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Diagnostic Strategies for Gout

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Abstract

Gout is a complex form of arthritis and is commonly seen and treated by the primary care provider. When a swollen, red, inflamed metatarsophalangeal joint is seen on exam it is easy to jump to the conclusion of a diagnosis of gout. A single clinical finding of gout is not enough information to diagnose gout. It is important to know what type of fluid is causing the inflamed joint in order to treat it appropriately. A literature search was conducted using the Harley French Library at the University of North Dakota. The author began the search by using two of the most familiar literature databases in health sciences, Medline (PubMed) and CINAHL. The search was narrowed by using Medical Subject Headings (MeSH) terms, limiting the search to RCTs, meta-analysis, systematic reviews, and dates of publication within the last eight years. The MeSH search included the terms "gout and synovial fluid." The literature continues to affirm that a synovial joint aspiration is the gold standard for diagnosing gout. It is an immediate procedure that primary care providers should be performing if gout is suspected and can be used to diagnose gout during the intercritical period of the disease.

Background

Gout indicates a group of disorders that is related to hyperuricemia and is the main cause of inflammatory monoarthritis (Cruz-Knight, 2014). Hyperuricemia is necessary for the development of gout but it is only one contributing factor to the diagnosis. It is a disorder that is characterized by monosodium urate (MSU) crystals in tissue (Conway & Schwartz, 2009). The crystals result in acute and chronic arthritis, soft tissues masses called tophi, urate nephropathy, and uric acid nephrolithiasis (Cruz-Knight, 2014). Acute gout attacks can affect more than one joint and it commonly affects the first metatarsophalangeal joint (Schlesinger, 2007). In an acute gouty flare, severe joint pain has a rapid onset and can reach maximal intensity within hours (Rakieh & Conaghan, 2011). The joint or joints that are affected appear to be swollen, red, warm and painful (Rakieh & Conaghan, 2011). Risk factors for developing gout include hyperuricemia, male gender, increasing age, alcohol ingestion, obesity, hypertension, diabetes, metabolic syndrome, diuretics, high purine diet, family history, renal impairment, hypothyroidism, hyperproliferative skin disorders, and surgery or trauma (Cruz-Knight, 2014).

The purpose of this literature review is to examine the current recommendations of diagnosing gout and how this information can be of value to the primary care provider. Currently, the gold standard continues to be the detection of MSU crystals in the synovial fluid by the technique of joint aspiration (Conway & Schwartz, 2009; Courtney & Doherty, 2013; Cruz-Knight, 2014; Dore, 2008; Pascual, Sivera, & Andres, 2011; Rakieh & Conaghan, 2011; Schlesinger, 2007; Wijnands et al., 2011). Although synovial fluid aspiration has been the standard for diagnosis of gout, many providers continue to diagnosis gout based on clinical diagnostic criteria (Dore, 2008). These clinical diagnostic criteria include American Rheumatism Association (ARA) criteria, New York criteria, and Rome criteria (Malik,

Schumacher, Dinnella, Clayburne, & Gilda, 2009). Along with using clinical criteria for diagnosis, many providers evaluate a serum urate level, complete blood count and thorough history and physical exam to make their diagnosis of gout (Malik et al., 2009).

This review seeks to unfold the reasons why providers may not adhere to the current diagnostic criteria for gout, how to diagnosis gout clinically, current recommendations for the diagnosis of gout and strategies for synovial fluid aspiration and analysis.

Case Report

Chief Complaint: Pain and swelling of right great toe

History of Present Illness: J.R. is a 46 year old female that presents today with pain, redness, and swelling to her right great toe. The pain has been occurring for the past four hours and she describes it as a burning sensation. The pain continued to increase in severity and caused her to stay home from work. She currently rates the pain a 5/10 on the pain scale and it is worse with walking. She has not taken any medications for the pain. She has not recently injured her toe that she is aware of. No history of arthritis or joint disease. She denies fever, chills, or drainage from her right great toe. No numbness or tingling to lower extremities. No other concerns expressed.

Past Medical History: Hypertension, Dyslipidemia, Diabetes Mellitus Type 2, Kidney stones.

Past Surgical History: Lithotrispy

Social History: Works as a landscaper and enjoys curling one day a week for activity.

Medications

Hydrochlorothiazide 25 mg oral daily
Lisinopril 20 mg oral daily
Metformin 500 mg oral daily
Simvastatin 20 mg oral nightly
Aspirin 81 mg oral daily

Allergies: No known allergies

Review of Systems

Skin, hair, nails: See HPI.
Throat and Mouth: Patient denies difficulties in swallowing. No nausea or vomiting.
Chest and Lungs: Patient denies any recent respiratory infections. Denies cough, dyspnea on exertion or wheezing.
Heart and blood vessels: Patient denies chest pain, pressure or palpitations.
Gastrointestinal: Patient denies abdominal pain.
Urinary: Patient denies dysuria, frequency or hematuria.
Musculoskeletal: Patient denies any history of arthralgias or myalgias. No change in range of motion to upper or lower extremities. Patient complains of pain to her right great toe.
Psychiatric: Patient is oriented to person, place, and time.

Physical Exam

Vitals: BP 126/78| Pulse 72 |temperature 37.4 C| BMI 29
GEN: Alert and oriented. Verbally responds to questions appropriately.
HEAD: Head is round, symmetrical and atraumatic.
MOUTH and THROAT: Patient speaks clearly with no hoarseness.
CV: Regular, S1 and S2 present, no murmurs/rubs/gallops. Radial pulses moderate and equal bilaterally. Posterior tibial and dorsalis pedis pulses are moderate and symmetrical bilaterally.
RESP: Breathing appears non-labored. Respiratory rate is regular. Lungs are clear in all quadrants. No wheezes/rales/rhonchi/crackles. No presence of retractions or accessory muscle use.
SKIN: Right great toe is swollen, red, and warm to the touch over the metatarsophalangeal joint. There are no drainage or open lesions to lower extremities bilaterally. Capillary refill less than 3 seconds.
MSK: Normal gait, full range of motion to upper and lower extremities. No joint effusions, clubbing or cyanosis.
NEURO: Mood and affect appropriate for situation. Sensation to feet intact. Absence of neuropathy to lower extremities. No depression/anxiety/manic symptoms.

Differentials

1. Gout
2. Cellulitis
3. Septic joint arthritis

Labs

WBC: within normal limits.
BMP: within normal limits.
Uric acid level: elevated (was above 7 mg/dL)

Diagnosis: Gout

Plan

1. Colchine 1mg followed by 0.5 mg every two hours until absence of symptoms. Educated patient that the main side effects from the medication are nausea, vomiting and diarrhea. If patient unable to tolerate medication, call the clinic and systemic corticosteroid may need to be initiated.

2. Diet: Instructed patient of the importance of a diet low in purine rich foods (such as anchovies, sardines, herring, organ meats, dried beans, peas, gravy, mushrooms, spinach, asparagus, cauliflower, baking or brewer's yeast) and avoid alcoholic beverages. Increase low fat dairy foods, fruits such as cherries and bananas, green leafy vegetables and maintain adequate hydration with water.

3. Follow up in one week for a uric acid level recheck. Return sooner if patient develops a fever, increase in swelling, redness, or drainage to the right great toe.

Literature Review

Many providers understand that synovial fluid aspiration is the gold standard for the diagnosis of gout but still many do not perform the procedure and diagnose gout based on clinical findings (Dore, 2008; Schlesinger, 2007). As gout continues to be one of the most common rheumatic diseases in adulthood, with self reported prevalence in the USA of roughly

3.9 % of adults (8.3 million), it is critical to diagnose the disease correctly and efficiently in primary care (Khanna et al., 2012).

Provider Adherence to Diagnostic Recommendations

Pascual et al. (2011) investigated the shortcomings of the clinical diagnosis of gout and shared that "due to its characteristic clinical features gout was recognized as a distinct condition in the antiquity and was known by physicians through the ages" (p. 162). When MSU crystals were found in an acute inflamed joint, many physicians felt confident in their clinical diagnostic skills that MSU crystal identification was seen as elegant but dispensable (Pascual et al., 2011). This could lead to a missed diagnoses and not properly treating the underlining disease. Their confidence in clinical skills outweighed the recommendations to perform a synovial fluid aspiration for a clear diagnosis of gout.

Dore (2008) points to multiple factors that contribute to providers not performing a synovial fluid joint aspiration to diagnose gout. One factor is the concern that the clinician may have the possibility of a "dry tap" and not be able to pull any joint fluid on aspiration (Dore, 2008). If no fluid is able to be tested, a provider could cause the patient pain with the aspiration without gaining information to contribute to their diagnosis. Other factors include lack of experience in synovial fluid aspiration, lack of experience in evaluation, not enough time to perform the aspiration and limited access to the standard of care using a polarizing microscope for synovial fluid examination (Dore, 2008). These factors may not affect the skilled clinician working in a large facility but could potentially impact the novice provider in a rural community where resources are scarce.

The Clinical Diagnosis

In a clinical scenario where a synovial joint aspiration cannot be completed potentially due to patient refusal, lack of experience by clinicians, or limited access to a polarizing microscope a diagnosis of gout can be made on the basis of typical clinical symptoms and presence of hyperuricemia (Dore, 2008). This may be the case in remote areas of practice or practices that don't regularly treat gout patients. European League Against Rheumatism (EULAR) identifies typical clinical symptoms of gout as a rapid development of severe pain, swelling and redness (Dore, 2008). These symptoms are highly suggestive of crystal inflammation in the joint if it is during an acute gouty attack (Dore, 2008). Even if the patient presents with typical symptoms of gout, there is a chance that a diagnosis may be missed if the synovial fluid is not tested.

EULAR does recommend that in a typical case presentation of gout, as in pain in the great toe with hyperuricemia, a clinical diagnosis alone is reasonably accurate (Dore, 2008). The American College of Rheumatology (ACR) and EULAR endorse that the gold diagnostic standard for gout is the presence of urate crystals on synovial fluid analysis, but if a clinical diagnosis of gout needs to be made there are criteria to make a presumptive diagnosis (Dore, 2008). The criteria include:

> "a careful patient and family history, including questions regarding co-morbid conditions frequently associated with gout (such as hypertriglycemia, diabetes, coronary artery disease, hypertension, and metabolic syndrome) and whether the patient has had previous similar episodes of acute joint pain and swelling in the absence of trauma, thorough identification of all current medication some of which may be associated with hyperuricemia, and thorough physical examination" (Dore, 2008, p. S18).

Other criterion that has been used in the past to diagnose gout as a clinical diagnosis include the ACR criteria, New York criteria, and Rome criteria (Pascual et al., 2011). The clinical ACR criteria have been validated against synovial fluid analysis and were found to have poor sensitivity and specificity (Pascual et al., 2011). ACR testing of sensitivity was 70.0%, specificity 78.8% and positive predictive value 65.5% (Malik et al., 2009). The poor sensitivity and specificity of diagnosing gout based on the ACR clinical criteria should alert the clinician to use other methods of diagnostic criteria. The ACR criteria is defined by having MSU crystals in joint fluid or clinically by having the patient meet six of the following criteria:

> "greater than one acute arthritis attack, maximum inflammation within one day, monoarthritis attack, redness observed over joints, first metatarsophalangeal painful or swollen, unilateral first metatarsophalangeal joint attack, unilateral tarsal joint attack , tophus, hyperuricemia, asymmetrical swelling within a joint on x-ray, subcortical cysts without erosions on x-ray and synovial fluid culture negative for organisms" (Malik et al., 2009, p.23).

In the study of clinical diagnostic criteria for gout that Malik et al. (2009) completed, the New York criteria has a 70.0% sensitivity, 82.7% specificity and a positive predictive value of 70.0%. The New York criteria consists of MSU crystals in joint fluid, tissue, or tophus and is clinically diagnosed by having the patient meet two of the following criteria: "two attacks of painful limb joint swelling, abrupt onset and remission in one to two weeks initially, first metatarsophalangeal attack, presence of a tophus, and response to colchicines-major reduction in inflammation within 48 hours" (Malik et al., 2009, p.23). New York criteria has slightly higher sensitivity and specificity than the ACR criteria but it is still not a reliable method to base the diagnosis of gout on.

The Rome clinical criteria had the highest positive predictive value at 76.9% with a sensitivity of 66.7% and specificity of 88.5% (Malik et al., 2009). The criteria includes the patient meeting two of the following: "painful joint swelling, abrupt onset, clearing in one-two weeks initially, serum uric acid level of greater than seven in males and greater than six in females, presence of tophi, and presence of MSU crystals in synovial fluid or tissues" (Malik et al., 2009,p. 23). If a clinical diagnosis needs to be made, the Rome criteria is the best option for clinicians to follow. The gold standard of a synovial fluid aspiration surpasses the Rome criteria for a clear diagnoses of gout. Efforts are ongoing to potentially allow the diagnosis of gout based on clinical findings but the concern remains that if this were to occur less typical presentations of gout will never be diagnosed and result in weak criteria to be used in a primary care setting (Pascual et al., 2011).

Current Recommendations for Diagnosis Gout

Crystal proven diagnosis by synovial fluid aspiration once required retrieving a fluid sample from the inflamed joint (Pascual et al., 2011). It was then discovered that that MSU crystals can be present with asymptomatic gouty first metatarsophalangeal and knee joints (Pascual et al., 2011). If gout is left untreated, the presence of MSU crystals is constant in joints that have been previously inflamed, which allows the provider to have a precise diagnosis in the intercritical periods of the disease (Pascual et al., 2011). If the patient has been treated with uric lowering treatments, such as febuxostat, the crystals disappear from the joints (Pascual et al., 2011). If a provider is questioning if the patient has gout compared to septic arthritis or osteoarthritis, a diagnosis can be made in the intercritical period of the disease by joint aspiration.

In a large epidemiologic study of the challenges of diagnosing gout Wijnands et al. (2010) discuss that the identification of MSU crystals is considered the gold standard for diagnosis, but its application is difficult in large studies. In several studies multiple approaches have been used to classify patients having gout including ICD-9 codes, Rome criteria, and EULAR criteria (Wijnands et al., 2010). This makes it challenging to clearly study gout, its diagnostics and treatment. Another challenge is that gout is a disease that is typically intermittent, which can limit the ability to use MSU crystals as the gold standard in large studies in order to get an accurate sensitivity, specificity and positive predictive value of the use of synovial fluid joint aspiration in diagnosing gout (Wijnands et al., 2010).

The 3e (Evidence, Expertise, Exchange) Initiative is a multinational collaboration that aims their initiatives at promoting evidence-based practice in rheumatology by developing practical recommendations for providers and addressing clinical obstacles (Sivera et al., 2014). Their objective was to provide evidence based and practical recommendations for diagnosing gout and managing the disorder. They did this by a dissemination of the results of systematic literature reviews on gout. "Experts showed a strong consensus that identification of MSU crystals in a joint fluid sample or in a tophi aspirate is required for a definite diagnosis of gout" (Sivera et al., 2014, p. 330). Since patients are placed on lifelong urate lowering medications, a joint fluid aspiration should be routinely done to confirm the diagnosis of gout (Sivera et al., 2014). They recognized that this may be difficult in some settings and if that is the case, clinical or imaging findings could support a diagnosis of gout (Sivera et al., 2014). Rural clinic settings may be one area where clinical findings are used solely due to the unavailability of imaging. For example, a positive response to colchicine would support a clinical diagnosis of gout. The difficulty in using solely clinical findings is that the provider is unable to distinguish between the

type of crystal arthritis. The 3e Initiative continues to recommend synovial fluid aspiration as the gold standard of diagnosis for gout and a diagnosis solely established on hyperuricemia is not sufficient for diagnosis alone (Sivera et al., 2014).

Ostovic et al. (2010) desired to motivate clinicians to use urgent cytological examination of synovial fluids in order to define a specific diagnosis within arthropathies. They aimed their study specifically at synovial fluid aspiration and obtained 115 synovial fluids by fine need aspiration of patients with a chief complaint of a swollen knee (Ostovic et al., 2010). The exam of the synovial fluids consisted of analyzing volume, color, viscosity, clarity, mucin clot test, microscopic analysis for crystals and tissue fragments, total nucleated cell count, and neutrophil granulocyte percentage with Hemacolor rapid staining (Ostovic et al., 2010). All cytological analyses were completed in one hour of joint aspiration (Ostovic et al., 2010). Crystals were detected in only 12 samples of synovial fluids and all 12 samples identified MSU crystals. The authors were able to diagnose these 12 patients with gout based on MSU crystals (Ostovic et al., 2010). This study is relevant to primary care because it shows the reliability of synovial fluid analysis. It is a test that if performed correctly can be used solely as a diagnostic test for gout. It could lead to a decrease in treatment failure for gout if performed on the initial visit of an acute gouty flare. Ostovic et al. (2010) concluded that urgent cytological analysis of synovial fluid is a simple and reliable diagnostic screening test that is used to differentiate inflammatory and non-inflammatory joint diseases. It should be performed on every patient if gout is a differential diagnosis.

Is synovial fluid aspiration the only diagnostic procedure to diagnose gout? Gruber et al. (2014) sought to compare dual energy CT (DECT), ultrasound, and synovial fluid aspiration in the diagnosis of gout. They recruited 21 patients who presented with clinical symptoms of acute

or chronic gout (Gruber et al., 2014). DECT scans were completed of hands, wrists, feet, ankles, knees, and elbows and ultrasounds were completed of these same joints (Gruber et al., 2014). Joint fluid aspiration was performed in a total of 14 joints (Gruber et al., 2014). The results demonstrated positive MSU crystals by DECT scans in 25 of 37 joints and ultrasound findings were positive in 24 of 37 examined joints (Gruber et al., 2014). In correlating these findings with synovial fluid aspiration, DECT and synovial fluid results correlated 12 of 14 joints (86.5%) and ultrasound and synovial fluid in 14 of 14 joints (100%) (Gruber et al., 2014). Can ultrasound be used interchangeably with synovial fluid aspiration? Although the study points out that ultrasound detected 100% of the gout cases as synovial fluid aspiration, synovial fluid aspiration continues to be a faster, more inexpensive and a precise method to diagnosis gout. The study concluded that DECT can potentially result in some false-negative findings but can be a helpful examination in the assessment of patient with gout (Gruber et al., 2014). DECT may be helpful if joint aspiration and ultrasound are not available to the clinician but is a costly method of diagnosing gout. The authors of the study do recommend that ultrasound can be performed in patients with typical clinical presentation of gout to confirm a diagnosis and assert that the gold standard for diagnoses continues to be synovial fluid aspiration (Gruber et al., 2014).

Strategies for Synovial Fluid Aspiration and Analysis

Courtney and Doherty (2013) performed an analysis of the benefits of joint aspiration, steroid injections, and synovial fluid analysis and their use for diagnosis and treatment of various disorders. They addressed the "indications, technical principles, benefits and risks of aspiration and injection of intra-articular corticosteroids, and practical aspects relating to synovial fluid analysis" (Courtney & Doherty, 2013, p. 137). For the purpose of this literature review, the findings on indications for joint aspiration and synovial fluid analysis will be discussed.

Indications for joint aspiration include acute synovitis that can be related to sepsis or crystals in the joint and chronic arthropathy (Courtney & Doherty, 2013). This can include differential diagnoses of inflamed arthritic joint, acute gouty flare, septic arthritis, or inflammation around a joint with unknown origin. The goal of a joint aspiration is to identify the type of crystals present in the joint in order to treat appropriately. If not completed, it may result in incorrect treatment, treatment failure, and an incorrect diagnosis. It is the obligation of the clinician to diagnosis and treat patients based on current recommendations and standards. We are called to do no harm and an inaccurate diagnosis and treatment is doing hard to the patient. This is precisely the reason why clinicians need to be skilled in the procedure of synovial joint aspiration to provide an accurate diagnosis of gout when it is present.

Synovial fluid aspiration can be completed within the office setting and a thin 29 gauge needle is used to allow for arthrocentesis of asymptomatic first metatarsophalangeal joint or a thin 25-29 gauge needle for other small joints with only a small amount of discomfort for the patient (Pascual et al., 2011). In untreated gout, aspiration of the first metatarsophalangeal joint with a 29-gauge needle indicates a definite MSU identification in over 90% of cases (Courtney & Doherty, 2013). Larger gauge needles, such as 21-23 gauge, may need to be used in large joint aspirations or injections (Courtney & Doherty, 2013). Clinicians have the option of using sterile gloves or unsterile gloves when performing the procedure but must understand that a no-touch technique needs to be used if wearing unsterile gloves. Roughly one quarter to one third of providers routinely use sterile gloves when performing a joint aspiration or steroid injection (Courtney & Doherty, 2013). Swabbing the site with alcohol is effective in killing skin flora as is the use of chlorhexidine (Courtney & Doherty, 2013). Clinicians should be comfortable and confident in their aseptic technique for a joint aspiration in order to properly diagnose gout.

Once the synovial fluid is aspirated it is then analyzed using a compensated polarized microscope (Pascual et al., 2011). The compensated polarized microscope is the standard for crystal identification in synovial fluid because it allows for identification of the crystals by their birefringence (Pascual et al., 2011). It is important to note that both MSU and calcium pyrophosphate dehydrate (CPPD) crystals can be distinguished by their morphological characteristic alone using an ordinary light microscope if a polarized microscopy is unavailable (Courtney & Doherty, 2013). The factor that some clinicians have limited access to the standard of care using a polarizing microscope should not be used to defer a synovial fluid aspiration. An ordinary light microscope can be used and even most rural remote clinics should have access to one in their laboratory.

Learning Points

- Synovial fluid analysis for crystal identification is an immediate procedure which allows for diagnosis of gout.
- Clinical diagnosis of monosodium urate in joints can be unreliable especially when clinical features are atypical.
- Compensated polarized microscopy is the current standard for crystal identification, if unavailable, simple polarized light microscopy is a useful tool for identification of monosodium urate crystals.
- Monosodium urate crystals are regularly found in asymptomatic joint of patients with gout permitting for confirmation of the diagnosis of crystal deposition during the intercritical period.

Conclusion

Synovial joint aspiration is the gold standard for the diagnosis of gout. Further research is needed to explore a diagnosis of gout based on clinical findings alone. The danger in diagnosing gout based solely on clinical findings puts patients at risk for an incorrect diagnosis, especially in patients with an atypical presentation of gout. Atypical presentation can include elderly with polyarticular disease that resembles rheumatoid arthritis, patients with benign nodules over multiple joints or patients with tophi located in their elbow and wrist. Classic features of gout such as red, swollen, warm great toe is easier to identify but can lead providers to a quick diagnoses without testing the joint fluid for a clear diagnosis. Synovial fluid analysis is an immediate procedure and should be used in the primary care setting in the diagnosis of gout.

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