whether a different cytokine phenotype might be considered predictive of clinical outcome.

Authors' affiliations
F Meloni, A Marone Bianco, E Paschetto, M Morosini, A M Fietta, E Pozzi, Department of Haematological, Pneumological and Cardiovascular Sciences, Section of Pneumology, University of Pavia and IRCCS Policlinico San Matteo, Pavia, Italy
R Caporali, F Bobbio-Pallavicini, C Montecucco, Department of Internal Medicine and Medical Therapy, Section of Rheumatology, University of Pavia and IRCCS Policlinico San Matteo, Pavia, Italy

Correspondence to: Dr F Meloni, Dipartimento di Scienze Ematologiche, Pneumologiche e Cardiovascolari Mediche e Chirurgiche, Sezione di Pneumologia, Università di Pavia, IRCCS Policlinico San Matteo, Via Taramelli 5, 27100 Pavia, Italy; federica_meloni@libero.it

Accepted 26 July 2003

REFERENCES

1 **Bouros D**, Wells AU, Nicholson AG, Colby TV, Polychronopoulos V, Pantelidis P, *et al*. Histopathologic subsets of fibrosing alveolitis in patients with systemic sclerosis and their relationship to outcome. *Am J Respir Crit Care Med* 2002;**165**:1581–6.
2 **Cheema GS**, Quismorio FP Jr. Interstitial lung disease in systemic sclerosis. *Curr Opin Pulm Med* 2001;**7**:283–90.
3 **Lukacs NW**, Hogaboam C, Chensue SW, Blease K, Kunkel SL. Type 1/type 2 cytokine paradigm and the progression of pulmonary fibrosis. *Chest* 2001;**120**:5–8S.
4 **Anonymous**. Preliminary criteria for the classification of systemic sclerosis (scleroderma). Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostics and Therapeutics Criteria Committee. Preliminary criteria for the classification of systemic sclerosis (scleroderma). *Arthritis Rheum* 1990;**23**:581–90.
5 **Medsger TA**, Silman AJ, Steen VD, Black CM, Akesson A, Bacon PA, *et al*. A disease severity scale for systemic sclerosis: development and testing. *J Rheumatol* 1999;**26**:2159–67.
6 **Keane MP**, Belperio JA, Burdick MD, Strieter RM. IL-12 attenuates bleomycin-induced pulmonary fibrosis. *Am J Physiol Lung Cell Mol Physiol* 2001;**281**:L92–7.
7 **Sakamoto H**, Zhao LH, Jain F, Kradin R. IL12p40(-/-) mice treated with intratracheal bleomycin exhibit decreased pulmonary inflammation and increased fibrosis. *Exp Mol Pathol* 2002;**72**:1–9.
8 **Anonymous**. Technical recommendations and guidelines for bronchoalveolar lavage (BAL). Report of the European Society of Pneumology Task Group. *Eur Respir J* 1989;**2**:561–85.
9 **Johnston CJ**, Williams JP, Okunieff P, Finkelstein JN. Radiation-induced pulmonary fibrosis: examination of chemokine and chemokine receptor families. *Radiat Res* 2002;**157**:256–65.
10 **Zhang Y**, McCormick LL, Desai SR, Wu C, Gilliam AC. Murine sclerodermatous graft-versus-host disease, a model for human scleroderma: cutaneous cytokines, chemokines, and immune cell activation. *J Immunol* 2002;**168**:3088–98.

Gout in liver transplant patients receiving tacrolimus

J C Gerster, M Dudler, N Halkic, M Gillet

Ann Rheum Dis 2004;**63**:894–895. doi: 10.1136/ard.2003.006478

Hyperuricaemia and gout have been reported in organ transplant patients treated with cyclosporin, an immunosuppressant inhibiting calcineurin.[1 2] Tacrolimus, another calcineurin inhibitor, is nowadays widely used in place of cyclosporin. Hyperuricaemia has been seen in patients receiving tacrolimus[3] but, to our knowledge, only rare cases of gout have been mentioned so far.[4]

Since 1998, 31 patients (22 men, 9 women; current mean age 53 years (range 24–67)) have regularly received tacrolimus for immunosuppression after liver transplantation in the surgical department of Lausanne University Hospital. The mean duration of follow up with tacrolimus treatment was 27.8 months (range 7–57).

In two cases the first manifestations of gout appeared after liver transplantation when these two patients were receiving tacrolimus for immunosuppression.

CASE REPORTS

Patient 1

A 31 year old man received a liver transplant in November 1998. He was treated with tacrolimus at a daily dose of 6 mg, as well as prednisone. He also was receiving treatment with furosemide. In July 1999 he presented episodes of acute arthritis of the right wrist and both elbows. The serum uric acid level was 421 µmol/l and creatinine 105 µmol/l. Gout was not diagnosed until March 2000, when he started to have severe compression of the right median nerve, owing to a voluminous mass located in the anterolateral part of the wrist (fig 1A), which was suspected to be tumoral. Histological examination of the resected material revealed typical gouty tophi (fig 1B). After surgery, he was treated with allopurinol and colchicine. To treat hypertension, he received furosemide and losartan; this latter drug was chosen because it has been shown to have uricosuric properties[5] and has proved to be beneficial in hypertensive gouty subjects.[6]

Patient 2

A 25 year old woman who received a transplant in 1996 for type 1 A glycogen storage disease has been treated with tacrolimus since then. Attacks of podagra and arthritis of the left wrist occurred 5 years later when she was receiving tacrolimus 4 mg/day. No tophi could be seen. The serum level of uric acid was 452 µmol/l and of creatinine 190 µmol/l. From the time of diagnosis she has been receiving allopurinol 100 mg/day, and the attacks of gout have resolved.

DISCUSSION

In a large series of patients who had received a liver allograft, hyperuricaemia was detected in about half, in both cyclosporin and tacrolimus treated patients.[4] It was assumed that both drugs can impair renal uric acid excretion.[3 4]

In our series of liver transplant recipients receiving tacrolimus, gout was directly related to tacrolimus treatment in two. In case No 1, large tophaceous deposits developed

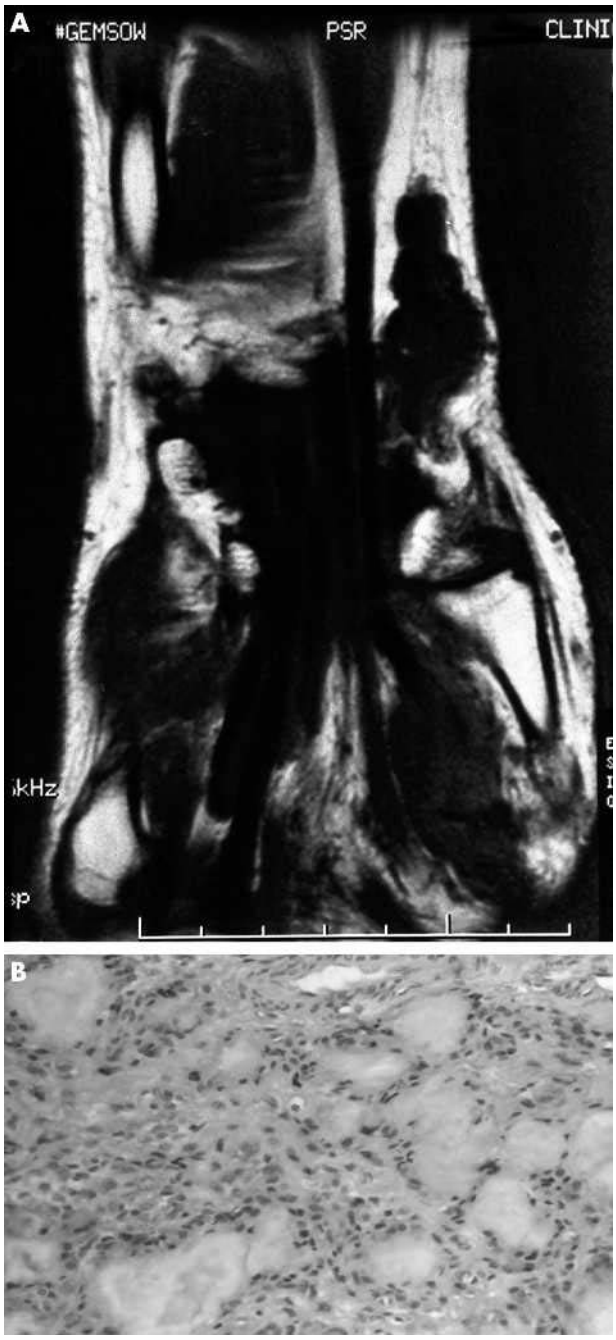

Figure 1 (A) Magnetic resonance T_1 coronal view showing a polylobed mass of low signal intensity in the radial aspect of the wrist. (B) Histological picture of the mass: large amorphous areas of monosodium urate crystal deposits surrounded by macrophages and giant cells (haematoxylin and eosin ×20).

very quickly within an interval of 8 months. The same observation has been frequently made with cyclosporin.[1 2] Although that patient was also taking diuretics, the causal relationship between tophaceous gout and tacrolimus treatment seems very probable. In case No 2, it is unlikely that her glycogen storage disease could have been a favouring factor for gout because liver transplantation cures the metabolic abnormalities associated with such disease.[7]

Although no case of gout has been found in the series of patients receiving liver transplants reported by Taillandier *et al*,[8] gout was diagnosed in 6% of the series of Neal *et al*.[4] Although until now cyclosporin has been considered to be the main cause of gout in transplant recipients, our study supports the idea that tacrolimus can similarly induce gout. It appears important to recognise that tacrolimus is a drug favouring hyperuricaemia and gout in some transplant patients, even if probably less likely than cyclosporin. Being aware of this possibility is important so that gout can be treated as early as possible to avoid occurrence of dramatic tophaceous gout, as illustrated in one of our cases.

ACKNOWLEDGEMENTS

We thank Dr L Guillou of the Institut Universitaire de Pathologie, CHUV, Lausanne, for the histological examinations.

Authors' affiliations

J C Gerster, M Dudler, Department of Rheumatology, University Hospital (CHUV), Lausanne, Switzerland
N Halkic, M Gillet, Department of Surgery, University Hospital (CHUV), Lausanne, Switzerland

Correspondence to: Professeur J C Gerster, Service de Rhumatologie, CHUV, 1011 Lausanne, Switzerland; Jean-Charles.Gerster@chuv.hospvd.ch

Accepted 24 August 2003

REFERENCES

1 **Lin HY**, Rocher LL, McQuillan MA, Schmaltz S, Palella T, Fox IH. Cyclosporine-induced hyperuricemia and gout. *N Engl J Med* 1989;**321**:287–92.
2 **George T**, Mandell BF. Gout in the transplant patient. *J Clin Rheumatol* 1995;**1**:328–34.
3 **Van Thiel DH**, Iqbal M, Jain A, Fung J, Todo S, Starzl TE. Gastrointestinal and metabolic problems associated with immunosuppression with either CyA or FK 506 in liver transplantation. *Transplant Proc* 1990;**22**:37–50.
4 **Neal DA**, Tom BD, Gimson AE, Bibbs P, Alexander GJ. Hyperuricemia, gout, and renal function after liver transplantation. *Transplantation* 2001;**72**:1689–91.
5 **Minghelli G**, Seydoux C, Goy JJ, Burnier M. Uricosuric effect of the angiotensin II receptor antagonist losartan in heart transplant recipients. *Transplantation* 1998;**66**:268–71.
6 **Würzner G**, Gerster JC, Chiolero A, Maillard M, Fallab-Stubi CL, Brunner HR, *et al*. Comparative effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricaemia and gout. *J Hypertens* 2001;**19**:1855–90.
7 **Matern D**, Starzl TE, Arnaout W, Barnard J, Bynon JS, Dhawan A, *et al*. Liver transplantation for glycogen storage disease types I, III and IV. *Eur J Pediatr* 1999;**158**(Suppl 2):S43–8.
8 **Taillandier J**, Alemanni M, Lioté F, Rucay P, Samuel D, Bismuth H. Serum uric acid and liver transplantation. *Transplant Proc* 1995;**27**:2108–90.