 2 phases. First, there is angiogenesis and movement of undifferentiated mesenchymal cells from adjacent living bone tissue growing into the dead marrow spaces, as well as entry of macrophages that degrade dead cellular and fat debris. Second, there is cellular differentiation of mesenchymal cells into osteoblasts or fibroblasts. Under favorable conditions, the remaining inorganic mineral volume forms a framework for establishment of new, fully functional bone tissue.

Avascular necrosis of the femoral head occurs due to disruption of blood supply to the proximal femur. It can occur due to a variety of causes, either traumatic or Non traumatic in origin. Femur head AVN is the most common type of necrosis because the artery supplying to that area is very narrow so it gets injured easily followed by mere dislocation or a subcapital fracture which leads to lack of nourishment resulting in necrosis. [15]

Steroid-associated osteonecrosis represents the second most common cause of osteonecrosis overall, after trauma. Despite of it, the exact pathophysiology is not clear and probably multifactorial. These causes most likely aggregate factors such as fat emboli, fat cell hypertrophy leading to increased intraosseous pressure, endothelial dysfunction, hyperlipidemia, and abnormality of the stem cell pool of the bone marrow; all of which contribute to ischemia and subsequent necrosis. [16] Autoimmune and chronic inflammatory disorders, e.g., Systemic lupus erythematosus (SLE), are well-known to be associated with osteonecrosis of the femoral head. The risk of developing the condition in these patients is usually attributed to long-term steroid treatment, though there are reports of cases in those who are steroid naive. [17]

Alcohol-induced osteonecrosis is similarly not well understood. But most likely stems from bone marrow fat cell hypertrophy and proliferation, serum lipid level changes, blood vessel occlusion, increased intraosseous pressure, and subsequent lack of perfusion cause similar pathology as that of steroid-associated osteonecrosis. [18]

Sickle cell disease can often precipitate osteonecrosis. The misshapen and rigid red blood cells impede blood flow leading to ischemia and bony infarction, with the femoral head being the most common site of osteonecrosis in these patients. [19] Legg-Calve-Perthes is idiopathic avascular necrosis of the femoral head that affects paediatric populations. Lack of blood supply causes necrosis of the femoral head leading to a deformity that puts the patient at high risk of developing osteoarthritis or losing Range of Motion (ROM).

3.4 Clinical signs and symptoms

In the beginning, this disease is asymptomatic. It is also possible there is a segmental collapse present and the patient doesn't feel it. As the disease progresses, the hip can become stiffer, which is visible in the gait of the patient when he starts to limp. Pain is also observed by support on the leg, in the buttock, groin and thigh. [20]

Non-traumatic cases will typically present with mechanical pain of variable onset, severity and often difficult to localize.

Symptoms include pain and decreased range of motion in the affected joint. In some cases, the condition is diagnosed during routine x-ray imaging, due to a lack of overt symptoms. The most common location for this condition to manifest is the head or neck of the femur or humerus and the knee joint.

3.4.1 Avascular necrosis can be classified into five different stages [21]

- Stage 1: - Radiographic changes are absent or show minor osteopenia. An MRI scan is required for identification (can show oedema). The onset of this disease is asymptomatic.
- Stage 2: - First stage with radiographic changes. This stage is characterized by sclerosis of the superior central portion of the joint head and/or osteopenia and/or subchondral cysts.
- Stage 3: - In this stage, the articular surface is depressed so that the round contour is compromised, without being significantly deformed. This leads to a joint space narrowing. A plain radiograph shows a crescent sign.
- Stage 4: - This stage is characterized by a wide collapse of the subchondral bone and destruction of the underlying trabecular pattern. This can lead to secondary arthritis.
- Stage 5: - The final stage where both articular surfaces are affected, which leads to a dysfunctional joint.

3.5 Complications

Complications include progressively worsening joint pain, restricted range of motion and osteoarthritis. [22] The end stage of the process is severe destruction of the femoral head with resultant degeneration of the hip joint. These complications can cause significant disability in patients.

3.6 Diagnosis procedure

Osteonecrosis can be diagnosed with a systematic check of the historical background of the patient combined with physical examination. Assessment of risk factors and age of the patient can also provide clues to the disease.

A laboratory workup is done to rule out other causes of hip pain as well as to assess for comorbid factors in patients with suspected osteonecrosis. Rheumatoid arthritis and sickle cell disease are two conditions that can precipitate the development of osteonecrosis in the femoral head and can cause hip pain even without osteonecrosis. [23]

This workup include a Complete Blood Count (CBC), lipid Profile, Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), Rheumatoid factor (RF), anti-nuclear antibody (ANA), anti-cyclic citrullinated peptide (anti-CCP) and hemoglobin electrophoresis.

In the early stages, this condition is asymptomatic, which makes diagnosis almost impossible. However early screening with MRI is currently the best modality for diagnosis due to its sensitivity. The double line sign is an MRI finding seen at the periphery of a region of osteonecrosis. It consists of an inner bright line representing granulation tissue and an outer dark line representing sclerotic bone. Measurement of the size and location of the necrotic lesion is a crucial prognostic parameter to predict collapse and can be better defined on an MRI. [24]

At a more advanced stage, standard radiograph can confirm the diagnosis. Tissue affected by avascular necrosis will appear denser (increased whiteness) and possibly sclerotic (patchy) on the radiograph [25]. An MRI can assist in making the diagnosis. It can show a subchondral radiolucency called a “crescent sign”, it indicates imminent articular collapse.

4 *Anukta vyadhi* In Ayurveda

The literary meaning of “*Anukta”* is unstated or unspecified. *Anukta vyadhi* means the *Vyadhi* which is not explained in Ayurved Samhitas. As per Ayurveda *Vata, Pitta* and *Kapha* are tripods of life. Their harmony result in good health and its vitiation by any cause leads to disease. There are innumerable diseases as the same vitiated *Dosha* causes various disorders according to variations in etiology and location. According to Ayurveda a disease pathogenesis should involve the basic *Samprapti* factors like *Dosha, Dhatu, Mala, Agni*, *Strotasa;* without the involvement of these, the disease can’t be manifested and hence the detailed knowledge of these basic factors helps to understand the pathology involved and accordingly the treatment can be proposed.

In Chikitsa Sthana, Charak mentioned that, the disease which are not described here due to their various names and clinical presentations shall also be treated according to the dominance of *Dosha, Hetu, Samutthan* etc. factors.

Also, the medicines shall be prescribed after due consideration of Desha (Habitat), Kala (Season), Pramana (Dosage), Satmya (Adaptability) and Asatmya (Non-adaptability). If this is properly considered, then it is Pathya (beneficial to body systems), otherwise it is Apathya. [26]

Acharya Sushruta explained a different concept to understand the disease i.e., *Shatkriya Kala*.[27] If *Vyadhi* is treated in earlier stage it will not proceed to the next, so a wise physician should begin the treatment at an early stage if possible, to prevent further manifestation.

The treatment that is opposite to *Dosha*, *Dushya* and *Nidana* is always beneficial. The diseases that are told and untold in Ayurvedic texts can be treated with proper implementation of principles like *Anukta vyadhi, Shatkriyakala* etc.

Taking all this into consideration, the critical study of any disease which is not mentioned in classical Ayurveda text can be done.

5 Femoral head avascular necrosis from Ayurveda perspective

5.1 *Hetu* of AVN

Hetu or *Nidana* means the factors responsible for producing disease i.e. etiological factors. A particular factor can be called as *Nidana* only when it develops a complete disease process in the body either immediately or after certain period. [28]

Avascular necrosis *Hetu* can be classified as

- *Nija Hetu* includes causes like Cigarette smoking, Heavy alcohol intake etc.
- *Sahaj Hetu* Sickle cell anemia can be considered as *Sahaj Hetu*.
- *Aagantuja Hetu*:-Trauma, Injury or fracture of bone.
- *Nidanarthakar Roga* :- Vascular defects secondary to disease like Diabetes mellitus.
- *Purvajanmakrut* :- No exact cause

5.2 *Samprapti*: - Complete process of manifestation of disease is called *Samprapti*. The Pathogenesis of AVN can be understood in terms of *Samprapti Ghataka* and *Shatakriyakala*.

The events occurring in Pathogenesis of AVN are as follows

- *Rakta Dushti*
- *Dosha Dushti (Vyan Vayu)*
- *Asthi Dhatu Dushti*
- *Asthivaha Strotas Dushti.*

Rakta Dushti is the first step in the pathogenesis of AVN. *Hetu* like *Aaghata, Madyapana*, Fat embolism, Sickle cell disease etc. causes *Raktadushti*. *Raktadushti* causes *Strotorodha (Margavrodha)* which lead to vitiation of *Vata Dosha*. *Aahar Hetu* that precipitates the vitiation of *Vata Dosha* is also responsible for *Asthivaha Strotas Dushti and Asthi Dhatu Dushti*. This ultimately causes AVN *Vyadhi.*

5.2.1 Samprapti Ghataka of AVN

Samprapti Ghataka includes *Dosha, Dushya, Strotodushti, Agnimandya, Ama* etc.

Dosha – Predominantly *Vata, Dushya – Rakta ,Asthi and Majja Dhatu, Updhatu-Sira, Pradhan strotasa – Asthivaha, Strotodushti - Sanga, Vimarga-gamana, Adhishtana - Vankshansandhi, Vyaktisthana – Vankshansandhi , Vyadhi Swabhava - Chirakari , Rogmarga – Madhyam*.

5.2.2 Shatakriyakala

• *Sanchaya – Vata sanchay* due to *Raktadushti • Prakopa – Vata • Prasara – Vata* in *Asthi-Majjavaha Strotasa • Sthansamshraya - Vankshansandhi. • Vyakti – Vatavyadhi • Bheda – Vankshangatvata*

5.2.3 Lakshana

Clinical picture of AVN shows the dominance of *Vata Dosha*. The *Vata Prakopak* symptoms of AVN include *Vankshan Sandhishool, Graha, Sthanik Mansa Peshishosh, Chankraman Kashtata.* The *Vata Dosha Prakopa* is due to *Strotorodha*.

Rakta Dushti causes *Strotorodha* and it causes vitiation of *Vata Dosha*, which plays the important role in the pathogenesis of AVN. Also, *Asthi Dhatu Dusthi* causes *Sthanvaigunya*.

6 Discussion

Ayurveda considers *Dosha*, *Dhatu* and *Mala* as the basic constituents of body. Equilibrium of these along with *Sama Agni* and cheerful mind, intellect and sense organs is termed as healthy state of body similarly its disturbance leads to disease state.

As the time progresses, new diseases are emerging due to change in lifestyle and other infections. Ayurveda principles and concepts are endless and its application can be useful in present era as well. *Anukta vyadhi Sankalpana* is one amongst such concepts.

"Anukta" means any disease or drug which is not explained in Ayurvedic text. It helps not only in the understanding classical concept but also becomes base for understanding new diseases.

Acharya Charaka mentioned that it is not necessary to name each and every disease, but identification of causative factors, site affected and vitiated *Dosha* will help in appropriate treatment of disease.

Femoral head avascular necrosis can be considered as *Anukta vyadhi* which is caused due to trauma to the bone or non traumatic conditions like alcohol intake, cigarette smoking, sickle cell anaemia, SLE etc. When the blood supply to the head of the femur is disrupted partially or completely it leads to avascular necrosis.

After traumatic cause, chronic steroid use and excessive alcohol consumption represent the bulk of non-traumatic etiologies, contributing to more than 80% of them. Steroids helped save many lives during the second wave of COVID 19. Steroids were administered to patients suffering from moderate to severe Covid during the second wave to reduce the inflammatory response and lung injury caused by the viral infection. But the drug use has also left many with prolonged side effects. AVN due to lack of blood supply, is one of them.

Hyperlipidemia, vascular diseases and Excess consumption of alcohol cause Deposition of fats in blood vessels eventually block the small blood vessels that will reduce the blood flow to the bone causing death of bone tissue.

In Ayurveda avascular necrosis can be correlated with *Asthimajjagata Vata* as per resemblance of the symptoms.

Due to *Nija, Aagantuja, Sahaj, Anyavyadhi Upadrava Kruta* or *Purvjanmakruta Hetu, Rakta Dushti* occurs. This *Raktadushti* is of *Margavarodhajanya* which leads to *Vimarga-gaman* of *Vata* at *Asthi*. It causes the death of cellular components of the bone and in advanced disease state it may result in subchondral collapse. *Samprapti Ghataka* of AVN includes *Raktadushti* and *Siravikruti* followed by *Vataprakop.* The most common site to get affected is neck of Femur. As it is *Asthidhatu Dushti Janya Vata Vikar*, it can be considered as a *Kashtasadhya Vyadhi.*

Thus, *Anukta vyadhi Samprapti* can be understood by considering *Hetu, Dosha Dushti* and *Samutthan* with the help of *Anukta Sankalpa.*

7 Conclusion

In Ayurveda diseases mentioned are classified on the basis of etiology, appearance, site, symptoms, type of pain etc. As the time progress new diseases are identified, the pathology of such newly emerged diseases can be understood by using the principles like *Anuktavyadhi Sankalpana*, *Shatakriyakala* or *Dashavidha Parikshyabhava* etc. Understanding of disease pathology in terms of Ayurveda will definitely helpful to initiate appropriate line of treatment for the patients well -being.

Compliance with ethical standards

Disclosure of conflict of interest

Authors declare that there is no conflict of interest.

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