Gout- from a primary care perspective

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Abstract

Gout is a type of inflammatory arthritis which can cause recurrent episodes of acute pain and joint inflammation.

Epidemiological studies show it is 2-6 folds more common in men than in women. It is caused by raised serum uric acid levels which, when gets deposited in joints and tissues can cause significant pain and morbidity. Untreated gout can cause permanent joint damage. Hyperuricemia can also cause urate nephropathy and renal stones. It is associated with other cardiovascular diseases.

Risk factors include male sex, obesity, genetics, purine rich food, alcohol, certain medications, chronic kidney disease, hypertension and diabetes mellitus.

Gout can present as rapid onset pain and swelling of any joint, predominantly of the first metatarsophalangeal joint. Tophi can present as painless, nodules on extensor surfaces of joints or other body parts.

Diagnosis is by identification of uric acid crystals in joint fluid aspirates.

Management involves modifying risk factors, treatment of acute attacks using non- steroidal anti-inflammatory drugs, colchicine, steroids and long-term prophylaxis medications. Prophylaxis is based on treat to target approach and involves urate lowering drugs like allopurinol, febuxostat. There are other newer drugs available in secondary care.

Despite the availability of effective prophylactic medications to lower uric acid levels, the prevalence of gout is increasing. It stresses the importance of patient education as well as initiating urate lowering drugs in patients presenting with recurrent attacks and those with other co-morbid risk factors.

The aim of this article is to provide an overview of gout and its management in primary care. We, as authors also highlight the importance of patient education and empowerment in better understanding of their disease and adherence to long term management. We also strongly advocate starting urate lowering therapy for at risk patients by primary care physicians. This will not only prevent future gout attacks, but also reduces long term complications like joint damage, tophi, renal stones, renal impairment and reduce the risks of cardiovascular disease.

Key words: Gout, inflammatory arthritis, hyperuricemia, urate lowering therapy, prophylaxis

Introduction

Gout has been referred to as “disease of kings” in the past, because of their high consumption of purine rich food and high consumption of alcohol (1).

Gout is a type of inflammatory arthritis caused by deposition of monosodium urate crystals. It is a chronic condition usually caused by elevated serum uric acid levels (2). Although hyperuricemia causes gout, not everyone with raised serum uric acid levels develop gout. The diagnosis is mainly by identifying uric acid crystals in the joint fluid aspirate. It usually presents as a rapid, onset severe pain and swelling of a joint, mainly the first metatarsophalangeal joint. Presence of tophi indicate longstanding untreated gout. It can also cause urate nephropathy and renal stones. Lifestyle modification along with urate lowering therapy to reduce serum urate levels below the target, is the mainstay of gout management (3).

Primary care physicians are very good at managing acute gout attacks. However, only one third of UK patients with gout, are started on urate lowering therapy, despite the availability of good prophylactic medications. This could be multifactorial. Patient education and understanding of the disease is key in effective management (4).

The aim of this article is to raise awareness among primary care physicians, on managing gout, focussing on prompt use of urate lowering therapies, thereby reducing future risks of gout flares and reducing cardiovascular morbidity and mortality.

Epidemiology

Gout prevalence in the general population is 1-4%. It is 2-6 times more common in males than females. Premenopausal women are protected because of the uricosuric action of oestrogen. A UK general practice survey in 2012 showed the prevalence of Gout to be 2.49%, with a male to female ratio of 4.3:1. The incidence has since been increasing worldwide due to poor unhealthy dietary habits, sedentary lifestyle and Obesity etc. (3,5).

Pathophysiology

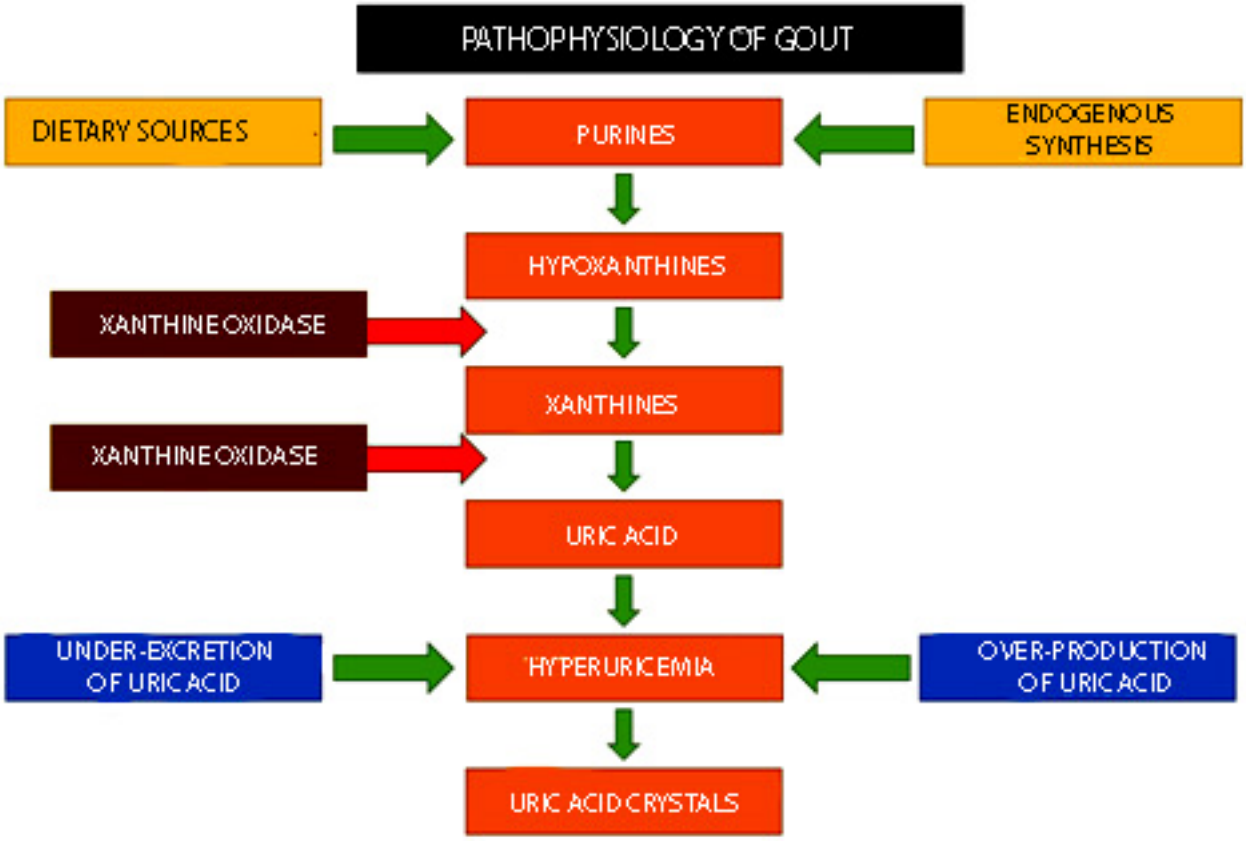
Purines from dietary sources and endogenous synthesis (by liver and small intestine) are broken down to produce uric acid as it’s end product. Uric acid is primarily excreted through the kidneys (60-75%) and the rest through the GI tract (6). Xanthine oxidase is an enzyme that helps conversion of Purines to its end product uric acid. Xanthine oxidase inhibitors like Allopurinol and Febuxostat help prevent this conversion into uric acid. Figure 1 illustrates pathophysiology of gout. Although hyperuricemia causes urate crystal formation, there are other local factors that come into play like temperature, PH, synovial and cartilage factors. This explains why, not everyone with hyperuricemia develop gout (6). Gout is caused by either under excretion or over production of uric acid. Under excretion contributes to 90% of cases of Gout, while only 10% of cases are due to over production. When uric acid levels reach above the threshold, it causes extracellular urate saturation and crystal formation in joints and tissues. These crystals activate inflammatory processes causing acute gouty arthritis. Over the years, chronic inflammation leads to destruction of the joints causing chronic gouty arthritis and tophi formation. Chronic hyperuricemia also leads to urate nephropathy and nephrolithiasis (3)

Aetiology

Gout occurs due to a combination of factors including genetics, dietary and other lifestyle choices, other comorbidities, some of them are listed in table below (3,5).

Risk Factors include
HTN
CKD
Hyperlipidemia
Psoriasis
Obesity
Diabetes mellitus
Metabolic syndrome
Chemotherapy
Drugs: Diuretics ; low dose aspirin and cyclosporin

Figure 1


PATHOPHYSIOLOGY OF GOUT
DIETARY SOURCES
PURINES
ENDOGENOUS SYNTHESIS
HYPOXANTHINES
XANTHINE OXIDASE
XANTHINES
XANTHINE OXIDASE
URIC ACID
UNDER-EXCRETION OF URIC ACID
HYPERURICEMIA
OVER-PRODUCTION OF URIC ACID
URIC ACID CRYSTALS

Diagnosis

Clinical features

Gout can present as an acute painful, swollen joint with redness that comes abruptly, usually overnight. The most affected joint is the first metatarsophalangeal joint, also called as Podagra. It accounts for 70% of first attacks. Other joints that can be affected are knee, midtarsal joints, wrists, ankles and joints of hands. On examination, the affected joint shows warmth, redness, swelling and tenderness. Tophi present as hard nodules on skin in and around joints (7).

American College of Rheumatology (ACR) Criteria for diagnosis of Gout (10) are:

- Finding of monosodium urate crystals in joint fluid or identified from tophi is diagnostic.
- Or 6 or more clinical features from the following:

1) More than 1 attack of acute arthritis
2) Maximum inflammation within 1 day
3) Monoarthritic attack, with redness observed over joint
4) First MTP joint swollen or painful
5) Unilateral first MTP joint attack
6) Unilateral tarsal joint attack
7) Tophus
8) Hyperuricemia
9) Asymmetrical swelling within a joint on Xray film
10) Subcortical cyst without erosions on Xray film
11) Joint culture negative for organisms during attack.

Investigations

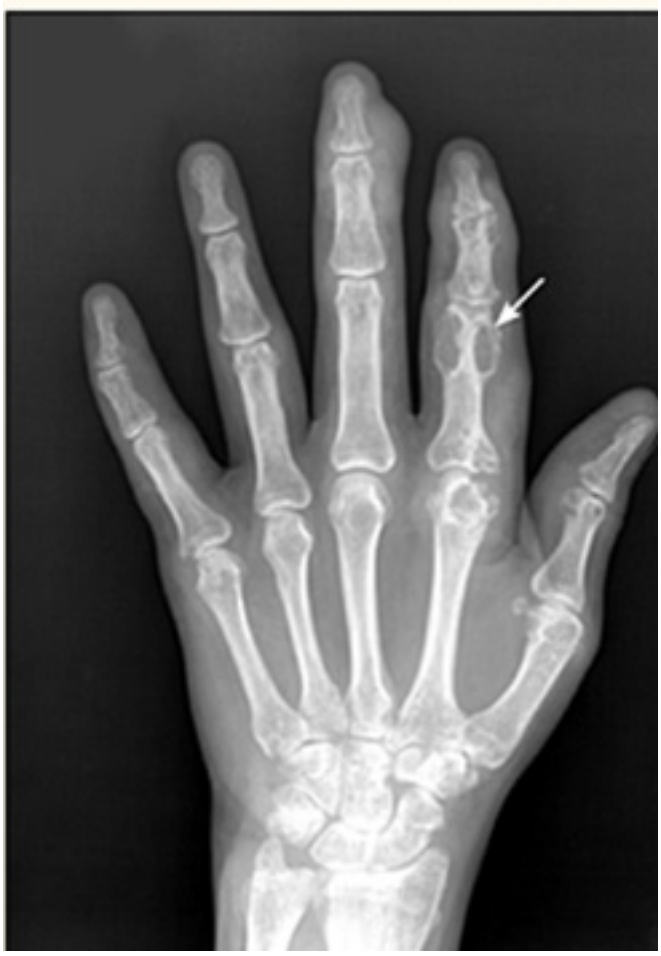
Serum urate levels are usually low during an acute attack. Hence, it is advisable to check serum urate levels 2-4 weeks after an acute attack.

Other blood tests like renal function, lipids, Hba1c, LFT may be ordered to screen other co-morbidities including metabolic syndrome.

The gold standard diagnosis of gout is by identification of uric acid crystals in joint fluid aspirate.

Plain Xray is still used mainly for imaging in gout. More recently there are more advanced imaging modalities like ultrasound, MRI, CT and dual energy CT. These can show early changes of joint damage and tophi. In future we may be able to rely on these advanced imaging methods rather than examining joint aspirates.

Another use of these advanced imaging might help us in objectively monitoring gout treatment response (8).



Erosive arthropathy in Gout of proximal phalanx Eggebeen, A.T., 2007. Gout: an update. American family physician, 76(6), pp.801-808 (9).

Differential Diagnoses:
The acute gout attacks can mimic other conditions like septic arthritis, pseudogout and cellulitis.

Chronic tophaceous gout should be differentiated from rheumatoid arthritis, nodal osteoarthritis (3,5).

Management of Gout

Management of gout involves nonpharmacological and pharmacological management.

Nonpharmacological management:
This includes advice to patients on smoking cessation, alcohol reduction, adapting healthy dietary habits, exercise.

As dietary factors are well known cause of gout, diet and lifestyle modification forms an important aspect of managing gout.

Dietary advice for patients: (10,11,12)
- Avoid high purine diet like red meat and seafoods like shellfish and organ meats like liver.
- Avoid high sugar or fructose containing drinks.
- Vegetables rich in purines like spinach, soybeans and mushrooms can be consumed.
- Patients should be encouraged to drink more than 2 Litres of water per day.-
- Increased dairy products intake is found to be protective against gout.
- Exercise, weight loss and reducing alcohol are all part of effective management, promoting healthy lifestyle and thereby preventing gout attacks in patients, as well as reduce the cardiovascular risks in patients.

Pharmacological management:
This mainly involves two components
a) Managing acute flares
b) Reducing serum uric acid to levels below the target threshold to prevent future flare ups (13)

Acute gout flares typically present as sudden severe acute inflammatory joint pain, it also lasts for a short period. Starting anti inflammatory medications early on like non-steroidal inflammatory drugs will stop the inflammatory processes, alleviate pain and preserve joint function. Commonly used medications are Naproxen, Diclofenac and Indomethacin are prescribed at the maximum dose for the shortest possible duration (5,7).

Colchicine, due to its anti-inflammatory properties is also used to treat acute gout flares as well as given as prophylaxis while initiating Urate lowering therapies. It is prescribed at a dose of 500mcg given 2 to 4 times a day, with a maximum of 6mg per course. The common side effects include gastro-intestinal effects like nausea, vomiting and diarrhoea, which occurs in 5-10% of cases (5,14).

In cases where above medications are intolerant or contra-indicated, steroids- either systemic or intra-articular provide symptomatic relief during acute attacks (7). Prednisolone at a dose of 30-35mg per day for 3-5 days is recommended.

Hypertensive patients on loop or thiazide diuretics, who develop gout, should be switched to losartan or a calcium channel blocker (15).

Prophylactic Medications in primary care:
Lack of patient knowledge about their disease, creates a barrier when initiating Urate lowering therapy. Patients see Gout as an acute disease with intermittent flares, rather than a chronic, progressive disease. Educating patients at diagnosis, discussing their risk factors, explaining that it is a lifelong condition and the role of medications in lowering their serum urate levels and thus preventing long term complications, will help patients in adherence to their treatment (7,16).

When to offer Urate lowering therapy (ULT):
NICE recommends offering ULT using a treat to target approach, in those with multiple gout attacks, chronic kidney disease stages 3-5, those with tophi, on diuretics and those with chronic gouty arthritis (7).

2020 American College of Rheumatology guideline for the management of gout strongly recommends initiating ULT for those with more than 1 subcutaneous tophi, evidence of radiographic damage attributable to gout or more than or equal to 2 gout flares per year (17).

ULT should be initiated with a treat to target strategy, aiming for serum uric acid levels below 360 micromol/L or 6 mg/dL, but consider a lower target serum urate level of 300 micromol/L for those with gout, who have tophi or chronic gouty arthritis (7).

Initiating Urate lowering therapy can precipitate acute gout attacks. Hence it is recommended to use prophylaxis against these by using either NSAID's (along with PPI cover) or Colchicine cover for 3-6 months until serum urate target levels are reached. This will help patients' compliance in lifelong treatment (7,18,19).

NICE recommends Allopurinol and Febuxostat as first line prophylactic agents. These drugs should not be stopped during an acute attack (7).

Allopurinol:
Allopurinol is a xanthine oxidase inhibitor-an enzyme involved in the production of uric acid. It is one of the first line prophylactic medications used in gout. It should be initiated at a dose of 100mg/day, with a gradual 50-100mg increments every 4 weeks, till target serum urate levels are reached. The usual dose is 100- 600mg, with a maximum dose of 900mg. It should be used with caution in those with renal impairment. In certain ethnic populations like Han Chinese, Thai and Korean, it is common to have HLA-B*5801 allele. Such patients develop allopurinol hypersensitivity syndrome, steven johnson syndrome/ toxic epidermal necrolysis, which can be fatal. Allopurinol should be avoided in such people (7,20).

Febuxostat:
Febuxostat is a non-purine xanthine oxidase inhibitor. It is recommended at a dose of 80mg once daily, slowly titrated up by 2-4 weeks to 120mg daily, until target serum urate levels are reached. It is not recommended in those with ischaemic heart disease and congestive cardiac failure. If hypersensitivity reactions occur, it should be stopped straight away (7,11).

Other medications like probenecid, sulfinpyrazone, pegloticase, lesinurad are available to use in secondary care.

When to refer to secondary care:
Most cases of gout are managed in primary care. However certain patients mentioned below, need secondary care referral: (7)

a) When the diagnosis is uncertain
b) When the patient is intolerant to the usual medications or does not respond to them.
c) When treatment is contraindicated.
d) In cases of CKD stages 3b to 5.
e) When a patient has an organ transplant.

Conclusion

Gout is a common and well-studied type of inflammatory arthritis. We, as primary care physicians are best placed to manage gout, help patients better understand their disease. Accepting a chronic disease diagnosis and taking lifelong medications, can be daunting for patients. By educating and empowering patients on the relationship between their gout attacks and cardiovascular risks, we can help them adopt a healthy lifestyle and prevent further complications.

We advocate the importance of patient education by giving patients all the information they need to know about their disease at the time of diagnosis. We also recommend early initiation of urate lowering therapy among at risk patients by primary care physicians and maintaining a treat to target approach until target serum urate levels are reached. To help better compliance, it is advisable to start prophylaxis against acute gout flares while initiating ULT. It is imperative to utilise this opportunity to screen for all other cardiovascular diseases, to treat patients in a timely manner and prevent longer term complications. It is also advisable to check serum urate levels annually, to make sure targets are being met.

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