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Objective To review the epidemiology, pathophysiology, clinical manifestations, diagnosis, and treatment of gouty arthritis of the hand and wrist, with a focus on the surgical aspects.

Data sources and extraction Electronic databases including MEDLINE, PubMed, and the Cochrane library were searched with the key words of "gouty arthritis", "hand", "wrist", and "surgical".

Study selection A total of 55 articles were selected for inclusion in this review.

Data synthesis There is no existing study for the overall prevalence of gout in Asia, though one study showed that it was 3.1% in Taiwan. Its pathophysiology entails hyperuricaemia, trauma, lower temperatures, and previous diseases. Gouty arthritis of hand and wrist presents as acute wrist pain, subcutaneous or peritendinous tophi, tenosynovitis, entrapment neuropathy, tendon rupture, or even bone destruction. Demonstration of negatively birefringent crystals in the absence of organisms and a normal white cell count in synovial fluid confirm the diagnosis. Medical treatment including non-steroidal anti-inflammatory drugs, colchicines, allopurinol, uricosuric agents, and lifestyle modifications remain the mainstay of treatment. Surgical treatment options for tophaceous gout involve decompression by aspiration, incision and drainage, tenosynovectomy, shaving procedures, and complex surgical approach.

Conclusion While medical treatment remains the mainstay of treatment for gouty arthritis of the hand and wrist, 5% of patients may not respond. In this group, surgery is often performed in advanced stages, but yields less-than-satisfactory outcomes. Gouty arthritis is difficult to treat when it starts to cause stiffness and deformities. Although more studies are needed to evaluate the outcomes, the authors suggest that one possible solution is pre-emptive surgery.

Introduction

Gout is an ancient medical disorder recognised since the time of Hippocrates.¹ Its prevalence in western populations was 1.4%.² The overall male-to-female ratio was 3.6:1. The prevalence peaked in men between the ages of 75 and 84 years (7.3%), while in women its prevalence continued to rise beyond the age of 85 years (being about 2.8%). The epidemiology of gout is difficult to quantify precisely as there are variations in methodology between studies, especially in terms of case definitions. One paper concluded that the prevalence of gout in Taiwan to be 3.1%,³ but this cannot be generalised to Asia. Gouty arthritis is an intense and painful inflammatory response elicited by subcutaneous or bursal deposits of monosodium urate (MSU) crystals, which commonly manifest as a monoarticular arthropathy of the first metatarsophalangeal joint, better known as podagra. In contrast to podagra, only a few articles review gouty arthritis of the hand and wrist. This paper reviews the less prominent, but by no means less important, involvement of gouty arthritis in the hand and wrist, with a focus on currently available surgical interventions.

Methods

Multiple online electronic databases including MEDLINE, PubMed, and the Cochrane library were used for article collection. The key words searched included: "gouty arthritis", "hand", "wrist", and "surgical". Articles published in English in the past 60 years

Key words

Anti-inflammatory agents, non-steroidal;
Antirheumatic agents; Gout/surgery;
Prevalence

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were included. Epidemiology, pathophysiology, clinical manifestations, diagnosis, and treatment were reviewed. Bibliographies of chosen articles were screened for additional relevant articles not discovered through database searches.

Pathophysiology

Hyperuricaemia is an important component in the development of gout. It is defined as a serum uric acid level of more than 7.0 mg/dL (0.42 mmol/L) in men and 6.0 mg/dL (0.36 mmol/L) in women.⁴ One study showed that 18.8% of patients with hyperuricaemia develop gout in 5 years. The only predictor of gout at baseline was the uric acid level, but other contributing factors included alcohol consumption, diuretics use, and excess weight gain; all of which increased the risk of a gouty attack in patients with hyperuricaemia.⁵

Hyperuricaemia can be the result of overproduction or underexcretion of uric acid. For the production of uric acid, the source of urate either may be exogenous (ingestion of purine-containing food) or endogenous (synthesis of purine nucleotides). For excretion of uric acid, during evolution, there was loss of the enzyme, uricase, which oxidised uric acid (to a highly soluble compound, allantoin).⁶ As a result, renal excretion became an important pathway of uric acid elimination; 80 to 90% of the patients with hyperuricaemia or gout are underexcretors.⁷

Other contributing factors besides hyperuricaemia include: trauma, lower temperatures, and previous diseases.⁸ The first metatarsophalangeal joint is often affected in gout, partly because it is a site of mechanical stress and prone to minute trauma. Lower temperature favours crystal deposition.⁹ This explains why the helix of ear and foot are often affected. Previous disease, such as osteoarthritis in the fingers, can increase the chance of crystal deposition in the previously diseased joint.⁸

The mechanism by which MSU crystals cause gouty arthritis entails two phases. The first requires phagocytic cells such as monocytes to internalise MSU crystals and activate c complex called inflammasome, followed by the release of interleukin (IL)-1 β . The second involves an inflammatory response driven by IL-1R, resulting in the production of chemokines and inflammatory mediators. All of these eventually result in a neutrophil influx into the joints, which is the characteristic of gouty inflammation.¹⁰

There are four different phases in gout. They include: asymptomatic hyperuricaemia, acute gouty arthritis, intercritical gout, and chronic tophaceous gout.¹¹ During the intercritical gout period, the joints appear to return to normal between attacks.¹² The disease progresses to chronic tophaceous gout if there are excessive MSU deposits around the tissues,

最後防線？手部和手腕痛風症的手術治療

目的	回顧有關手部和手腕痛風症的流行病學、病理生理學、臨床病徵、診斷和治療方法，討論特別集中在手術治療方面。
資料來源及研究選取	使用以下關鍵詞搜索 MEDLINE、PubMed 及 Cochrane Library 資料庫發表的文獻：「痛風症」、「手部」、「手腕」及「手術」。
資料選取	共 55 份學術文章被納入研究範圍。
資料綜合	未發現有關亞洲人痛風症總患病率的文獻，只有一研究顯示台灣的痛風症患病率為 3.1%。痛風症的病理生理學包括血液尿酸含量過多、創傷、較低的溫度和過往的患病紀錄。臨床病徵有急性手腕疼痛、皮下或腱附近的痛風石、腱鞘炎、受壓性神經病變、腱斷裂，甚至損害骨組織。當發現患者在關節液中出現負性雙折光尿酸鹽結晶，沒有微生物和白血球處於正常水平，便可確診為痛風症。藥物治療包括非類固醇類消炎鎮痛藥、秋水仙鹼、別嘌醇、促進尿酸排泄藥，以及培養良好的生活習慣。手術治療方法包括引流以達至減壓、切開引流、腱鞘切除術、切削技術和進行較複雜的手術等。
結論	雖然藥物治療仍然是治療痛風症的主要方法，但有 5% 的病人對藥物治療並沒有反應。在這群病人中，手術治療往往只在痛風症的後期使用，導致手術的結果不理想。從我們的經驗觀察到，一旦痛風症引致關節僵硬和畸形，便很難治理此病。縱然仍須進行更多研究來評估痛風症手術治療的效果，我們認為其中一種改善治療效果的方法是盡早為痛風症患者進行手術治療。

and usually develops after 10 years or more of acute intercritical gout.¹³ Crystallographic analyses show that tophi consist of macroscopic collections of MSU crystals.¹⁴

Clinical manifestations

Gouty arthritis of the wrist usually manifests as acute wrist pain and subcutaneous or peritendinous tophi.^{15,16} It may progress to destructive bone lesions and ligament disruption. It is usually painful with the presence of acute tophi. It is believed that the pain in a tophaceous deposit is caused by the increasing tension following rapid deposition of urate crystals in a semi-fluid state.¹⁷ The tophi are often associated with degenerative changes of the involved joint.¹⁸

Periarticular or articular tophi (Fig) in the fingers cause limitation of finger motion. Mallet finger, boutonniere and hyperextension deformities may result when there is loss of balance between the flexor and extensor-tendon mechanisms.¹⁹ The frequency of tophaceous gout in carpal tunnel syndrome was reported to be 0.6%.²⁰ The median



FIG. Gouty tophi in the thumb

nerve is compressed due to increased volume of carpal tunnel contents by the tophaceous material.²¹ Tendon involvement can lead to tenosynovitis, entrapment neuropathy, or even tendon rupture.²² Involvement of tendons can also present as pain and local warmth, which is difficult to distinguish from infection.²³

Diagnosis

Arthrocentesis and synovial fluid analysis remains the gold standard for diagnosis of gouty arthritis. Pathological samples obtained from biopsy of the synovium, tendon, ligament, and tophi should be transported in alcohol instead of formalin so as to prevent MSU crystal degradation.²⁴ Gouty arthritis is confirmed with the presence of negatively birefringent crystals, an absence of organisms, and a white cell count in synovial fluid within normal ranges.²⁵

Treatment

Medical treatment

In the acute attack, rest and topical ice are effective.^{26,27} Oral non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine are the drugs used most often.¹³ Oral colchicine is the conventional drug for gout and is most effective during the first 12 to 24 hours of a gouty attack.¹³ A recent study²⁸ showed that low-dose oral colchicine (1.2 mg followed by 0.6 mg 1 hour later) is as effective as high-dose oral colchicine (1.2 mg followed by 0.6 mg every hour for 6 hours), but gave rise to lower rates of diarrhoea, vomiting, and other side-effects. Although NSAIDs are the drugs of choice in gouty arthritis in patients without other co-morbidities, they should be used cautiously in patients with peptic ulcer disease,²⁹ renal disease,³⁰ and in those receiving anti-coagulants.¹³ Intra-articular and systemic corticosteroids are other options.^{31,32}

Lowering serum urate concentrations to levels of less than 6.0 mg/dL (360 µmol/L) may prevent gout and reduction to less than 5.0 mg/dL may be necessary to resorb tophi.³³ Lifestyle and dietary modification including reduction of alcohol intake,³⁴ weight reduction in men,³⁵ decreased intake of purine-rich foods of animal origin,³⁶ and increased dairy food consumption can lower serum urate level.³⁷ In 2006, the European League Against Rheumatism³⁸ recommended that allopurinol should be started at a low dose (100 mg daily), especially for those with renal impairment. The dose should be increased by 100 mg every 2 to 4 weeks if required. Uricosuric agents, such as probenecid, are used in patients with normal renal function, but 4 times daily administration is advocated for full therapeutic efficacy.³⁹ A new non-purine xanthine oxidase inhibitor,⁴⁰ febuxostat, has comparative efficacy to allopurinol (40 mg daily of febuxostat is comparable to 300 mg daily of allopurinol).⁴¹ A newly developed uricase attached to a polyethylene glycol moiety is currently undergoing trials. This drug breaks down uric acid, converting it to allantoin, which is highly soluble. It can be used as a 'debulking' agent in severe tophaceous gout, but its residual immunogenic properties can render the disease refractory to ongoing use.⁴²

Surgical treatment

Despite the use of optimal medical treatment, 5% of patients may not respond and some may progress to tophaceous stage.⁴³ The traditional indications for surgery are^{15,19}: (1) functional, which includes excision to allow wearing of clothing and gloves, restoration of motion, and joint stability; (2) symptomatic, which includes reduction of pain, decompression of nerves, control of infection, discharging sinus, and skin ulceration; and (3) cosmetic restoration, especially for tophaceous gout in the hand and wrist.

Although various methods can be used to operate on patients with gouty arthritis in the hand, some general principles are the same. The tissues, especially the skin overlying a large subcutaneous tophi, should be handled gently because it may have impaired vascular supply.⁴⁴ Sharp dissection and curettage are commonly employed for most infiltrative lesions involving tendon and joint capsules in the hand. Most of the time, the tendons can be kept intact by just shaving the tophus down to the original size of the tendon, followed by medical management which causes slow absorption of the remaining tophus.¹⁵ Every effort should be directed at preservation of hand function. However, if there is advanced tophaceous infiltration of the tendon, resection followed by primary repair or subsequent tendon transfer can be performed.⁴⁵

If the involved areas are clean and have intact covering skin, primary closure can be achieved

following debridement, as the wounds are likely to heal well.⁴⁶ The wounds should be closed with a minimal number of interrupted subcutaneous sutures, since a large number of subcutaneous sutures jeopardise the network of blood vessels just beneath the skin overlying any tophus.⁴³ Frequent irrigation of the wound in the operation is recommended. Not only does this wash away urates, it also prevents drying of the wound and tissue damage. Furthermore, the crystals are moderately hygroscopic and tend to dry out the surrounding tissues during curettage.⁴³ Since the solubility of urate has a two-fold rise between 25°C and 37°C,⁴⁷ warm normal saline irrigation can theoretically decrease the rate of clogging, and therefore increase the efficiency of urate removal.

The method chosen for removal of tophi depends on their consistency. For soft and fluctuant tophi, Cassagrande¹⁵ recommended decompression by aspiration or incision, whilst drainage was the best option. This is because primary closure of the fluctuant areas by surgery delays healing and infrequently may exacerbate gout.

For hard tophi, surgery is often needed for removal. Surgical procedures used to remove tophaceous deposits involve tenosynovectomy, shaving, and other complex surgical approaches.

Tenosynovectomy involves debridement of tophi, and release of relatively unimportant but heavily infiltrated tendon sheaths. For important tendon sheath, removal can cause bow-stringing of the corresponding tendon. However, the tendon could be shaved to improve gliding between the residual tendon and the tendon sheath. It is indicated for tendons that are heavily infiltrated by the tophaceous substance and loss of active digital motion but without overlying skin ulcerations. The procedure can rapidly improve the range of motility with a small chance of postoperative complications. Its limitation is that it is associated with a significant risk of tendon adhesions, which may be reduced by early physiotherapy.⁴⁸ The shaving procedure involves a shaver that performs oscillating movements at high speed. This is faster and more efficient than manual curetting movements. In a study of 32 patients, each tophaceous lesion was removed in less than 15 minutes with uneventful postoperative recovery, except that two patients endured recurrent acute attacks of gouty arthritis that were controlled by colchicine and analgesics.⁴⁹ The authors made no mention of any flexor tendon involvement nor did they state whether the procedure was feasible with carpal tunnel syndrome. The shaving procedure is indicated if tophaceous deposits are not excessive and in the absence of significant skin ulceration.⁴⁸ This less-invasive technique tends to spare the skin. Its limitation is that it cannot be performed where

there are important nerves and tendons, (eg proximal interphalangeal finger joints), since it is a blind procedure and the chance of injuring surrounding structures is relatively high. Based on their experience of 29 cases, Tripoli et al⁴⁸ recommended that a complex surgical approach should be the first-choice operation for gouty tophi. This involves an 'S-shaped incision' overlying the tophaceous deposits and excision of the gouty tophi after identification of important structures. Its advantages are: better exposure of the important structures, better range of motion and cosmesis, less pain, and a prolonged disease-free period. From their experience, they recommend this complex surgical approach as the treatment of first choice. The indications include: unremitting single joint pain uncontrolled despite drug treatment, infection, significant deformity, and joint stiffness. The limitation of this approach is that it needs considerable expertise. The handling of soft tissue entails careful removal, while not compromising skin circulation. Preoperatively, the patient must be educated regarding postoperative management to facilitate an improved outcome. Postoperatively, wound and joint pain are common but should not be allowed to hinder mobilisation exercise, lest the mobility of hand becomes much worse. Moreover, postoperative wound and joint pain are temporary and after wound healing its extent diminishes to levels less than those in the preoperative state.

Gouty tophi also occur over interphalangeal joints. In tophaceous gout involving proximal interphalangeal joints, tophectomy and extensor mechanism reconstruction are performed if medical treatment fails. Tophectomy should be carried out earlier in patients who are allergic to allopurinol or who have renal disease.⁵⁰ For tophaceous gout involving the distal interphalangeal joint, Mudgal¹⁸ recommended aspiration through neighbouring uninvolved skin, in order to overcome delayed wound healing. Ideally, arthrodesis should be considered for persistently symptomatic and unstable distal interphalangeal joints.

Hydrosurgery was described by Vanwijck et al⁵¹ in 2010. It removes target tissue and creates a smoother, less irregular wound surface, making it more feasible to receive a skin graft. Its pressurised pulsatile lavage effect is believed to reduce the bacterial load and prevent the diffusion of microbial contaminants deeper into the wound.⁵² Lee et al⁵³ reported two cases of subcutaneous tophaceous gout on the lateral malleolar area with successful skin graft and local flap coverage after hydrosurgery. Studies have shown that the hand usually has better wound healing than the foot, due to its better blood supply.⁴⁹ The authors of that report therefore believed that this technique produces better results when applied to the hand, despite the paucity of studies to support this contention.

Discussion

Medical treatment remains the mainstay for managing gouty arthritis of the hand and wrist. It is very effective, especially in those with occasional attacks. In patients with repeated gouty attacks and tophi, urate-lowering therapy is indicated. However, about 5% of the patients may not respond and this group may present to orthopaedic surgeons under three categories: infection of the affected area; poor hand function (operation requested to improve function); or intolerable deformity (operation requested for cosmesis). When infection is present, the primary goal is to control the infection, so the vital structures including skin and tendons in the hand may have to be sacrificed. However, severe infection is uncommon in tophaceous gout, because tophaceous material is generally regarded as bacteriostatic.¹⁹ Regarding patients with deformity and poor hand function, they usually present to the orthopaedic surgeons late, and the disease is so advanced and severe that vital structures in the hand may need to be removed. In advanced gout with large tophaceous deposits, there is high risk of delayed postoperative wound healing because of the poor circulation to overlying skin. Inadequate removal of uric acid deposits causes uric acid to seep through the wound, which also contributes to delayed wound healing. Since the tophaceous deposits in advanced disease are large, adequate removal often entails removal of affected vital structures including tendons. As a result, there may be no improvement of hand function after operation for advanced disease. On the other hand, cosmesis cannot be restored without an operation. The orthopaedic surgeons therefore always face a dilemma in deciding whether or not to operate on these patients. In mitigating this dilemma, in this group of patients there is a need for the timing of surgery to be reconsidered.

The hand and wrist are functionally very important for humans to perform daily activities. Although the traditional indications for surgery in gouty arthritis involve restoration of function, symptomatic relief and cosmetic restoration, the authors propose that a fourth indication, namely 'pre-emptive surgery', should be added. For patients who have repeated attacks of gouty arthritis, a few tophaceous deposits and mild stiffness of the joint but failure of medical treatment, there is a high chance of disease progression. Operations performed after bone, joint, tendon or skin involvement, have a high morbidity, especially delayed wound healing. Moreover, sometimes tophi can grow silently for years without episodes of acute gout,¹² which gives a false impression that the disease is controlled. Thus, one study showed that there is frequent hand function impairment in patients with chronic tophaceous gout, as the deposits

may damage the joint, causing synovitis and/or a mechanical obstruction to joint movement.⁵⁴ Such gouty arthritis may ultimately require a debulking operation. The authors recommend that once joint stiffness has developed as a result of gouty deposits infiltrating into the tendon and joint area, debulking surgery should be performed. This may retard progress of the gouty arthritis and decrease the chance of gouty tophi eroding vital structures in the hand and wrist. Otherwise (in advanced disease), it might only be possible to restore minimal hand function by surgery.

Surgery for advanced stages of gouty arthritis has a lot of disadvantages. Curettage and debulking of large tophi is time-consuming. Besides, the crystals are hard and there is fibrotic tissue around the tophi, making manual curettage inefficient. In addition, large tophi cause local ischaemia to surrounding skin. As a result, there is a risk of necrosis of the overlying skin, if skin incisions are inappropriate.⁵⁵ Kumar and Gow⁵⁶ found that in surgery for gouty tophi, 53% of patients experienced delayed wound healing. This study was quoted in the literatures as the major reason of reserving surgery for the advanced-staged gout. However, prior to surgery, the majority of their patients (67%) had infected or ulcerated tophi. We believe that if earlier surgery were to be performed, these patients would not have had infected or ulcerated tophi, and resulted in better postoperative recovery. The advantages of pre-emptive surgery include better wound healing as there is no skin infiltration. The postoperative hand function will also be better as there is less tendon infiltration.

Throughout the years, various surgical techniques for gouty arthritis, including tenosynovectomy, shaving procedures, a complex surgical approach, and hydrosurgery have been developed. All these aim to remove the gouty deposits more efficiently. Yet the results of surgical management of gouty arthritis cannot improve if the operation is performed at suboptimal time.

One potential selection bias for this review is that it only involved literature covering the past 60 years. Earlier literature was not reviewed. However, most of the principles discussed here only appeared in later review articles. Also, with rapid developments in the field of medicine, newer evidence could have more impact on our clinical practice.

Finally, while a lot of effort has gone into the development of surgical techniques, optimal timing for such operations should be reconsidered. Earlier operations for gouty arthritis can reduce the technical difficulties and improve the functional outcomes. With the ideas proposed in this article, it is hoped that surgery will not become the last defence in gouty arthritis, as earlier surgery may well improve outcomes.

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