The Journal of Dermatology (2010.06) 37巻6号:578～580.

Chronic tophaceous gout secondary to self-induced vomiting in anorexia nervosa
(神経性無食欲症における自己誘発性嘔吐後に発生した慢性結節性痛風)

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Letters to the Editor-

A case of chronic tophaceous gout secondary to self-induced vomiting in anorexia nervosa

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Short running title: chronic tophaceous gout in anorexia nervosa

Dear Editor,

A 50-year-old Japanese woman noticed asymptomatic nodular masses on her right elbow, right second finger, and left fifth finger in 2005. Two years later, she developed painful erythema and swelling in these regions. She was treated with oral antibiotics by an orthopedic physician, but no improvement was seen. The erythema and swelling worsened and spread over the other joints. She was referred to our hospital on June 21, 2007. Her past medical history included hyperuricemia at 20 years of age, unexplained acute renal failure at 40 years of age, and hypokalemia since the age of 41 years. Physical examination revealed an afebrile, remarkably slender woman, weighing 36 kg (-37% of ideal body mass index). Elastic soft, dome-shaped, reddish tumors were noted on bilateral elbows. The tumor on the right elbow contained several whitish, stony-hard nodules with spontaneous discharge of whitish chalky liquid material (Fig. 1a). Several metatarsophalangeal joints, bilateral knees and ankles, and the lateral sides of the feet also showed marked swelling with overlying dark red erythema. Small whitish subcutaneous nodules were also noticed on her left ear helix and several fingers. Her left fifth finger was swollen and shortened (Fig. 1b). Aspirates from these swollen lesions showed white chalk-like material. Light microscopic examination of the spontaneous discharge demonstrated numerous needle-shaped, monosodium urate crystals (Fig. 2). Roentgenographic examination revealed bone destruction of the metacarpophalangeal (MCP) joint of the left fifth finger (Fig. 1c) and multiple punched-out lesions of the tarsal bones. Laboratory

analyses showed renal insufficiency (blood urea nitrogen 42.4 mg/dL, serum creatinine 1.51 mg/dL), hyperuricemia（serum uric acid 12.2 mg/dL）. Pelvic computed tomography scanning disclosed bilateral renal stones. Plasma renin activity, plasma aldosterone concentration, angiotensin, and other endocrine examinations were all within normal limits. Antinuclear antibody and rheumatoid factor were negative. A myelogram showed no abnormal findings. The patient was diagnosed as having gout. Treatment with oral allopurinol, etodolac, cimetidine, and potassium sodium hydrogen citrate lowered her serum uric acid and alleviated her painful joint swellings. To investigate the etiology of her gout, her detailed medical records were examined. She had lost weight at 20 years of age and developed amenorrhea at 27 years. She was admitted to hospital for hypokalemia (2.8 mEq/L) and renal failure due to self-induced vomiting at 40 years of age. At that time, her serum uric acid was already elevated (8.9 mg/dL), and she was diagnosed as having AN. After discharge, she was treated for hypokalemia by another physician, but she never received appropriate treatment for AN or hyperuricemia.

Gout is a disorder of uric acid metabolism that leads to deposition of urate crystals in tissues and body fluids. It is clinically characterized by acute gouty arthritis, destructive arthritis, chronic tophi, nephrolithiasis, and nephropathy. Premenopausal women rarely suffer from gout because estrogen enhances renal excretion of uric acid.[1] However, gout may develop in women with predisposing factors such as obesity, diuretic therapy for hypertension, and renal insufficiency.[1] The main skin

finding of gout is a tophus, which is initially a small white to yellow, movable nodule. Typical sites include digital joints, elbows, helix of the ear, and Achilles tendons. The chronic tophi sometimes grow insidiously for years without recurrent episodes of acute inflammatory attacks and, therefore, may cause difficulties in diagnosis. It has been shown that hyperuricemia is found in 9% of AN patients.[2] Several mechanisms are involved in the pathogenesis of AN-induced hyperuricemia. AN, which can be interpreted as self-starvation, could elevate serum ketone levels that reduce renal uric acid clearance, resulting in hyperuricemia.[3] The lowered serum gonadotropin and estrogen levels commonly seen in AN also reduce renal uric acid clearance, besides inducing amenorrhea. Although hyperuricemia is occasionally observed in AN, multiple tophaceous gout rarely develops in AN patients. To the best of our knowledge, only seven such cases have been reported in the English medical literature. In these patients, gout was considered to be secondary to abuse of diuretics or laxatives, [4-7] as well as alcoholism.[8] The present patient never abused diuretics or laxatives, however, she had habitual self-induced vomiting, which often causes hypokalemia and hypovolemia. Prolonged hypokalemia could cause tubulointerstitial nephritis that would reduce the renal uric acid clearance, which in turn induces uric acid deposition in the kidney. In conclusion, her multiple tophaceous gout can be regarded as a late manifestation of AN.

Previous reports indicate that various dermatoses, **including xerosis, telogen effluvium, lanugo-like body hair, carotenoderma, acne, seborrheic dermatitis, and so on,** might develop in AN

patients.[9] However, gout is not a well-recognized complication of AN. Considering its pathophysiology, patients with AN may readily develop hyperuricemia, and gout should be included in the list of complications of AN. Skin lesions such as tophi may provide a clue for underlying eating disorders.

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FIGURE LEGENDS

Fig.1. (a) Subcutaneous nodules with white chalky material on the right elbow.

(b) Shortened left fifth finger and swollen MCP joints of left index and fifth fingers.

(c) Radiograph showing erosion and bone destruction (white arrow head) around the MCP joint.

Fig.2. Monosodium urate crystals from a tophus, observed with polarized light microscopy.