Treatment of tophaceous gout: When medication is not enough

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\section*{A R T I C L E  I N F O

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\section*{A B S T R A C T

Objectives: To review the literature concerning surgical intervention of tophaceous gout and propose clinical circumstances for when it may be considered.

Introduction: Tophi develop in approximately 12–35\% of patients with gout. Tophaceous disease is usually preventable given the availability of effective urate lowering therapies (ULT) including allopurinol, febuxostat, probenecid, lesinurad, and pegloticase. Despite medical therapy, there remains a subset of patients who develop significant complications of tophi including infection, ulceration, and entrapment neuropathy. Tophi in close proximity to joints can cause joint instability, severely limited range of motion, and significant functional impairment. For the rare circumstance when a tophus is causing an urgent complication or if a patient has a contraindication to all available ULTs, surgery may be an appropriate option. This review summarizes the published experience with surgical interventions for tophaceous gout and offers recommendations for its consideration.

Methods: Using Medline and Google Scholar, all available series of surgery for tophaceous gout were reviewed.

Results: Overall, 7 published surgical series were identified. In all, 6 of these 7 series were published between 2002 and 2014. The reported outcomes of surgical interventions for tophaceous gout were generally positive without major post-surgical complications.

Conclusion: Although medical therapy with ULTs should be the first-line approach to tophaceous gout, surgery should be considered for the rare patient with impending or severe, debilitating complications including infections, entrapment neuropathy or those at risk for permanent joint destruction. In these selected clinical circumstances, surgical intervention for tophaceous gout may be appropriate.

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\section*{Introduction

Tophaceous gout is present in approximately 12–35\% of patients \cite{1-4}. The presence of tophi have been associated with significant morbidity including poor quality of life and increased healthcare resource use \cite{1}. Depending on their anatomic location, tophi have the potential to cause irreversible joint damage with bony destruction \cite{5,6}. Tophi can also entrap nerves causing compressive neuropathy, such as carpal tunnel syndrome \cite{7,8} or radiculopathy \cite{9}. Superficial tophi are also susceptible to infection, especially if the overlying skin is ulcerated.

Urate lowering therapy (ULT) is widely accepted as the initial treatment for tophaceous gout \cite{10}. ULT should be advanced in a step-wise, “treat-to-target” approach. A common goal is a target serum urate of less than 6 mg/dL as this level of uric acid suppression has been associated with increased functionality of joints, a decrease in the number and size of tophi, and improved overall control of symptoms \cite{11,12}. Even lower levels of serum urate may be necessary to prevent attacks of gouty arthritis and tophus resolution \cite{10,13}.

Current guidelines recommend beginning therapy with a single agent xanthine oxidase inhibitor (XOI), either allopurinol or febuxostat, with dosing adjustments to suppress the serum urate level to less than 6 mg/dL; levels of uric acid closer to 5 mg/dL may be necessary if attacks of gout continue \cite{10}. For refractory or tophaceous gout (e.g., persistently elevated serum urate and symptoms despite optimized management with oral ULTs), the recombinant uricase enzyme pegloticase is now an option \cite{10,14}. However, the utility of this medication has been limited by allergic reactions, cost, and the development of antibodies that diminish its effectiveness \cite{15}.

ULT is a beneficial treatment for the majority of patients suffering from tophaceous gout, however an estimated 100,000–300,000 of the nearly 3 million cases of gout in the United States...
are not adequately managed with current therapies [16,17]. Many gout patients have complex co-morbidities and medication profiles, making medical management challenging and even prohibitive in some circumstances. Barriers to adequate medical treatment include delayed medication prescribing, inadequate medication dosage [18] and non-adherence [19]. Furthermore, it takes months to years for tophi to resolve even with appropriate medical treatment [11]. The duration of time it takes ULT to resolve tophi significantly prolongs patient morbidity associated with tophi, and likely increases the chance of complications such as permanent joint destruction or associated infections. Finally, treatment for tophaceous gout may be deferred altogether if a more severe or life threatening medical condition takes precedence.

The surgical treatment of gout is an ancient remedy, and before effective medical treatment, surgery was frequently performed. It was most commonly recommended for cosmetic reasons or for the removal of large deposits of sodium urate (“debulking”) [20]. Hippocrates describes the relief of severe gouty pain by burning tophi with crude flax. Several centuries later, Pare surgically opened tophi and then rubbed them with hermodactyl (colchicine). The first descriptions of excision of hard tophi and amputation date from the late 19th and early 20th centuries [21]. Fortunately, we now understand that tophaceous gout results from prolonged hyperuricemia and that medications to lower uric acid are usually effective.

Historically, Straub et al. [21] classified indications for surgery into several categories including functional and symptomatic. Surgery was considered appropriate in the following circumstances: when tophi interfered with normal tendon or joint function, caused skin necrosis or ulceration (or when these complications seemed imminent), caused symptomatic nerve compression, or caused joint destruction [22]. Uncontrollable local infection or sepsis were considered the most compelling surgical indications for tophaceous gout [23].

Though controlled trials comparing medical and surgical therapy are lacking, surgery can potentially restore function faster than medical therapy and prevent complications in some individuals with persistent tophi. However, in considering surgical intervention for tophaceous gout, it is often challenging to balance these potential advantages against the risks associated with surgery, especially poor wound healing and infection.

In general the surgical approach is determined by tophus consistency and degree of joint involvement (Table 2). For infiltrative tophi involving the joints or tendons, sharp debridement and curettage is preferred. Tendons seldom have to be sacrificed in this process; rather, debridement of the tophus to restore the normal appearance of the tendon will allow for a return of the normal gliding function of the tendon. Copious irrigation with warm saline solution not only aids in mechanically removing tophi but also prevents drying of the tissue which is common in the setting of crystal deposition.

Here, we have reviewed the rather limited published experience of surgical treatment of tophaceous gout. As summarized below, this literature consists of small cases series with generally positive outcomes.

Methods

We performed a literature search using the PubMed and Google Scholar databases to identify medical literature regarding surgery for tophaceous gout. The search was limited to publications in English from 1950 through 2015. The database search was conducted using the following terms: tophaceous AND gout AND surgery, or “Surgical case series” AND “tophaceous gout.” Articles were excluded for the following reasons: duplicate, nonrelevance, or when neither an abstract nor the full text were available.

Results

Our database search using the above listed keywords in PubMed yielded 171 articles and Google Scholar yielded approximately 800 articles. No retrospective or prospective clinical trials were identified. In all, 7 retrospective surgical case series were deemed appropriate for review. The results of individual studies are summarized in Table 1. In total, 6 of the 7 case series were published between 2002 and 2015. A total of 317 patients were included in these 7 studies. Anatomic regions varied and included hands, wrists, elbows, knees, ankles, and feet. Indications for surgery were most commonly reported to be sepsis control, pain control, and functional impairment. The most common surgical techniques were arthroscopic shaver and open tophectomy. The reported outcomes were generally positive with restoration of function while the most common adverse outcome was delayed wound healing.

Kumar [23] conducted a retrospective study on the results and complications associated with surgery for tophaceous gout over a 6-year period. The major indication for surgery was sepsis control secondary to infected and ulcerated tophi (51% of patients), followed by mechanical problems as a result of tophi on the foot, elbow, or hand (27% of patients). Only 4% of patients underwent surgery for pain control. Prior to surgery, hyperuricemia was present in 68% of patients but 12% did not have urate levels checked. In all, 31% of patients were taking allopurinol. The major complication of surgery was delayed wound healing occurring in 53% of patients. The majority of patients with delayed wound healing (67%) had an infected or ulcerated tophus prior to surgery. The remaining 47% of patients were completely healed 1 week after surgery. A total of 3 patients had to undergo digit amputation that resulted in only minor debility.

Lee et al. [24] enrolled 32 patients with chronic tophaceous deposits involving the hands or elbows. Using a soft tissue shaving technique he found that there were no major complications in any of the 32 patients. Overall, 80% of patients had the operation during the inter-critical phase, and 2 patients suffered a recurrent attack of gouty arthritis within 12 h after the operation. The acute gouty attack was treated with NSAIDS and colchicine. Swelling at the operative site usually lasted about 10 days. Medical therapy and serum urate levels were not noted in this study.

Lee et al. [25] in a follow-up, retrospective study of 147 patients using the shaver technique showed that patients with positive wound cultures, renal impairment, elevated CRP, white blood cell count greater than 10,000 cells/mL, and lower extremity tophi had significantly longer hospitalizations than patients without these features. The data from this study suggested that if surgery was performed prior to the development of overlying skin infection or infection of the tophaceous mass itself, there tended to be fewer post-surgical complications and shorter hospitalizations. No serum urate measurement or medical therapy was reported in this study. The authors emphasized that use of the shaver technique was associated with only minor surgical complications.

Wang et al. [26] conducted a case series consisting of 28 male patients with hyperuricemia and repeated attacks of gouty arthritis of the first MTP joint. In all, 15 patients chose to undergo arthroscopic intervention followed by post-surgical urate lowering therapy while the other 13 patients were treated with medication alone. Exclusion criteria of this study included symptoms of an acute gout attack or possible infections including inflamed joints, ulcerated skin, or a draining sinus. The follow-up period was 3.9 years in group 1 and 2.4 years in group 2. Although the authors state that patients were given adequate treatment to control hyperuricemia, all of the patients in the medically treated group had serum uric acid levels above 6 mg/dL at follow-up. Both the medical and surgical group had significant improvement in the