Review Article

Evaluative Role of Family Physician in Diagnosis and Management of Gout in Primary Health Care Centers: A Simple Literature Review

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Abstract

Background: Gout is a painful condition that is common in developing countries such as Saudi Arabia. When a patient is referred to a doctor with symptoms suggestive of gouty arthritis, a metabolic screening is ultimately requested. Diseases enclosing obesity, hyperlipidemia, diabetes mellitus, hypertension, and cardiovascular disease should be investigated as they are indirectly associated with gout. The latest practice-updated general physicians should determine the cause and effect of this disease and manage it in primary health care settings. Objective: In this literature review, we will discuss gout as a disease within a primary healthcare setting with a diagnosis and management approach. Method: PubMed database was used for articles selection, and the following keywords were used in the MeSH: Gout, Evaluation, Management, Treatment, and Primary Healthcare. This review includes epidemiology, pathophysiology, clinical features, diagnostic evaluation, and management of gout. Conclusion: Chronic diseases such as diabetes and hypertension should be accounted for in diagnostic workup and help in the long-term management of gout patients. Urate lowering agents are recommended in patients suffering from attacks. Colchicine may help in preventing the resurgence of painful episodes. Patients with renal disease should have their allopurinol doses adjusted appropriately. Adherence to medication and motivation of both clinicians and patients are key factors in the successful management and control of acute gout attacks and a better lifestyle for patients suffering from this illness. Physicians should always approach and evaluate the patients' condition, work with them, and guide them to suitable drugs and lifestyle modifications to ensure their health improvement.

Keywords: Gout, Management, Primary Health Care Centers

Introduction

Gout is a painful medical condition and a frequent cause of acute and chronic arthritis worldwide, with a propensity for a cure if management is optimized. This inflammatory arthritis affects the first metatarsophalangeal joint. It occurs as a response to the presence of monosodium urate crystals in joints, bones, and/or soft tissues. Even though there is a clear protocol of management that is recognized globally, there is notable low compliance among patients. Around one-third of patients in the UK are currently on sub-therapeutic anti-gout medication dosage with adherence below 40% in twelve months [1]. In this review, we will help physicians to have a general understanding of the disease to help in the daily life of the patients encountering this problem. This paper will include discussing gout by integrating epidemiology, pathophysiology, clinical features, diagnostic evaluation, and management of this painful ailment in modern clinical practice.

Methods

PubMed database was used to select articles and the following keywords were used in MeSH: Gout, Evaluation, Management, Treatment, and Primary Healthcare. Many articles on the topic were found with further restriction by PubMed filters and reviewing the titles and abstracts of the

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articles, the final results were included in this paper. With regard to the inclusion criteria, the articles were selected based on the relevance to the project, which should include one of the following topics; gout evaluation, gout management, the pathophysiology of gout, and primary health care role. The exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint, or were repeated studies, systematic reviews, or meta-analysis.

Discussion

When a patient is referred to a physician with symptoms of gout, metabolic screening should be performed. Diseases such as obesity, hyperlipidemia, diabetes mellitus, hypertension, and cardiovascular diseases are investigated as they are associated with gout [2, 3]. Al-Arfaj et al. interestingly showed that uric acid levels are positively correlated with age, weight, serum creatinine, and erythrocyte sedimentation rate, and they are negatively associated with serum cholesterol or triglycerides. In men, uric acid levels only correlate significantly with BMI and serum creatinine [4]. Elevated inflammation markers and neutrophils with lowered negative phase reactants mainly affect serum uric acid during an acute episode. Serum uric acid is commonly around 360 μmol/L in males and 16.3% in females [5]. Joint aspiration with polarized light microscopy of the synovial joint is the definitive investigation for gout diagnosis. The effusion would appear turbid with low viscosity, and on microscopy, the needle-shaped monosodium urate crystals appear without birefringence. The primary care doctor may not have the former tools such as joint aspiration kit at hand, so based on the acute features of inflammation and typically affected joints such as podagra, a well-sought clinical diagnosis can be made [6]. In a recent study [4] from Saudi Arabia, hyperuricemia was reported to reach 8.42% in a sample from 14 primary health care clinics; however, hyperuricemia is usually high in the population with only a few developing gouty arthritis; hence, it should not be a factor in diagnosing gout. In the United Kingdom, the report prevalence was 2.49%, making gout a common condition in the developed world [1].

Gout is more common among men over 40 and increases with age; however, women may also suffer from this painful disease [1]. Premenopausal women have a lower risk of gout as uricemia is opposed by estrogen, progesterone, and lowered insulin resistance in this population and these gender differences disappear by the age of 60 [1, 7]. Evidence shows that increased consumption of spirits, beers, fructose-heavy beverages, red meat, and seafood puts people at risk of gout [1, 7]. Gout is also linked to certain chronic medical conditions like renal impairment, hypertension, and insulin resistance, along with medications especially diuretics [1, 7-9]. Uric acid is an end-product of endogenous and dietary extracted purine and its levels are decided by purine metabolism. Notably, the elimination is two-third from the kidney and one-third from the intestines. Most of the gout patients have an impaired excretion (90%). There is more than one step in the excretion process of the uric acid that can be disturbed leading to hyperuricemia such as reabsorption via urate transporter-1, active re-secretion, and GLUT9, which transports uric acid back to circulation. Hyperuricemia (high levels of uric acid) is almost always present in gout patients (even in non-inflammatory status). However, the majority of hyperuricemic patients never develop gout [10]. So, individual differences in the formation of crystals and/or in inflammatory responses might be the key to develop this condition. Multiple risk factors may cause hyperuricemia, such as absolute or relative impairment of renal uric acid excretion, overproduction of uric acid, and/or overconsumption of purine-rich foods that are metabolized to urate (e.g. red meat) [11]. Fortunately, we can detect extracellular fluid urate levels by measurement of serum or plasma urate. Uric acid tends to form urate crystals (along with other chemical compounds –e.g. sodium) that precipitate (e.g. in joints) and are less soluble under certain circumstances such as acid conditions and at low temperatures (like in metatarsophalangeal joint of the big toe) [12, 13].

On the other hand, consumption of skimmed milk, yogurt, coffee, and vitamin C reduces the risk of gout disease; while, eating cherry reduces recurrent attacks. Nevertheless, there are other non-modifiable and modifiable risk factors being recognized. Non-modifiable risk factors include male gender, advanced age, and ethnicity (e.g., Pacific Islanders). Associations of at least 28 genetic loci with hyperuricemia have been established by genome-wide association studies (GWAS) [14]. Single nucleotide polymorphism (SNP) analyses at these loci have identified polymorphic alleles that also alter gout risk [15, 16]. Modifiable risk factors include obesity, diets rich in meat and seafood content, alcohol-containing beverages (especially beer and distilled spirits), sodas, and fruit juices high in fructose or sucrose content, hypertension, thiazide or loop diuretic use, chronic kidney disease, postmenopausal and organ transplant recipient status, and use of certain medications (e.g., cyclosporine A or low-dose aspirin, although cardioprotective aspirin doses of only 81 to 325 mg/day do not warrant discontinuation). Consumption of alcohol or intermittent use of diuretics, which may result in abrupt changes in extracellular fluid urate levels, appear to increase the risk of an attack [7, 17].

Signs and symptoms may slightly vary by type; acute, chronic, and transplant induced gout. Acute gout is presented with acute crystal synovitis and within half a day an excruciating tender pain occurs in the joints with erythematous swelling [18, 19]. The acute attack fades within a week or two and commonly affects the first metatarsophalangeal joint, knees, ankles, and midfoot. Once the crystals are formed, the immune system recognizes them as “foreign bodies” (NLRP3 receptor is associated) and starts the process to eliminate them by activating the cytokine cascade. This will result in the activation of interleukin-1β, leading to activated whole inflammatory cascade (including

the influx of neutrophils –by IL-8- and leucocytes into the joint). The ingestion of urate crystals causes even more release of pro-inflammatory cytokines (mainly interleukin-1β) leading to this vicious cycle and more inflammation and thus more pronounced symptoms (acute gouty arthritis). Moreover, even if the acute flares resolve, the crystals remain in the joints [20, 21]. The attacks are precipitated by injury, excessive purine intake, dehydration, infection, and imitation of hyperuricemic medications [17]. The solution for preventing acute attacks by anti-gout drugs is to slow up the titration of urate-lowering treatment [6, 22]. With the recurrence of attacks, and as years pass by, patients develop chronic tophaceous gout. These tophi are monosodium urate crystals appearing as subcutaneous nodules in finger and toe tips, bursa, and olecranon. This chronic form of gout is presented with long-standing joint pain and tenderness, stiff joints, and occasional acute gout episodes. Transplant recipients are in immunosuppressant medications like calcineurin inhibitors and prednisolone, usually developing a rapidly progressive tophaceous gout. In patients with non-transplants, it would take around 10 years for gout to develop, transplant recipients have it worse as it would take half that period or less for tophi to form [6].

When it comes to gout, it is important to have the right amount of the right drug at the right time. The physician should converse with empathy towards patients in pain, educating them on the importance of adhering to medication and actively involving them in management decisions. When patients present an acute attack, it is important that they have adequate bed rest, apply cold ice on inflamed joint and intake non-steroidal anti-inflammatory drugs as a first-line therapy while considering colchicine or corticosteroids [6, 14, 22, 23]. Dietary modifications, especially in obese individuals, are necessary as exemplified by daily supplements of vitamin C, which help reduce serum uric acid, and cherry reducing the recurrence of attacks [7, 6, 17]. Urate lowering agents are recommended in patients who have more than one attack of gout per year or developed tophi, transplant recipients with acute gout, renal impaired patients, and nephrolithiasis cases [6, 14, 22]. Guidelines vary on whether treatment should be initiated during the acute phase or 1-2 weeks after the attack [14]. Starting initially at a low dose and steadily incrementing with a goal of serum uric acid below <300 μmol/L is optimal [6]. If the patient, unfortunately, develops acute episodes while on urate-lowering medication, he/she should still continue his/her regimen [6, 14, 22]. Consider colchicine if tolerable by your patient, as it would aid in preventing recurrence of attacks. A potential dose of 0.5 mg once or twice daily for six months would reduce recurrence. If colchicine cannot be tolerated, then a choice should be made on an alternative of NSAIDs, COX-2, and low-dose steroids [6, 24]. Allopurinol is a xanthine oxidase inhibitor, its metabolite oxypurinol is excreted by the kidneys and is long-acting. An initial dose of 100 mg per day is increased gradually, but not above the maximum licensed dose until serum acid levels are satisfactorily below 300 μmol/L. In renal impaired patients, the initial dose of allopurinol is 50 mg per day and the maximum dose should be reduced with referral to a specialist [14]. Febuxostat is another drug that can be used if allopurinol is strongly contraindicated in a patient. It is a non-purine analog inhibitor of xanthine oxidase exclusively and generally was well tolerated and was as effective as allopurinol in trials. Moreover, it is safer in renal impairment than allopurinol as it is metabolized in the liver and not excreted by the kidneys. There are other drugs such as pegloticase, benzbromarone, and probenecid that are all used in different scenarios but with more restrictions due to their side effects. If the clinical evaluation was done in finesse and co-morbidities were detected, then they should be managed appropriately. If a heart failure patient is on aspirin, although it is associated with gout, its use should be continued as benefits outweigh the risk margin [6]. It would be unwise to treat hypertension with beta-blockers or diuretics as they are affiliated with gout, and it is preferred to prescribe amlodipine or losartan. Atorvastatin or fenofibrate should be used with hyperlipidemia [15].

To conclude, we found that all of them agreed to consider sodium mono-urate crystals target in the patient with gout and hyperuricemia should be < 6.0mg/ dL to archive long-term control. Urate lowering agents and mainly Allopurinol are considered in case of recurrent attacks. In the case of acute attacks, NSAIDs are considered in the first line of management.

Conclusion

Gout arthritis is a painful and common condition that affects tens of thousands of people and as a physician, it is one of the most orthopedic conditions that are seen in our setting. Fortunately, for gout patients, it has a high propensity for cure if done and followed by the patient appropriately. The research on this topic was variable starting from the mechanisms behind this disease, risk factors, and associations to the drugs' efficacy and lifestyle modifications effect. However, there is still a new scope that can be explored especially with drugs that target the inflammatory markers seen in gout (e.g. IL-2) and their rule in the overall treatment approach. The physician should always approach and evaluate the condition of their patients' work with them and guide them to suitable drugs and lifestyle modifications to ensure the betterment of their patients' health and near-normal lifestyle.

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