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Review Article

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Gout Management in Primary Care Approach; Literature Review

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ABSTRACT

Gout is considered one of the most common causes of arthritis worldwide. It has approximately a prevalence of 2.5%. The pathophysiology behind it mainly increases uric acid in the blood, either by increasing production or decreased excretion by the kidney. It usually manifests as a tender, erythematous, and swollen joint. The gold standard to diagnosis is the aspiration of synovial fluid of the affected joint. Acute treatment should be in the emergency department; however, the maintenance can be done at the primary care clinics. The objective of this review is to discuss Gout disease in clinical presentations, diagnosis, and management, mainly at primary care. We searched the PubMed database looking for relevant articles to the topic using Mesh terms, "Gout disease." Gout disease is considered one of the most common rheumatological disorders globally. A number can be increased by a poor lifestyle such as alcohol consumption and increased red and white meat-eating. Diagnosis can be based on some blood tests, radiological imaging, and aspiration of the joint. Maintenance treatment usually is done at the primary care in which the patient can be given Allopurinol or other urate-lowering drugs.

Key words: *Gout disease, Uric acid, Syniovial aspiration, Allopurinol, Primary care*

INTRODUCTION

Gout is the most common prevalent disease of arthritis (joint inflammation), and it has the most significant potential for safe treatment between arthritis diseases [1-3]. The underlying cause of this disease is increasing uric acid in the body either by increasing production or decreasing excretion, so it can be treated by lowering the production by Xanthine Oxidase inhibitor or increasing the excretion by the kidney [4-6]. In this review, we will talk briefly about the epidemiology, pathophysiology, and treatment of the disease, and we will focus on Gout management in primary care.

Epidemiology

As mentioned in the introduction, gout is one of the most prevalent diseases in clinics; it generally makes up approximately 2.5% of the population [7]. The disease is more prevalent in men than women; it is estimated that the prevalence of gout in men is 3-6%, and in women, it is 1-2% [7]. Nowadays, the prevalence of gout is increasing rapidly, in some countries it is around 10% and is considered a highly prevalent disease due to the increase of bad habits such as: increasing eating junk foods and decreasing physical activity both of which play an essential role in developing the disease [7].

Pathogenesis

Urate is the ionized form of uric acid; urate crystals deposition in tissues occurs when the serum uric acid rises above the pathological potential threshold of uric acid about 6.8mg/dl [8]. Urate deposition can be caused by increased uric acid production, which is responsible for only 10% of the disease, or it can be caused by decreased renal excretion, which is the most common underlying mechanism and causes about 90% of gout cases [9]. We will mention some causes of increased uric acid production:

- Overproduction caused by enzymatic deficiency such as Lesch-Nyhan syndrome, which is x-linked recessive [10]. In this syndrome, an enzyme deficiency in purine metabolism will lead to the accumulation of uric acid [10].
- Diet is one of the most critical factors that increase the uric acid level in the body [11]. It is mostly found in animal proteins such as red and white meat, so gout patients should avoid excessive eating of meat and increase their vegetable intake, and if they drink alcohol, they should stop it, because it is known that alcohol increases uric acid [11].

The uric acid increase can be due to endogenous causes such as malignancy or chemotherapy, which will accelerate cell turnover and increase purine in the body [12]. The second cause, and the most important one, is decreasing renal excretion of uric acid, which causes 90% of gout cases [8]. Hence, uric acid is insoluble and needs a specific transporter such as URAT1 (uric acid transporter 1) and OAT (organic anionic transporter) [13]. The normal excretion of uric acid is 10% in urine [13]. However, in uromodulin mutation, this percentage will drop sharply, and this is the primary mutation that will cause a decrease of uric acid excretion and an increase in serum uric acid [13]. When we talk about gout, there is acute onset gout, and there is a chronic one, and indeed the treatment differs from one to one. In acute gout, uric acid crystals' deposition activates synovial macrophages to engulf those crystals [14]. Mature macrophages can quickly engulf the crystals without inducing an inflammatory response [14]. However, when the non-mature one, engulfs the crystals, it may lead to trigger the immune reaction and activating the inflammatory cytokines, mast cells, and neutrophils [14]. Usually, in the acute onset of gout, the treatment is limited to NSAIDs (non-steroidal anti-inflammatory drugs) or Colchicine since they stop the inflammatory reaction [14].

Chronic gout occurs due to repetitive recurrence of acute attacks; chronicity is one of the gout features [15]. The researches have shown that the underlying cause of chronic gout is the activation of chondrocytes to produce an inflammatory reaction and increasing level of MMP (matric metalloproteases), which increase the damage of the surrounding cartilages [16]. Chronic gout can occur even if the management is optimal and the acute flare-up is under control [8]. However, nowadays, the incidence of chronic gout is dropping due to improved health care, treatment of chronic gout is mainly Allopurinol, which is a xanthine oxidase inhibitor, and the physician stops the NSAIDs and Colchicines [17].

Clinical manifestation

The typical clinical features in acute gout patients are pain and swelling in the metatarsophalangeal joint, knee, foot, olecranon, and pre-patellar bursa this pain, erythrma, swollen and stiffness of the joint, usually it is precipitated by infection dehydration or trauma **(Figure 1)** [18]. Chronic gout is caused by recurrent attacks of acute gout crystals of MSU (monosodium urate crystals) in the form of hard, subcutaneous white to yellow deposits and heterogeneous consistency with chronic joint stiffness pain (2).

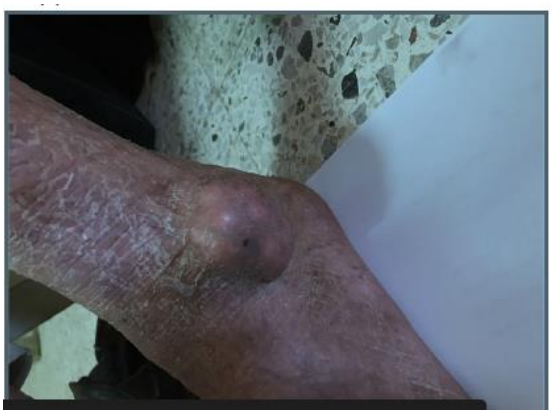

Figure 1. Gouty arthritis

Investigation

The definite diagnosis of gout depends on joint aspiration and polarized light microscopy of the synovial fluid, which is considered an invasive procedure [19]. The most crucial differential diagnoses in gout are septic arthritis, pseudo-gout, and reactive arthritis, so these should be ruled out to confirm gout diagnosing [4]. In blood tests, increased neutrophils and inflammatory biomarkers, as well as hyperuricemia are very important findings, but it is not enough to confirm a gout diagnosis [20].

Synovial fluid aspiration is an effective way to rule out septic arthritis after culturing the aspirated synovial fluid; under polarized light microscopy of synovial fluid, we can confirm negative MSU crystals (monosodium urate) **(Figure 2)** [21]. Urinary uric acid excretion is not significant because it is only beneficial in the early stage of the disease, so a 24-hour collection of uric acid creatinine ratio is performed [19]. In terms of imaging techniques, ultrasonography is very sensitive to detect the monosodium urate crystals deposition [22]. It has a double contour sign, which deposes the monosodium urate crystals on the surface of the hyaline cartilage, but the problem is that this test is not 100% specific **(Figure 3)** [22].

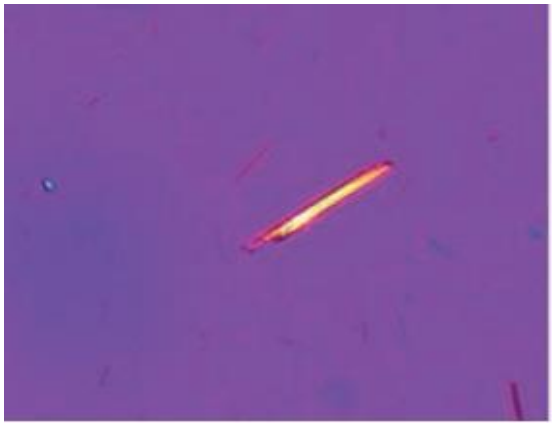

Figure 2. monosodium urate crystal under Polarised light microscopy

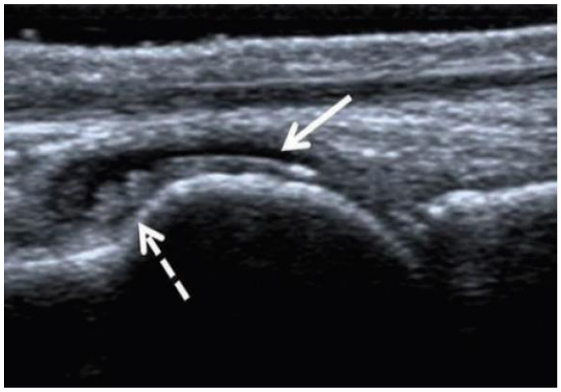

Figure 3. Radiographic appearance of Gouty arthritis.

Management of gout in primary care

According to the 2017 guidelines of the British Society of Rheumatology and British Health Professional in Rheumatology, NSAIDs or Colchicine (low dose; 500mcg, 2 to 4 times daily) are the first-line treatment of acute gout attack, according to the patient profile and preferences [23]. If the patient has contraindications for using NSAIDs or colchicines, a low dose of prednisolone (35mg daily for five days) is recommended [23]. Adherence to short-term gout management is crucial to decrease recurrence risk and prevent chronic gout attacks [23]. Lifestyle modification is very important in gout patients, so they should avoid alcohol and decrease the intake of high purine food content such as white and red meat [23].

Gout patients should increase their physical activity since they are at increased risk of cardiovascular disease and diabetes mellitus [23]. Furthermore, they should pay attention to drugs that increase the uric acid level, such as thiazide and loop diuretics, both of which should be avoided in gout patients, and alternative treatment for hypertensive patients should be used [23]. For ULT (urate-lowering therapy), the most used and effective drug is Allopurinol, which is a xanthine oxidase inhibitor [23]. According to guidelines, the doctor should prescribe ULT for all patients without waiting for any complications or recurrent gout attacks. Also, the patient should be informed and taught how to take the drugs and simplify the regimen and explain the aim of the therapy [23].

In addition, the complication that can occur if the regimen is neglected will show a full adherence to the regimen. According to the guidelines, the standard dose of Allopurinol is 50-100 mg daily as a starting dose; then the dose is increased by 50-100 mg every four weeks to achieve the serum uric acid's optimal level, which is 300 micro mol/L according to British guidelines [23]. However, according to the European and American guidelines, the serum uric acid that should be achieved is 360 micro mol/L [23]. The maximum dose that can be given of Allopurinol is 900 mg daily by divided doses [23]. Some recent research shows that a very low serum uric acid level increases the risk of developing dementia and Parkinsonism, so a very low serum uric acid should be avoided [23]. The guidelines again recommend 500mcg of Colchicine as a prophylactic treatment for six months to prevent any recurrence of a gout attack. For patients who are intolerant to Colchicine, NSAIDs are prescribed as prophylaxis with gastroprotective therapy to prevent ulcer formation [23].

CONCLUSION

Gout has a prevalence of 2.5%, and in some countries, this prevalence can reach 10% by increasing the bad habits of eating fast food and no physical activity. The leading underlying causes of gout is increasing in uric acid or urate crystals due to an imbalance between the production of uric acid and excretion, so the main concerns for the treatment of gout are by reducing the level of uric acid by Allopurinol and in acute attacks prescribing NSAIDs and Colchicine is crucial with a prophylactic treatment to prevent and recurrent attacks.

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