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Gout: Pathophysiology

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A B S T R A C T

Gout is a type of arthritis characterized by sudden, severe pain, swelling, redness, and tenderness in the joints, most commonly affecting the big toe. It is caused by the buildup of uric acid crystals in the joints, which leads to inflammation and intense pain.

Uric acid is a natural waste product that is produced when the body breaks down purines, substances found in certain foods and beverages. Normally, uric acid dissolves in the blood and is excreted through the kidneys. However, in some cases, the body either produces too much uric acid or fails to eliminate it properly, resulting in a high level of uric acid in the blood, a condition known as hyperuricemia.

Keywords: **GOUT**

INTRODUCTION

When there is an excess of uric acid in the blood, it can form needle-like crystals that accumulate in the joints, tendons, and surrounding tissues. The deposition of these crystals triggers an inflammatory response, leading to the characteristic symptoms of gout.

Gout attacks often occur suddenly, often at night, and are accompanied by intense pain that can be described as throbbing, crushing, or excruciating. The affected joint becomes swollen, red, and extremely tender to the touch. The pain and swelling usually peak within a few hours and can last for days or weeks if left untreated. As the attack subsides, the symptoms gradually resolve, but repeated attacks can occur over time.

Although the big toe is the most commonly affected joint, gout can also affect other joints such as the ankles, knees, elbows, wrists, and fingers. The pain and inflammation can significantly limit mobility and disrupt daily activities.

Several factors can increase the risk of developing gout, including genetics, obesity, a diet high in purine-rich foods (such as red meat, seafood, and alcohol), certain medical conditions (such as kidney disease and diabetes), and certain medications (such as diuretics and low-dose aspiri

Causes

Hyperuricemia, an excess of uric acid in the blood, is the main cause of gout.The body produces uric acid during the breakdown of purines. These are chemicals found in high amounts in certain foods and drinks, such as alcohol, turkey and goose, liver, and seafood.

People trying to limit their intake of purines may wish to opt for duck or chicken instead and should avoid organ meats altogether.Typically, uric acid is dissolved in the blood and excreted in urine via the kidneys. If the body produces too much uric acid or does not excrete enough, it can build up and form needle-like crystals. These trigger inflammation and pain in the joints and surrounding tissues.

Risk factors

Several factors can increase the risk of hyperuricemia and gout, including:

- **Advanced age:** Gout is more commonTrusted Source in older adults and rarely develops in children.
- **Sex:** In people younger than 65, gout is four timesTrusted Source as prevalent among males as females. It is three times as prevalent in males after the age of 65.
- **Genetics:** A family history of gout can increase a person's risk.

- **Dietary choices:** Alcohol interferes with the removal of uric acid from the body, and a high-purine diet increases the amount of uric acid in the body. Consuming alcohol and having this type of diet can increase the risk of gout.
- **Lead exposure:** Studies have suggested a link between chronic lead exposure and an increased risk of gout.
- **Medications:** Certain medications can increase the levels of uric acid in the body. These include some diuretics and drugs containing salicylate.
- **Weight:** Being overweight or obese and having high levels of visceral body fat are linked with an increased riskTrusted Source of gout. None of these factors directly causes the condition, however.
- **Other health conditions:** Renal insufficiency and other kidney conditions can reduce the body's ability to remove waste, leading to elevated uric acid levels. Other conditions associated with gout include high blood pressure and diabetes

Epidemiology

The general prevalence of gout is 1–4% of the general populationIn western countries, it occurs in 3–6% in men and 1–2% in women. In some countries, prevalence may increase up to 10%. Prevalence rises up to 10% in men and 6% in women more than 80 years old. Annual incidence of gout is 2.68 per 1000 persons.It occurs in men 2–6 folds more than women. Worldwide incidence of gout increases gradually due to poor dietary habits such as fast foods, lack of exercises, increased incidence of obesity and metabolic syndrome.

Pathogenesis of hyperuricemia

Urate is the ionized form of uric acid present in the body. Uric acid is a weak acid with pH of 5.8. Urate crystals deposition in tissues starts to occur when serum uric acid level rises above the normal threshold. Pathological threshold of hyperuricemia is defined as 6.8 mg/dL .

Some factors may affect the solubility of uric acid in the joint. These include synovial fluid pH, water concentration, electrolytes level, and other synovial components such as proteoglycans and collagen. SUA level in the body is determined by the balance between its production either from purine intake in diet or endogenous production by cellular turnover and its excretion by the kidneys and GIT. Increased production of UA is responsible for only 10% of cases of gout while the remaining 90% are caused by its renal under-excretion.

Factors affecting SUA levels include age and gender. SUA is low in children. After puberty, SUA levels start to increase to reach their normal levels. In men, levels are higher than in women. However, SUA levels in postmenopausal women increase to reachmen's levels.

This explains why gout is usually a disease of middle aged and older men, and postmenopausal women. Rarely, it may happen in children and young adults in some rare inborn errors of purine metabolism.

These enzymatic defects result in increased SUA with consequent production of UA crystals in kidneys and joints . Overproduction of uric acid Deficiency of enzymes involved in purine metabolism leads to overproduction of UA. For example, Lesch-Nyhan syndrome is an inborn error of metabolism resulting from deficiency of an enzyme involved in UA metabolism named hypoxanthine–guanine phosphoribosyltransferase. It is a genetic X-linked recessive disorder with varying degrees of severity according to the type of mutation. The clinical picture of this disease involves neurological abnormalities such as dystonia, chorea, cognitive dysfunction, compulsive injurious behavior, self-mutilation and articular manifestations (early onset gout) in addition to renal stones. If left untreated, it may lead to tophi formation and renal failure [9].

Another enzymatic abnormality that causes gout in the young is the superactivity of phosphoribosyl pyrophosphate synthetase. It is an X-linked dominant inherited disorder. The syndrome has two clinical forms, a severe early onset form in children and a mild late juvenile or early adult onset form. Clinical picture includes neurological abnormalities such as sensorineural hearing loss, hypotonia and ataxia in the severe form. The mild form manifests as uric acid renal stones and arthritis. However, these enzymatic disorders constitute only less than 10% of cases of overproduction of urates [10].

Treatment

An excess of uric acid in the body, or hyperuricemia, is the main cause of gout. Treatment typically involves prescription medication. These drugs can help treat the symptoms, prevent future flares, and reduce the risk of complications, such as kidney stones and acid crystals forming white growths in the affected areas, an issue called tophi. Common treatments include nonsteroidal anti-inflammatory drugs and corticosteroids, which also combat inflammation. These reduce swelling and pain in the areas that gout affects. Excessive uric acid levels typicallyTrusted Source stem from an overproduction of uric acid or issues that affect how the kidneys excrete this substance. Some medicines reduce uric acid production and improve the kidney's ability to remove uric acid from the body.

Without treatment, an acute gout attack is at its worst 12–24 hoursTrusted Source after it begins. A person can expect to recover within 1–2 weeks without treatment, but there may be significant pain during this period.

Tests and diagnosis

Gout can often be challenging to diagnose, as its symptoms are similar to those of other conditions.

Most people who develop gout have high levels of uric acid, but this may not be detectable during a flare-up. As a result, a person does not need to have hyperuricemia to receive a gout diagnosis. Still, high levels of uric acid in the blood or uric acid crystals in joint fluid are the main diagnostic criteria for gout. To assess this, a rheumatologist orders a blood test and may also extract fluid from an affected joint for analysis.

In addition, they can use an ultrasound scan to locate uric acid crystals around affected joints or within growths. X-rays cannot detect these signs, but healthcare professionals may use them to rule out other causes of the symptoms.

DISCUSSION

Gout has been estimated to account for almost 5% of nonsurgical joint disease (Coodley, 1958). Although it still most commonly presents in its classical form, the disease can manifest in a wide array of presentations (Ning & Keenan, 2010). It is theorized that such atypical presentations are a result of a complexity of contributing factors to the disease (Ning & Keenan, 2010). Premorbids such as advanced age, obesity, and metabolic syndrome are among the most important predisposing factors in the development of gout (Walker et al, 2014). In our patient, however, none of these comorbids existed. In this case, before the confirmation through microscopic examination of the synovial fluid_ and based solely on the history_ the diagnosis of gouty arthritis essentially became a diagnosis of exclusion. On physical examination, there was no hepatosplenomegaly or lymphadenopathy, thus ruling out Still's Disease. There was no history of sexual contact or alcohol consumption, hence, ruling out Reiter's Syndrome. Rheumatoid Arthritis (RA) was excluded based on the absence of any extrapulmonary manifestations of RA, and negative reports for both RA factor and anti-CCP. Currently, the absence of any rash, oral ulcers, Raynaud's phenomenon, dryness of eyes and mouth, numbness, tingling sensation, or photosensitivity meant that Systemic Lupus Erythematosus could be ruled out. There was no complaint of backache, chest pain, dyspnea, or migratory arthritis, so ankylosing spondilytis was ruled out. Lesch-Nyhan syndrome, a rare disorder in which gout is inherited in a Mendelian manner, could have been suspected in our case due to the early age of onset of the disease and a positive family history; however, the absence of the associated clinical features such as mental retardation, self-mutilation, choreoathetosis, or ataxia, meant that this could not have been a working diagnosis (Walker et al, 2014). The clinical presentation of our patient was mostly in contrast with the classical clinical features of the disease, hence, the diagnosis of atypical gouty arthritis. The classical presentation is with an acute monoarthritis, whereas our patient presented with polyarthritis in each of his visits to the hospital, which accounts for only 10-20% of cases of patients with gout (TCD, 2021). Over 50% of the cases present with an affected first MTP joint, which was never a presentation with our patient (Walker et al, 2014). An acute attack of gout is typically self-limiting over 5-14 days, with complete resolution without treatment; however, the acute attack of our patient was not self-limiting and did not resolve without pharmacological intervention (Walker et al, 2014). It is said that simultaneous polyarticular attacks are unusual, which was the case with our patient (Walker et al, 2014). No severe bony deformities developed in our patient. Most importantly, no tophi were observed in any of the involved joints, whether axial or peripheral. Upon investigation, the most striking feature was a normal SUA level of our patient. Normal SUA levels are observed only in about 11% of the patients of gout, using the lower normal cut-off value of 0.36 mmol/L (Leiszler, Poddar & Fletcher, 2011). However uncommon, though, normal SUA levels during an attack do not exclude gout, as serum urate falls during the acute phase response (Leiszler, Poddar & Fletcher, 2011). Normal or low SUA levels are also found in patients of gout who are diabetics or alcoholic; however, our patient was neither diabetic nor alcoholic (Leiszler, Poddar & Fletcher, 2011). Elevated ESR and CRP are typical of acute gout (Walker et al, 2014). Our patient, however, had normal ESR and CRP levels. A biochemical screen, including RFTs, glucose levels, and lipid profile, is advised in patients of gout because of the association with metabolic syndrome (Walker et al, 2014). In our patient, however, this particular biochemical screen showed values within normal range for all components. The diagnosis of gout in our patient, therefore, was confirmed only by the identification of urate crystals in the aspirate from his left knee joint (Walker et al, 2014). 4. Conclusion Although gout is a common form of inflammatory arthritis, with its typical presentation being the most common, it can present in any atypical fashion. When presented with a diagnostic challenge in a patient with gout, the clinician should be aware of unusual manifestations of gout in all patients with a variety of signs and symptoms, and consider it in the differential (Ning & Keenan, 2010).

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