A Case Of Chronic Tophaceous Gout, Urate Nephropathy And Metabolic Syndrome

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ABSTRACT

Gout is one of the oldest diseases known to mankind. Since the earliest times it has been recognized as a life-style disease; having been associated with affluence, dietary indiscretion, alcohol abuse and lack of exercise. Predominantly a disease of peripheral joints, it is a true crystal arthropathy. Arthropathy may manifest as initial asymptomatic hyperuricaemia, recurrent acute attacks, a relatively quiescent inter-ictal period or as chronic symptomatic tophaceous gout. Renal involvement if present may be in the form of urolithiasis, Uric acid nephropathy or Urate nephropathy. Metabolic Syndrome or Syndrome 'X', a constellation of cardiovascular risk factors is a common co-morbidity in patients with gout; the prevalence ranging from 60% to 86%. Hyperuricaemia, the salient and pathogenetic feature of gout is the common link between the two. The pathogenetic overlap between the two conditions should prompt a vigorous look-out for Metabolic Syndrome in patients with gout and its aggressive management if present. To highlight the importance of gout as a surrogate marker of cardiovascular risk, we report a case of chronic tophaceous gout with urolithiasis and Metabolic Syndrome.

INTRODUCTON

Gout is one of the oldest diseases known to man. It was known as 'Podagra' (foot pain) to the Egyptians as early as 2640 BC; Hippocrates described it in the 5th Century BC as the 'unwalkable disease', mostly affecting the rich (1). It is the most common inflammatory arthritis in men over 40 years and post menopausal women (2, 3). It is characterized by hyperuricaemia and deposition of Monosodium Urate (MSU) crystals in the joints leading to true crystal arthropathy. Arthropathy may manifest as initial asymptomatic hyperuricaemia, recurrent acute attacks, relatively quiescent inter-ictal period or as chronic symptomatic tophaceous gout. Renal involvement may be in the form of urolithiasis, Uric acid nephropathy or Urate nephropathy.

Metabolic Syndrome is a constellation of cardiovascular disease risk factors (hypertension, hyperglycemia, central obesity, dyslipidaemia). Hyperuricaemia is an integral part of the Metabolic Syndrome which is a common co-morbidity in patients with gout. The prevalence of Metabolic Syndrome in gout is very high, ranging from 60 %(4) to 86% (5). Increased prevalence is probably due to common risk factors (over-eating, obesity, sedentary life-style). Presence of Metabolic Syndrome increases the risk for atherosclerotic cardiovascular disease up to 3 times. There is an increase in all causes of mortality from coronary heart disease in men with gout (6). The close association between gout and Metabolic Syndrome suggests a pathogenetic overlap between the two and thus gout can be considered a surrogate marker of cardiovascular disease risk.

Here we report a case of chronic tophaceous gout with urolithiasis and Metabolic Syndrome.

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CASE REPORT

A 50 years old male, a known Diabetic and hypertensive was admitted with swelling over right great toe since 12 years. There was history of similar swelling in right second toe from which there was chalky white discharge. It later healed leaving a deformity. He

complained of pain in the small joints of both feet. He also gave history of oliguria. On examination, he was afebrile with blood pressure of 150/90 mmHg. He had multiple firm swellings over right 1st metatarsophalangeal joint (podagra) & on lateral aspect of left foot (Figure 1) which were non-tender. There was no evidence of arthritis in the form of joint swelling, redness & tenderness. Systemic examination was within normal limits. Patient was investigated. His Serum uric acid was 11.1 mg/dl, Blood urea- 176 mg/dl, Serum creatinine - 3.5mg/dl; Hemoglobin and total count was normal. Fasting lipid profile showed hypertriglyceridemia (triglycerides – 183 mg %). X ray of right foot showed sclerosis & narrowing of joint space of 1st metatarsophalangeal joint (Figure 2), there were peri-articular erosions with over-hanging bony edges. Ultrasound of abdomen showed bilateral multiple renal calculi. Arthrocentesis revealed chalky white fluid (Figure 3). Fine needle aspiration showed needle shaped crystals (Figure 4).When examined under polarizing microscope, negatively birefringent needle shaped crystals were seen (Figure 5).Histopathology showed irregular gouty tophus surrounded by inflammatory cells (Figure 6) & typical flower shaped monosodium urate crystals(MSU) (Figure 7).With these investigations, diagnosis of gout was made. This patient also had type II DM, systemic hypertension & hypertriglyceridemia. So the final diagnosis of Gout with Metabolic syndrome with urolithiasis with urate nephropathy was made and Urate lowering therapy in the form of Allopurinol 100mg once daily was started. However after starting Allopurinol, patient developed an acute attack of arthritis which subsided with Colchicine.

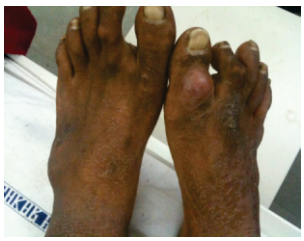

Figure1 showing tophi on the first meta-tarsophalangeal joint and lateral aspect of left foot

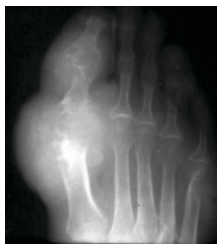

Figure 2. X-Ray foot showing peri-articular erosions & over hanging edges

DISCUSSION

Gout is a metabolic disorder of purine metabolism caused by increased endogenous production of uric acid or by reduced efficiency of renal urate clearance. In the majority of patients with gout, hyperuricaemia results from reduced renal urate clearance (7).Historically, gout has been considered a disease of the affluent class, linked to dietary indiscretion.(excess red meat and alcohol) and sedentary life-style. It is commoner in men and post-menopausal women. Men have higher urate levels whereas the uricosuric effect of Estrogen protects the younger women (3).

High purine content of certain alcoholic beverages like beer (8), increased purine production (9) and reduced urate clearance due to alcohol induced lactic acidaemia (10, 11) are the various pathogenetic mechanisms by which alcohol increases the risk of gout. Besides, genetics also seems to play a role, though monogenic disorders causing enzyme defects in purine metabolism resulting in over-production of uric acid are extremely rare (3).

Uric acid at physiological pH exists in its ionized form, urate. When the ionic product of Na and Uric acid exceeds the saturation level, MSU can form. MSU has limited solubility, its saturation level being 6.8 mg/ dl. MSU crystals are formed once this saturation level is exceeded. These are preferentially formed within the cartilage and fibrous tissues in the initial stages where they may remain quiescent for years together. On shedding into joint spaces or bursae, inflammatory damage ensues (3).

Our patient presented with Chronic tophaceous gout who developed an acute attack after initiation of urate lowering therapy. He also had Urolithiasis and Urate nephropathy.

Initiation of urate lowering therapy may precipitate an acute attack and hence prophylactic Colchicine is advocated with urate lowering therapy, at least initially. Besides, direct trauma to the joint, dehydration or acidosis, rapid weight loss or inter-current illnesses are other precipitating factors (3). Inter-current illness as well as ULT reduces the serum uric acid levels (through

increased urinary excretion), promoting dissolution of MSU crystals which encourages crystal 'shedding' (3, 12). An acute attack of gout characteristically targets the distal joints, especially of the lower limb (1st metatarsophalangeal joint, known as 'Podagra'), commonly at night. Lower temperatures of these joints reduce the solubility of MSU leading to its crystallization (13).

There is a two-fold increase in the risk for developing incident kidney stones as individuals with Gout have persistently acidic urine which favors precipitation of Uric acid leading to Uric acid stone formation. The acidic milieu also promotes Calcium Phosphate stone formation. Besides nephrolithiasis, Urate nephrosis (a late manifestation of severe disease marked by deposits of MSU crystals surrounded by giant inflammatory reaction in the medullary interstitium and pyramids) and Uric acid nephropathy (a reversible cause of acute renal failure seen in acute Gout) can occur in patients with Gout (14).

Our patient had diabetes, hypertension and central obesity (waist circumference – 88cm). Thus Metabolic syndrome was an additional co-morbidity.

Gout has a strong association with MS, hyperuricaemia being the common link between the two. Hyperuricaemia is closely associated with Insulin resistance; an integral component of the Metabolic syndrome. Higher Insulin levels not only reduce renal excretion of urate (15) but also probably enhance its re-absorption (16, 17).Amongst the components of Metabolic syndrome, Gout appears to be related with dyslipidemia and obesity more than hyperglycaemia or hypertension (5).

The gold standard for diagnosis of gout is to perform a joint or tophus aspiration. Identification of intracellular monosodium urate (MSU) crystals in the synovial fluid or tophus makes the diagnosis of gout definite. Under polarized light microscopy, these appear negatively bierfringent needle shaped crystals. The European League against Rheumatism (EULAR) Gout Task Force in 2006 (18) issued a set of recommendations on its diagnosis. The key recommendations for the diagnosis of gout include: “In acute attacks the rapid development of severe pain, swelling, and tenderness that reaches its maximum within just 6–12 hours, especially with overlying erythema, is highly suggestive of crystal inflammation, though not specific for gout” and “Demonstration of MSU crystals in synovial fluid or tophus aspirates permits a definitive diagnosis of gout. The validity and usefulness of these criteria still need to be defined. The diagnostic value of a SU level is limited. A normal SU level clearly does not exclude acute gout as almost 50% patients with acute gout may have normal SU levels during acute gout (19)despite their increased uric acid (UA) pool. Conversely, an elevated serum uric acid level alone does not serve as a sole criterion for gout. Most patients with hyperuricemia will never have an attack of gout.

While urate lowering therapy is the mainstay of management of chronic Gout, NSAIDs, Colchicine or steroids can be used for acute attacks. Allopurinol, in the dose of 100 to 800mg, is a commonly used urate lowering therapy. However increased toxicity with Allopurinol is a concern in patients with renal failure in whom dose reduction is required. Febuxostat, a newly approved Xanthine oxidase inhibitor, is advocated in patients with Allopurinol hypersensitivity or renal failure. Lifestyle modification in the form of weight reducing calorie restricted diet, exercise and abstinence from alcohol may be beneficial.

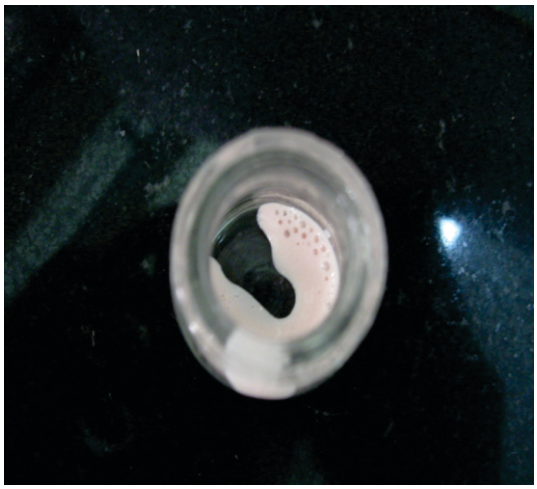

Figure 3. FNAC showing chalky white aspirate

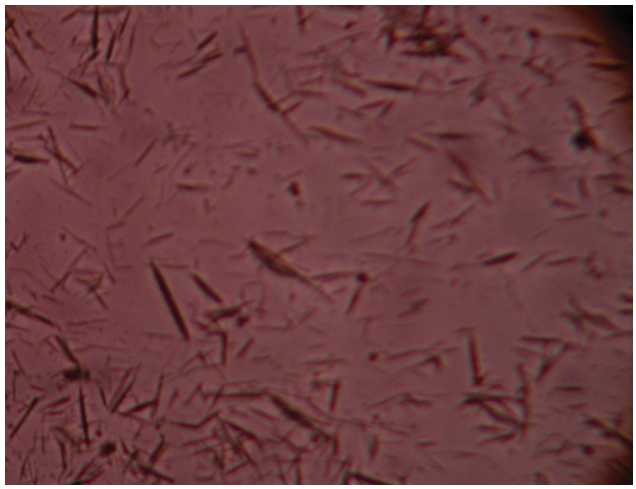

Figure 4. FNAC showing needle shaped crystals

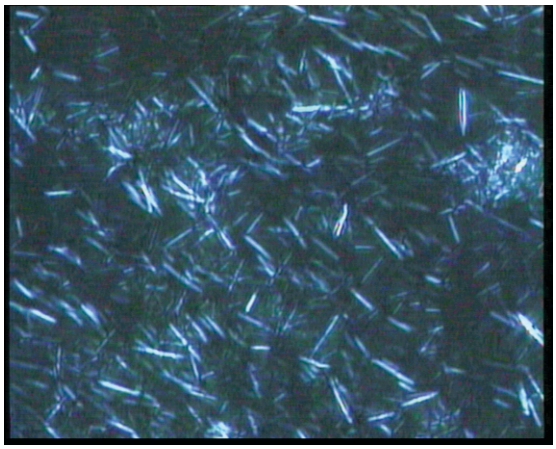

Figure 5. Negatively birefringent needle shaped crystals under polarizing microscope

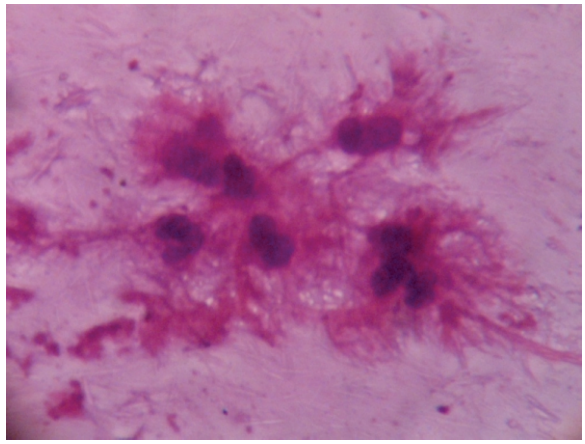

Figure 6 showing gouty tophus surrounded by inflammatory cells

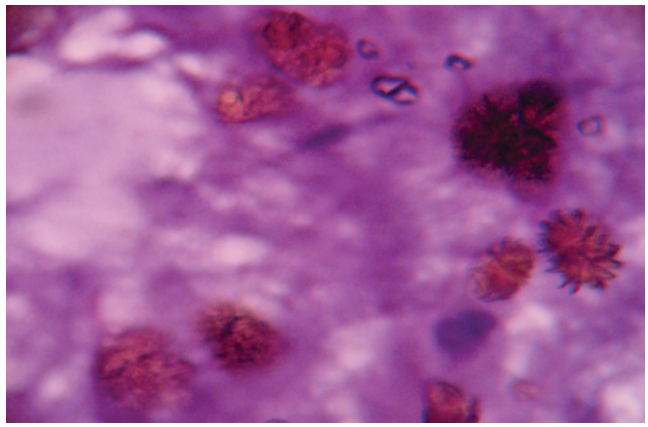

Figure 7 showing flower shaped gouty crystals

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