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Effects of hemodialysis on advanced bony tophi in a tophaceous gout patient with chronic renal failure

Sirs,

In most cases of gout, bony tophi can be conservatively controlled by therapies aimed at lowering serum urate concentrations (1). However, the management of gout

is not easy in patients with renal insufficiency (2). This is a report of a patient with severe tophaceous gout and renal failure treated with hemodialysis.

A 63-year-old Japanese woman was admitted to our department for joint deformities and arthralgia on January 13, 1996. She had suffered from acute glomerulonephritis at the age of 14. Her proteinuria had continued throughout this period. She had been treated with benzylhydrochlorothiazide for the past 20 years. Gout had initially been recognized 5 years ago. Her gout attacks involved the both metatarsophalangeal (MTP) and interphalangeal (IP). Subsequently, these gout attacks would also involve the hands and knees and persist for several days. Joint examination revealed swelling and tenderness involving both the interphalangeal (IP) and metatarsophalangeal (MTP) joints and a subcutaneous tophus (3 cm in diameter) was observed in upper area of the right tibial bone. Laboratory tests showed an elevated plasma urate concentration (8.4 mg/dl), serum BUN (74 mg/dl), and creatinine (3.4 mg/dl), and renal function was markedly impaired (creatinine clearance: 18.8 ml/min). Urinalysis revealed proteinuria (380 mg/day) and microhematuria. 24-hr uric acid excretion was 170-230 mg/day. Radiography revealed multiple punched out lesions with overhanging edges in the both MTP and IP joints (Fig. 1a).

She was diagnosed as having tophaceous gout and chronic renal failure. Treatment with allopurinol (100 mg/day) and potassium citrate/sodium citrate (2400 mg/day) were started. Her serum urate levels were maintained at less than 7 mg/dl and her gout attacks decreased in duration and frequency. However, joint swelling and the size of the tophi did not change despite these treatments.

At 13 months following the treatment, her X-ray findings for bony tophi had not changed except for the left first MTP joint which was beginning to resolve (Fig. 1b). Hemodialysis was started for azotemia and congestive heart failure on February 13, 1998. Subsequently, she has been treated with regular hemodialysis (4 hours HD, 3 times per week) without complications as an out-patient. Since she began hemodialysis, she has not experienced an attack of gout and her joint swelling and deformities have lessened. Her serum urate levels were controlled at less than 7.5 mg/dl (pre-dialysis point) without allopurinol. At 18 months from the start of hemodialysis, skeletal X-ray films showed marked improvement of osteolytic lesions (Fig. 1c).

Tophaceous gout, which occurs in cases of long-standing gout, is the consequence of the chronic inability to eliminate urates with deposits of urate crystal appearing in

the cartilage, synovial membrane, and soft tissues (3). In humans, the average urate pool size is about 1,200 mg and the turnover rate is also about 0.6 pools/day (3, 4). As the urate pool expands, deposits of urate crystals appear in the cartilage, tendon and soft tissue (5).

This patient had experienced an aggressive course of tophaceous gouty arthritis with extensive destruction of the IP and MTP joints. Decreased urinary excretion of urate caused by renal insufficiency and long-standing thiazide therapy may contribute to hyperuricemia and following tophaceous gout (6). Although allopurinol treatments corrected her serum urate concentration to less than 7.0 mg/dl, bony tophi were not improved by this therapy. For the resolution of tophi, serum urate level should be controlled to less than 6 mg/dl (7). In our case, the control of serum urate may not have been adequate; however, the dose of allopurinol had to be reduced due to renal failure. After the initiation of hemodialysis, her

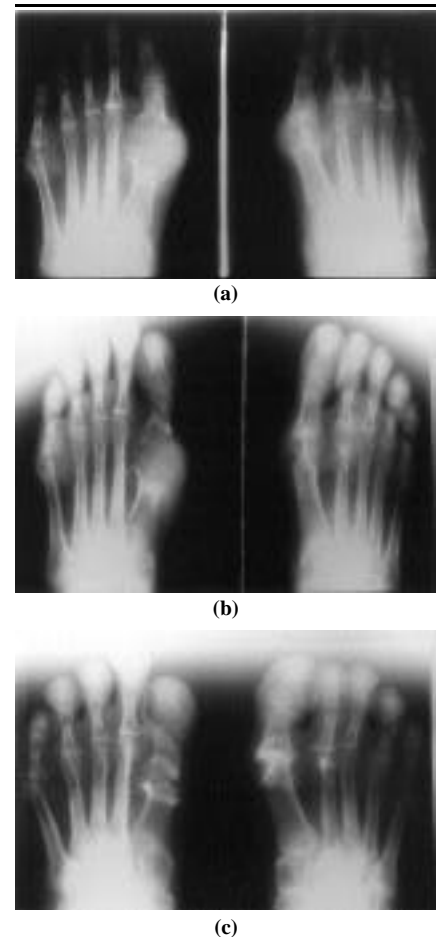


Fig. 1. Radiographic changes in gout. (a) A classical "punched out" para-articular erosions with a sclerotic margin of both the metatarsophalangeal joints. (First admission: January 13, 1996); (b) 13 months after allopurinol treatment (February 24, 1997); (c) 18 months after the initiation of hemodialysis (October 6, 1999).

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urinary excretion of urate was eliminated due to oliguria. Although the pre-dialysis serum urate was less than 7 mg/dl, the urate could be controlled to lower levels between each dialysis. Therefore, it is possible that hemodialysis treatment could modulate the body pool of urate negatively by the removal of urate. This negatively balanced body pool of urate by regular hemodialysis treatment may decrease the urate deposition in joints and subsequently reduce the osseous cystic lesions.

It is possible to control tophaceous gout by current medications. However, we propose that hemodialysis should be considered as one of the treatments for bony tophi in gout patients with severe end-stage renal disease as described previously (8, 9).

K. MIGITA, MD M. SAKAI², MD
K. ARATAKE, MD H. SHIMADA², MD
M. YONEDA, MD T. OTSUBO², MD
T. TSUKADA, MD K. EGUCHI, MD
H. IDA¹, MD

First Department of Internal Medicine,
Nagasaki University School of Medicine;

¹Department of Rheumatology, Nagasaki Kita
Hospital; ²Department of Nephrology, Kou-
seikai Hospital, Nagasaki City, Japan.

Address correspondence to: Kiyoshi Migita,
MD, First Department of Internal Medicine,
Nagasaki University School of Medicine,
Sakamoto 1-7-1, Nagasaki 852-8501, Japan.

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Pilot study using the combination of methotrexate and thalidomide in the treatment of rheumatoid arthritis

Sirs,

There have been three major clinical studies evaluating the use of thalidomide in the treatment of rheumatoid arthritis (RA) (1-3). Based on these studies thalidomide does seem to have a role in the treatment of RA but the dosages required to achieve benefit (> 200 mg/d) are associated with a high incidence of side effects (3). To determine if lower dosages of thalidomide (< 150 mg/d) combined with methotrexate (MTX) could show enhanced efficacy and improved tolerance, an open trial was performed and here are the results.

This study enrolled 10 female patients. All patients satisfied the ACR criteria for RA. All had disease onset after age 16 and showed 10 swollen joints at baseline evaluation. The average age was 48 yrs (range 34 - 69), average duration of disease 11 yrs (range 2 - 28 yrs), average number of previous DMARDs 3 (range 1 - 6), average MTX dose 17 mg/wk (range 10 - 30 mg/wk), and average prednisone dose 9 mg/d (range 0 - 20 mg/d). Only women of nonchildbearing potential were eligible. All DMARDs, except for MTX, had been discontinued in these patients because of adverse reactions or lack of benefit. All patients were required to be taking MTX at doses > 15 mg/wk for at least 3 months unless evidence of toxicity had occurred previously and required dosage reduction. All patients had to be taking a stable dosage of MTX for at least one month prior to entering the study. The total average duration of MTX use by these patients was 3 yrs (range 3 months to 8 yrs). All but 3 patients were taking NSAIDs regularly and all but 2 were taking corticoster-

oids regularly.

Patients on a stable dosage of MTX were started on thalidomide 50 mg/d for at least 2 weeks and then the dosage was increased by 50 mg/d every two weeks to a maximum of 150 mg/d, if tolerated. Patients were evaluated thoroughly every 2 weeks for 2 months and then monthly for the next 2 months (total 4 months).

Three patients withdrew from the study prematurely. Two of these, who were receiving thalidomide 50 mg/d, withdrew at 6 weeks due to drowsiness. The third patient withdrew at 3 months due to nausea attributed to MTX. These side effects resolved within 2 weeks after discontinuation of the given medication. Most patients experienced minor adverse events (60% experienced drowsiness, constipation, or paresthesias, and 30-40% experienced rash, lymphedema, sicca symptoms, dry skin, or tremor) that were easily remedied by reducing the thalidomide dosage or using simple, conservative measures. Although 60% of the patients experienced paresthesias, usually characterized by tingling in the fingertips, face, and/or toes, these symptoms were transient and resolved with a reduction in the thalidomide dosage.

Seven patients completed the open 4-month clinical trial using combination methotrexate and thalidomide in the treatment of RA. Five patients showed a favorable response using the ACR 20 criteria, of whom 3 patients were responders (meeting 4/6 criteria) and 2 patients were partial responders (meeting 3/6 criteria) (Table I). Two patients were non-responders. When evaluating each of the efficacy measurements used in determining the ACR scoring, there was improvement in most of the variables, but no single variable had a statistically significant improvement. The lack of statistical significance would be expected from a small sample size. The mean joint scores

Table I. Final results of the MTX/Thalidomide study: comparison of values at baseline and the final visit.

	Patient no. 2	Patient no. 3	Patient no. 4	Patient no. 5	Patient no. 6	Patient no. 9	Patient no. 10
Tender joint scores	2/0	9/25	23/3	54/50	3/2	32/20	13/7
Swollen joint scores	18/1	26/36	26/5	35/8	12/7	32/12	11/9
Physician's assessment*	3/1	3/3	3/2	3/2	2/2	3/3	2/2
Patient's assessment*	3/2	3/4	4/1	3/3	3/2	3/3	2/2
Morning stiffness (hrs)	0.5/0	0.25/8	2/0	5/6	2/2	8/6	0.5/0
C-reactive protein value	1.6/0.6	3.52/4.2	0.9/0.5	4.9/1.5	1.5/0.7	3.1/0.8	0.5/0
ACR 20 score	5/6	0/6	5/6	2/6	3/6	4/6	3/6

*Global Disease Assessment quantified as follows: 0 = no disease activity, 1 = slight disease activity, 2 = mild disease activity, 3 = moderate disease activity, 4 = severe disease activity.

Patients nos. 1, 7, and 8 withdrew from the study prematurely due to adverse events.