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GOUT-A REVIEW ON PATHOPHYSIOLOGY, ETIOLOGY, AND TREAMENT

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Abstract: Gout is a picturesque presentation of uric acid disturbance. It is the most well understood and described type of arthritis. Its epidemiology is studied. New insights into the Pathophysiology of hypeuracemia and gouty arthritis; acute and chronic allow for an even better understanding of the disease. The role of genetic predisposition is becoming more evident. The clinical picture of gout is divided into asymptomatic hypeuracemia, acute gouty arthritis, intercritical period, and chronic tophaceous gout. Diagnosis is based on laboratory and radiological features

Keyword: Gout, Pathophysiology, Etiology, Diagnosis, Treatment. Hypeuracemia. Risk factor.

GOUT

GOUT is a clinical syndrome resulting from the deposition of urate (monosodium urate monohydrate) crystals. The crystals may be deposited in a joint, leading to an acute inflammatory response, or in soft tissues, such as cartilage, causing no inflammation. Most cases of gout are characterized by the sudden onset of severe acute monarticular arthritis in a peripheral joint in the leg. The arthritis remits completely and then recurs with increasing frequency. After approximately 10 years of recurrent gouty arthritis, tophi develop in cartilage, tendons, and bursae in some patients. Established criteria for the diagnosis of gout include the presence of urate crystals in joint fluid, the development of a tophus, or the presence of the characteristic clinical pattern described above.[1] Occasionally, a patient may have a more chronic or less severe arthritis affecting more than one joint at a time, in which case the diagnosis depends entirely on the detection of urate crystals. In some patients, urate crystals have been detected in joints in which there has been no inflammation,[2,3] but most of these patients have had at least one previous attack of gout. There are also reports of tophi developing without prior arthritis,[4] chiefly in elderly women with renal insufficiency who were taking diuretic or nonsteroidal anti-inflammatory drugs.[5]

PATHOPHYSIOLOGY

Gout is form of inflammatory arthritis characterized by recurrent attacks of a red, tender, hot and swollen joint. it is associated with pain which comes in rapidly in less than 12 hours. in most of cases joint at the base of big toe is affected. Gout may also lead to topic, kidney stones or nephropathy.

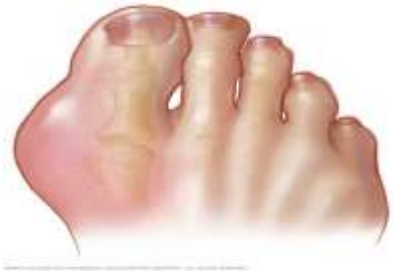

Fig.no 1 Gout Disease

Gout is a disorder of purine metabolism. Purines in the body are finally converted to uric acid which crystallizer in the form of mono-sodium urate, precipitating and forming deposits called as tophi, as joint, tendons and surrounding tissue. Microscopic tophi may be lined by ring of protein which blocks interaction of crystal with cell and thus avoid inflammation. Sometimes naked crystals may breakout from tophi due to minor physical damage to the joint, medical or surgical stress or rapid change in uric acid level. When crystal break out from tophi, they trigger a local immune-medicated informmatory reactions in macrophages. This reaction recruits the enzyme caspase 1, which converts pro-interleunkin 1 Beta into interleukin 1 Beta, one of the proteins in the informmatory cascade. other trigger which are imp in arthritis including cold temperature, rapid change in uric Level , acidosis , articular hydration and extracellular matrix protein like proteoglycans, collagen, and chondroitin sulphate.incresed precipitating at low temperatures explain why the joint in the feet are most commonly affected .rapid changes in uric acid occur due to trauma, surgery chemotherapy, diuretics and stopping or starting a drug , Allopurinol.in case of coexisting hypertension, use of calcium channel blockers and Lostarin are associated with Lower risk of gout.

Hypeuracemia

⇩

Deposition of urate crystals in joint and connective tissue.

⇩

Activation of monocytes and macrophages

⇩

Release of cytokines (IL-1Beta, TNF –alpha)

⇩

Neutrophils secrete inflammatory mediators at site (Histamine, Serotinin,etc)

⇩

Acids environment created further more deposition of urate crystals

⇩

Precipitation of gout. [6]

ETIOLOGY

Crystallization of uric acid, often related to its high level in the blood, is the underlying causes of gout . This can occur because of diet, genetic predisposition. Under excretion of Urate I.e. salts of uric acid . Under excretion of uric acid is the primary cause of hypeuracemia i.e. higher level of uric acid in blood in majority of cases while over production of uric acid is the minor cause.

Important factor are described below [7,8,9,10,11,12]

Life style : Dietary factors associated with gout are consumption of alcohol, fructose-sweetened drink , meat and sea food. Other trigger including physical trouma and surgery. Consumption of coffee, vitamins C dairy products and physical fitness appear to decrease the risk.

Genetic:

Gout is partially he genetic. The genes SLC2A9, SLC22A12 and ABCG21 have been found to be associated with gout. Loss of function mutation in SLC22A12 causes hereditary hypeuracemia By reducing urate absorption and unopposed urate secretion some rare genetic disorders are complicated by gout.

Medical condition

Metabolic syndrome a combination of abnormal obesity, hypertension, insulin resistant and abnormal lipid level often coexist with gout . Other condition completed by gout including lead poising, kidney failure, haemolytic anemia, solid organ transplant and polycythemia.a body mass index >35 increase risk of gout. Chronic lead exposure and lead contamination alcohol are risk factors of gout.

Diet.

Eating a diet rich in red meat and shellfish and drinking beverages sweetened with fruit sugar (fructose) increase levels of uric acid, which increase your risk of gout. Alcohol consumption, especially of beer, also increases the risk of gout.

Weight:

If you're overweight, your body produces more uric acid and your kidneys have a more difficult time eliminating uric acid.

Family history of gout.

If other members of your family have had gout, you're more likely to develop the disease.

Age and sex.

Gout occurs more often in men, primarily because women tend to have lower uric acid levels. After menopause, however, women's uric acid. levels approach those of men. Men are also more likely to develop gout earlier - usually between the ages of 30 and 50 whereas women generally develop signs and symptoms after menopause.

Medication

Diuretics are associated with attract of gout. Other medications which increases the risk of gout niacin, aspirin, ACE inhibitors, Angiotensin receptor blockers expect Lostarin, beta blockers, Ritonavair and Pyrazinamide. And combination of any of these drugs with hydrochlorothiazide further increase chances of gout

SIGN AND SYMPTOMS

The most common manifestation of gout is recurrent attract of acute inflammatory arthritis characterized bye a red, tender, hot swollen joint, in most of the cases metatarsal-phalangeal joint at the bases of big toe of affected. Other joint like that of heels, knees, wrists, and finger may also be affected. Joint pain usually begins over 2-4 hours and during night. This is mainly due to lower body temperature. Other symptoms along with joint pain including fatigue and high fever.

COMPLICATIONS

Following complications of gout can exist:

Recurrent Gout:

some people may never experience gout sing and symptoms again. But other Any may experience gout several times each year. Medication may help prevent gout attacks in people with recurrent gout.

Advanced Gout:

Untreated gout can cause deposit of Urate crystal under the skin. Tophi can develop in several areas like fingers , hands, feet, elbows, tendons, and ankles. They can become swollen and tender during attacks of gout.

KIDNEY STONES:

Urates crystal may collect in urinary tract in patients with gout causing kidney stone.

DIAGNOSIS

Joint fluid test: Joint fluid test is useful too observed uric acid crystal are present. This is the only test for diagnosis of gout.

Blood test: To measure the uric acid level in blood. Blood test results can be misleading through some people have high uric acid levels, but never experience gout. And some people have sings and symptoms of gout , but do not have unsual level of uric acid in their blood.

Urine test :A test to measure level of uric acid in urine.

X-rays:X-rays of extremities are sometimes useful in the late stages of the disease; X rays are not usually helpful in the early diagnosis. Pain often causes people to seek medical attention before any long term change can be seen on X-rays may help to rule out other causes of arthritis.

TREATMENT ON GOUT [13, 14,15]

The goals of treatment for gout are fast pain relief and prevention of future gout attacks and long-term complications, such as joint destruction and kidney damage.

NSAIDs: NSAIDsmay control inflammation and pain in people with gout. NSAIDs include indomethacin, ibuprofen, naproxen, and etoricoxib

Indomethacin, the first of these drugs to be used extensively, provides some pain relief within two to four hours. Depending on the severity of the attack and its duration, the appropriate dose ranges from 150 to 300 mg per day, given in divided doses, with a gradual reduction during a period of five to seven days as the attack subsides. Most other no steroidal anti-inflammatory drugs are effective but no better than indomethacin, although few

comparative data are available. The usefulness of no steroidal anti-inflammatory drugs is limited by their side effects, but in general, the risks are greatest in elderly patients, particularly those with renal dysfunction.

Colchicine: A type of pain reliever that effectively reduces gout pain, especially when started soon after symptoms appears. Colchicine. Your doctor may recommend colchicine (Colcrys, Gloperba, Mitigare), an anti-inflammatory drug that effectively reduces gout pain. The drug's effectiveness may be offset, however, by side effects such as nausea, vomiting and diarrhea.[17]

Corticosteroids: Corticosteroid medications, such as the drug prednisone, may control gout inflammation and pain. Corticosteroids may be administered in pill form, or they can be injected into joint. Corticosteroids are generally reserved for people who cannot take either NSAIDs or colchicine.

Medications that block uric acid production: Xanthine oxidase inhibitors, including Allopurinol.in and febuxostat, limit the amount of uric acid that body makes.This may lower blood's uric acid level and of reduce risk of gout. Side effects of Allopurinol.in include a rash and low blood counts. Febuxostat side effects include rash, nausea and reduced liver function.If gout symptoms have occurred OFF and ON without treatment for more than 10 years, uric acid crystals may have built up in the joints to form gritty, chalky nodules called tophi, If tophi are causing infection, pain, pressure, and deformed joints, treatment includes: Xanthine oxidase inhibitors, which may shrink the tophi until they disappear.

Medication that improves uric acid removal: Probenecid improves kidney's ability to remove uric acid from body. This may lower uric acid levels and reduce risk of gout, but the level of uric acid in urine is increased.

Pegloticase: This medicine is for gout that has lasted a long time and has not responded to other treatment.

Medications to prevent gout complications [17]

If you experience several gout attacks each year, or if your gout attacks are less frequent but particularly painful, your doctor may recommend medication to reduce your risk of gout-related complications. If you already have evidence of damage from gout on joint X-rays, or you have tophi, chronic kidney disease or kidney stones, medications to lower your body's level of uric acid may be recommended.

- **Medications that block uric acid production.** Drugs such as allopurinol (Aloprim, Lopurin, and Zyloprim) and febuxostat (Uloric) help limit the amount of uric acid your body makes. Side effects of allopurinol include fever, rash, hepatitis and kidney problems. Febuxostat side effects include rash, nausea and reduced liver function. Febuxostat also may increase the risk of heart-related death.
- **Medications that improve uric acid removal.** Drugs such as probenecid (Probalan) help improve your kidneys' ability to remove uric acid from your body. Side effects include a rash, stomach pain and kidney stones.

PREVENTION [16]

During symptom free periods, these dietary guidelines may help protect against future gout attacks.Drink 8 to 16 cups (about 2 to 4 liters) of fluid each day, with at least half being water. Eat a moderate amount of protein, preferably from healthy sources, such as low-fat or fat-free dairy, eggs, and nut butters. Limit daily intake of meat, fish and poultry to 4 to 6 ounces (113 to 170 grams). Maintain a desirable body weight.

CONCLUSION

Gout is an increasingly prevalent condition worldwide and creates a heavy economic burden. Available treatments are generally effective; however, they are not devoid of adverse events. Well-designed, long-term, controlled clinical trials evaluating the comparative efficacy and tolerability of treatments for gout are needed.

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