

GOUT

G1 Malignant Peripheral Nerve Sheath Tumor Presenting as Tophi in a Patient with Chronic Gout

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INTRODUCTION: Malignancy complicating established tophaceous deposition of gout is a rare occurrence. [2,4,5] Malignancies occurring in gouty tophi as well as mimicking malignancies like soft tissue tumor and/or sarcoma are cited in literature. In this report, we highlight chronic tophaceous gout as a niche for malignancy.

CLINICAL PRESENTATION: V.P. is a diagnosed case of gouty arthritis 20 years prior to admission. Five years prior to admission, he developed multiple masses consistent with tophi at the elbows, knees, and feet. A year prior to admission, there was pain and rapid increase in the sizes of these multiple tophi measuring 2.0 x 4.0 – 4.0 x 6.0 cm masses on the elbows, knees, and metatarsal joints of the feet. A year PTA, biopsy of the left elbow and left lateral knee masses was read as sarcoma, for which the patient underwent radiotherapy. Laboratory tests done at that time, showed metastatic foci on the proximal left radius and ulna by bone scintigraphy, liver by ultrasound and lungs by chest CT scan. 3 months PTA, tophi on dorsum of the feet underwent rapid enlargement. A week before admission, the right foot mass ulcerated, extruding white chalky material, and was bleeding profusely. Biopsy of the mass revealed a malignant peripheral nerve sheath tumor (MPNST). Review of the histologic specimen from the elbow was found to be consistent with tophi.

CONCLUSION: This is the first reported case of the occurrence of malignant peripheral nerve sheath tumor in tophi. The course of the patient showed that the tumor could be missed in this specific setting and delay of diagnosis results in spread of this relatively slow growing yet highly malignant tumor. A high index of suspicion for a malignant process in common and benign settings such as chronic tophaceous gout should be made when there is change in character of the background condition (in this case, gout), i.e., increase pain intensity, persistent continuous pain, bleeding and rapid growth of tophi.

G2 Associated Factors For Allopurinol Hypersensitivity Among Filipinos With Gout

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BACKGROUND: Allopurinol is the most widely-used urate-lowering agent. Although the drug is effective and generally well-tolerated, the literature reports allopurinol hypersensitivity in 2% of the general population. This paper describes the clinical features and possible contributory factors to allopurinol hypersensitivity (AHS) in a cohort of Filipino patients with gout.

METHODS: Twelve patients with AHS were identified among a cohort of Filipino patients with gout seen at the Rheumatology Clinics of the University of Santo Tomas Hospital, in Manila, Philippines from 2001 to 2006. The following data were retrospectively obtained from the medical records of these patients: demographic profile, type of AHS reaction, as well as management and outcome of the hypersensitivity. Also searched for were a family history of gout, history of allergies to other drugs, and co-morbidities including renal failure, hypertension, diabetes mellitus, alcoholism, and urolithiasis.

RESULTS: In a gout database of 320 patients, 12 (9 males) or 3.75% were identified to have AHS. Of these 12 patients, the average age at gout onset was 45.7 ±13.8 years old (range 32-60); 6 patients had tophaceous gout, and 2 had first degree relatives with gout. The hypersensitivity reactions consisted of cutaneous manifestations in 11, of whom 3 were diagnosed with Stevens Johnson syndrome and 1 with fixed drug eruption (FDR). One patient complained of dyspnea (without laryngo/ bronchial spasm) and paresthesias which recurred on every allopurinol re-challenge. Associated conditions and underlying factors included 2 each with renal impairment and urolithiasis, 3 with hypertension, 3 with a history of other drug allergies, and 4 with concurrent therapy for tuberculosis. Five patients reported a history of

heavy alcohol beverage consumption. Excluding the patient with FDR, all other patients tolerated successful de-sensitization.

Conclusion: We have described the clinical profile of 12 patients (3.75% of gout patients) with AHS. The possible contributory factors included renal impairment, hypertension, alcoholism, and prior drug allergies. This paper further demonstrates that with the exception of an FDR, majority of patients can tolerate careful allopurinol desensitization.

G3 A Survey of Clinical Management of Gout among Filipino Physicians

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BACKGROUND: Gout is commonly missed out in the clinics. Treatment practices among general care physicians are observed to vary. In effect, control of repeated flares of gout as well as tophaceous deposits has been considered inadequate. This survey aims to determine the practice of physicians from different areas of specialization in the management of gout.

METHODS: A random survey was conducted among different physicians during rheumatology round-table discussions and lecture symposia in Metro Manila and key cities in the Philippines, from April to August 2007. Respondents were asked to answer a set of questionnaires directed along clinical management of gout prior to the commencement of lectures. Respondents' demographic data included sex, age, length of medical practice/level of training, and field of specialization, excluding rheumatology

RESULT: Of the 412 questionnaires distributed, 287(69.7%) were available for evaluation. There were 112(39.02%) internists/family physicians, 18(6.27%) specialists of allied specialties, 117(40.77%) general practitioners, 22(7.66%) medical students/interns, and 18(6.27%) who did not indicate their field of practice. Mean age of respondents was 44.3 ± 12.6 years. Mean duration of practice was 14.6 ± 11.6 years.

Generally, 150(52.3%) respondents would prescribe urate lowering drug (ULD) during asymptomatic hyperuricemia, 94(32.8%) after the first gouty attack, while 18(6.3%) after at least 2-4 episodes of gout flares. For confirmatory diagnosis of gout, 173(60.3%) respondents would want synovial fluid to be examined in patients suspected for gout, 160(55.7%) of them agreed to examine it once. For the management of acute gouty arthritis in an otherwise healthy patient, 136(47.4%) chose colchicine, 57(19.9%) non-steroidal anti-inflammatory drugs (NSAIDs), and 80(27.9%) allopurinol. While for gout patients with renal impairment, 35(12.2%) chose corticosteroid, 57(19.9%) allopurinol, 44(15.3%) NSAIDs. For the dosage and frequency of colchicine during acute gout flare, 45(15.7%) 3x daily for 3 days, 44(15.3%) hourly until pain relief, 46(16%) hourly until abdominal toxicity occurs, 72(25%) until achievement of maximum dose. Ninety six (33.4%) preferred to initiate ULD 1-2 weeks after acute gouty flare, while 85(29.6%) during acute flare of gout. In chronic gouty arthritis, 95(33.1%) chose to use colchicine for prophylaxis and 124(43.2%) NSAIDs. Ninety eight (34.1%) would discontinue prophylaxis soon after achieving a normal serum uric acid in a patient without evident tophi, while 90(31.4%) in 1-3 weeks, 51(17.8%) in 1-6 months. Thirteen (4.5%) respondents would give ULD for life, while majority [148(51.6%)] would discontinue it when serum uric acid normalizes. There were 86(30%) would request follow up SUA level once a month, 33(11.5%) every 2 months, 120(41.8%) every 3-6 months. One hundred forty seven (51.2%) would set < 5mg/dl while 95 (33.1%) chose <6.0 mg/dl as the target SUA level in management of gout.

CONCLUSION: This survey evidently shows the various inconsistent practices among physicians in the clinical management of gout. Efficient educational program should be designed in order to improve physicians' skills in the diagnosis and clinical management of gout.

G4 A Review of Factors Related to Tophi Formation Among Patients with Gout on Prolonged Systemic Glucocorticoid Use

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14th PRA Annual Convention. Cagayan de Oro. Jan 2007

BACKGROUND: The development of tophi in crystal-induced arthropathy depends on the level of hyperuricemia and the duration of the disease. Usually, tophi are located in subcutaneous and tendinous extension surfaces of hands, feet, and olecranon bursa. Intradermal tophi were shown to be associated with long-term glucocorticoid self-medication and chronic renal failure in a study done by Vasquez-Mellado et al.

OBJECTIVE: The study aims to describe the risk factors among patients with chronic tophaceous gout in relation to chronic systemic corticosteroid use.

METHODOLOGY: A retrospective chart review was done on (tophaceous) gout among Filipino patients seen by rheumatologists from around the archipelago. A standard case report form was accomplished for each patient by the attending rheumatologist. This included demographic data, disease onset (gout), onset of tophi formation, co-morbidities, history of systemic corticosteroid use prior to tophi formation, serum uric acid level, serum creatinine level, use of urate-lowering agent and its dose, and use of antihypertensive medications. Univariate analysis (Chi-square, student's t-test) and multiple logistic regression analysis were performed.

RESULTS: A total of 295 males were included in the study with a mean age of 56.42 ± 14.42 years and mean of 12.41 ± 11.42 years of gouty arthritis. The mean disease duration among patients who have tophi was 15.09 ± 12.05 years, significantly longer than among those who have no tophi ($p < 0.001$). Among patients who have chronic tophaceous gout (CTG), 32.37% reported chronic use of systemic corticosteroids prior to tophi formation ($p < 0.001$). The most frequent initial sites of acute gouty arthritis were the lower extremity joints in 94.38% of patients and similarly the most common site of initial tophi formation in 52.34% of patients, specifically the MTPs ($n=50$), ankle joints ($n=35$), and knees ($n=24$). Significant co-morbidities found among CTG patients include urolithiasis in 21.53% ($p=0.006$) and prior renal disease in 35.25% ($p < 0.001$). Multiple logistic regression analysis showed patients with prior steroid use have 12 times risk (95% CI 3.90-37.29) of tophi formation. Other factors shown to have a significant association with tophi formation include elevated serum creatinine level, urolithiasis, hyperuricemia and non-usage of urate-lowering agent.

CONCLUSION: The study showed interplay of various risk factors in patients with tophaceous gout. Patients with significant oral glucocorticosteroid use have increased risk for tophi formation in this study. Other factors that may increase risk of tophi formation among gout patients include hyperuricemia, and renal disease.

G5 The Association of Glucocorticoids and Serum Uric Acid Levels Among Male Gouty Arthritis Patients

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OBJECTIVE: Hyperuricemia is central to gout but does not inevitably cause disease. Predictors of the development and progression of gouty arthritis other than serum uric acid level include hypertension, the use of thiazides and loop diuretics, excessive alcohol consumption and renal disease. In a study done by Vasquez-Mellado et al, intradermal tophi were shown to be associated with long-term glucocorticoid self-medication and chronic renal failure giving rise to the hypothesis that chronic exposure to systemic steroids may have a role in the progression of the disease. Although chronic use of steroids in high doses can induce a hypercatabolic state, there is no known direct effect of steroid use on hyperuricemia; and an association between these two variables have not been established. The study aims to determine the association between oral systemic steroid use and serum uric acid levels among patients with gouty arthritis.

METHODOLOGY: A retrospective chart review was done on gout among Filipino patients seen by rheumatologists from different tertiary centers around the archipelago. A standard case report form was accomplished for each patient by the attending rheumatologist. This included demographic data, disease onset (gout), onset of tophi formation, co-morbidities, history of systemic corticosteroid use prior to tophi formation, serum uric acid level, serum creatinine level, use of urate-lowering agent and its dose, and use of antihypertensive medications. Multiple logistic regression analysis was performed to determine odds ratio (OR) of steroid use and hyperuricemia.

RESULTS: Univariate analysis showed that steroid use was associated with hyperuricemia (OR= 2.74, p=0.008). However, in the multivariate analysis, steroid use did not appear to be a risk for hyperuricemia (OR=1.87, p=0.168). Significant confounders included dyslipidemia and renal disease.

CONCLUSION: Steroid use was not shown to be a risk factor for hyperuricemia. Although other factors interplay with steroid use and may affect serum uric acid levels and gouty arthritis, further investigation is warranted to clearly establish how these variables affect one another and eventually impact on disease progression.

G6 Clinical Profile of Gout among Filipinos

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1. **Poster Presentation. 12th APLAR Congress. Kuala Lumpur, Malaysia, August 2006**
2. **APLAR Journal of Rheumatology 2006; 9(suppl.1) A86**
3. **Poster Presentation. 14th PRA Annual Convention. Cagayan de Oro. Jan 2007**

BACKGROUND: Gout is observed to be common among Filipinos, whether residing in the Philippines or living abroad. This paper describes the demographic profile, clinical presentation, predisposing factors, and associated conditions in a cohort of Filipinos with gout.

METHODS: This describes the clinical profile Filipino patients diagnosed with gout, who were consecutively seen at the Rheumatology Clinics of the University of Santo Tomas Hospital, in Manila, Philippines from January to December 2005. The following data were analyzed: demographic profile, joint involvement, history of alcoholic beverage consumption, co-morbidities; presence of tophi, and renal involvement.

RESULTS: One hundred thirty one (131) patients diagnosed with gout according to the ACR criteria for gout were included in this study. Majority of patients were males comprising 87% of the population. The mean age at onset is 57 years old. Among these patients a history of occasional to habitual alcohol intake was noted in 99 patients. Seventy-one (54%) patients were hypertensive, and 17 (13%) had diabetes mellitus. In majority of the patients the attacks were monoarticular: the knee joint being the most common joint involved (45%). Tophi were present in 49 patients (37.4%). The sites commonly involved were the knee (45%), metatarsophalangeal (MTP) joint (31.3%), and ankle (18.3%). Twenty eight patients had renal calculi by ultrasound or reportedly passed out stones in their urine. The laboratory parameters showed 45 % with hyperuricemia (mean serum uric acid level 8 mg/dl), 9.8% had dyslipidemia, and 4.8% had renal insufficiency.

CONCLUSION: We have described the clinical profile of patients with gout seen in a tertiary hospital over a period of one year. Majority were males, with a significant alcohol intake. Joint involvement was commonly the knee, with monoarthritis as the most common presentation. This paper reinforces the usual clinical features of gout reported in other literature, and stresses the need to do further studies to identify and correct contributing factors to this potentially disabling disease.

G7 Non-Prescription Analgesic/anti-inflammatory Modalities Used by Patients for Acute Gout

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1. 13th PRA Annual Convention. Westin Hotel, Manila. Jan 2006
2. APLAR Journal of Rheumatology 2006; 9(suppl.1) A86

OBJECTIVE: To describe non-prescription anti-inflammatory and analgesic modalities being taken by patients with acute gout.

DESIGN: Descriptive cross-sectional study

METHODOLOGY: Patients diagnosed with acute gout, consecutively seen at the University of Santo Tomas Hospital from January 2003 to November 2005 were included. All met the American College of Rheumatology (ACR) 1977 criteria for acute gout. Patients with intercritical and non-flare chronic tophaceous gout were excluded. The patients were given an investigator assisted questionnaire and the results analyzed using SPSS descriptive statistics.

RESULTS: There were a total of 130 patients (87.6% males) with a mean age of 57.6 \pm 13.63 SD years old. The mean age of onset of gout was 48.33 years old (\pm 15.10 SD). Majority (40%) of episodes were mono-articular, with knee joints being the most frequently involved joint (35%). Tophi were noted in 39.6% of the patients, primarily located at the elbow (44%). Associated co-morbidities included hypertension (50%), coronary artery disease (12%), DM type 2 (10%), nephrolithiasis (7%) and PUD (7%). Medications taken without a prescription included (36.9%) colchicine (23%), non-opioids (16.9%), allopurinol (12.3%), steroids (10.7%), and analgesics (4%). Non-prescription medications included non-steroidal anti-inflammatory drugs (NSAIDs) (51.3%), allopurinol (30%), colchicine (29.2%), steroids (11.5%), non-opioids (tramadol) (6.1%), and other analgesic (paracetamol) (2.3%) drugs. These medications were either self medicated or were given by friends, neighbors, relatives and herbalists. There were patients who inappropriately combined NSAIDs and COX-2 inhibitors (23%) together during an acute attack. Non-pharmacologic modalities included warm compress (20%), mentholated liniments (13%), cold compresses and herbal (ginger) (4%) and chemical heat (kerosene) (2%).

CONCLUSIONS: This study showed the kinds and frequency of non-prescription modalities like NSAIDs, allopurinol, colchicine, non-opioids and steroids taken by patients for acute gout, without a prescription. This can potentially lead to inappropriate use of these drugs with a tendency to misuse and abuse. Patient education for this common painful condition thus becomes imperative.

G8 An Open label, 2-arm comparative 5-day Trial of the Effect and Tolerability of Rofecoxib and Tenoxicam in the Treatment of Acute Gout

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Poster Presentation. 9th PRA Annual Convention. Edsa Shangri la Hotel, Manila. Jan 2002

INTRODUCTION: There is a concern that newer NSAIDs with highly specific COX-2 inhibition discovered recently might be inferior to conventional NSAIDs with nonspecific COX-1/COX-2 inhibition in the treatment of severe pain of acute gouty arthritis because of some evidences that COX-1 is also present in some inflammatory process.

OBJECTIVE: To compare the clinical efficacy and tolerability of COX-2 specific inhibitor, Rofecoxib, with conventional NSAID, Tenoxicam, in the treatment of acute gout.

METHODS: This is an, open label, 2-arm comparative study demonstrating the effect of Rofecoxib and Tenoxicam in the treatment of acute gouty arthritis. Primary endpoint for efficacy was reduction of pain assessed through 10-point VAS. Secondary endpoints were resolution of swelling and erythema as well as change of ESR values from baseline. Adverse experiences were identified and recorded.

RESULTS: Rofecoxib demonstrated comparable efficacy with Tenoxicam in the treatment of acute gouty arthritis both in primary endpoint (patients assessment of pain) as well as secondary endpoints (investigators assessment of swelling and erythema). This is, however, a preliminary report because the

10-month recruitment period did not yield the computed sample size. Both treatment groups were well tolerated.

CONCLUSION: COX-2 specific inhibitor, aside from its excellent safety profile and tolerability, is also as effective as the conventional NSAID in relieving the pain of acute gouty arthritis.

G9 Chronic Tophaceous Gout in a Young Adult

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Poster Presentation. 9th PRA Annual Convention. Edsa Shangri la Hotel, Manila. Jan 2002

A 25 year old computer technician was first seen for chronic tophaceous gout. He reports recurrent monoarthritis usually involving the lower extremity joints since the age of 17, for which he took several NSAIDs, colchicine and allopurinol. By age 22, small nodular masses were noted over the hands, elbows and earlobes. He used to drink alcoholic beverages for 2 years (age 20 to 22). Except for hypertension, there are no other remarkable family illnesses. The patient is normotensive.

Laboratory tests revealed a markedly elevated serum uric acid at 15.3 mg/dl, normal urinalysis, creatinine and creatinine clearance with an ultrasound finding of a suspicious nephrolithiasis on the superior pole of the right kidney and normal sized kidneys. Urinary uric acid was 1.11 g/ 24 hours. Aspirate from a tophus confirmed the presence of MSU crystals. He was then maintained on allopurinol, colchicine, and NaHCO₃.

Issues: Management from Rheumatology and Orthopedic Surgery standpoint

G10 Renal Microtophi in a Patient with Lupus Nephritis and Tophaceous Gout.

Navarra STV, Saavedra SC, Cayco AV.

J Clin Rheumatol 7:268-272, 2001.

G11 The Spontaneous Resolution of Acute Gouty Arthritis does not Significantly Contribute to the Potent and Comparable Anti-inflammatory and Analgesic effect of Etoricoxib or Indomethacin over the First Four Days of Treatment.

Boice JA, MD, Ng J, MD, Rubin BR, MD, Schumacher HR, MD, Navarra SV, MD, Ozturk ZE, MD, Malmstrom K, MD, Reicin AS, MD

Arthritis Rheum Vol 50, No.9 (suppl).S338. Sept 2004.

G12 Treatment of Chronic Gout. Can We Determine What Urate Stores are Depleted Enough to Prevent Attack of Gout?

Julie Li-Yu, Gilda Clayburne, Marie Sieck, Anna Beutler, Marina Rull, Elana Eisner, H. Ralph Schumacher Jr.

J Rheumatol 2001; 28:577-80

OBJECTIVE: To determine if lowering of serum uric acid (SUA) concentrations below 6 mg/dl or longer duration of lowered SUA will result in depletion of urate crystals from the knee joints and prevent further attacks of gout.

METHODS: A prospective study was initiated 10 years ago at Philadelphia VA Medical Center to attempt to maintain SUA levels of patients with crystal proven gout at <6.0 mg/dl. We recalled all 57 patients who were available during 1999. Patients were divided into 2 groups: Group A, with SUA still >6mg/dl, and group B with SUA ≤6mg/dl. A knee joint aspirate was requested from all asymptomatic Group B patients and many in Group A. Aspirates were examined by polarized light microscopy for identification of crystals.

RESULTS: There were no differences between the groups in age, sex, duration of gout, or serum creatinine. Group A (n=38) had a mean of 6 attacks of gout for the recent year, those with tophi having the most frequent attacks. Among the 16 patients in this group who agreed to knee aspiration, monosodium urate (MSU) crystals were found in 14, although they were asymptomatic at the time. Nineteen patients (Group B) were able to maintain serum urate levels \leq mg/dl for 12 months. Nearly half of them had no attack of gout for 2 or more years, with a mean of 1 attack in the last year for the whole group. Three patients in whom tophi were found did not have major flares of gout within the past year. Knee joint aspiration was done on 16 asymptomatic patients. Seven (44%) still had MSU crystals present in their knees. Patients in this group who were taking prophylactic colchicine did not differ with respect to the character of synovial fluid from those who had discontinued it for up to several years, although the frequency of attacks was less in those who continued colchicine.

CONCLUSION: A majority of patients were able to deplete urate crystal stores in their knee joint fluids when their SUA levels were kept to \leq 6mg/dl for several years. The mechanisms for persistence in some patients, and whether such crystals have clinical implications, are not known. Patients with chronic gout need serum urate concentrations to be kept low to prevent further attacks.

Key Indexing Terms:

CHRONIC GOUT URATE CRYSTALS ALLOPURINOL COLCHICINE

G13 Invasive Tophaceous Pseudogout in the Temporomandibular Joint: Misdiagnosis as Tumor: Case Report and Review of the Literature.

Li-Yu, Julie; Schumacher, H. Ralph Jr.; Gratwick, Geoffrey

Journal of Clinical Rheumatology. 6(5):272-277, October 2000)

We report a case of focal calcium pyrophosphate dihydrate (CPPD) arthropathy in a 72-year-old, white woman that occurred in the temporomandibular joint (TMJ), a relatively unusual location for CPPD crystals. The patient underwent surgical exploration and radiation therapy because of histologic interpretation of an initial biopsy specimen as showing metastatic poorly differentiated carcinoma. Further evaluation of the specimen revealed the presence of positively birefringent crystals under compensated polarizing light microscopic examination. Previously reported cases of CPPD affecting the TMJ have also shown that this may mimic neoplastic or infectious conditions. Tophaceous pseudogout at the TMJ is a surprisingly common complication of CPPD deposition disease. As in our patient, it can occur without known CPPD at other sites.