patients with histologically proved TA. IgM directed against human para-influenza type 1 virus were associated with TA onset.¹⁵

In conclusion, intra-alveolar haemorrhage may be one of the various causes of cough in TA. Further studies are necessary to ascertain whether it is the expression of a primary vasculitis or the consequence of an as yet unknown viral infection.

Authors' affiliations

D Le Thi Huong, M R Andreu, P Duhaut, P Godeau, J C Piette,
Department of Internal Medicine, Groupe Hospitalier Pitié-Salpêtrière,
83 bd de l'Hôpital, 75013 Paris, France

Correspondence to: Dr D Le Thi Huong; du.boutin@wanadoo.fr

Accepted 20 June 2002

REFERENCES

- Hunder GG, Bloch DA, Michel BA, Stevens MB, Arend WP, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 1990;33:1122–8.
- Machado EBV, Michet CJ, Ballard DJ, Hunder GG, Beard CM, Chu CP, et al. Trends in incidence and clinical presentation of temporal arteritis in Olmsted County, Minnesota, 1950–1985. *Arthritis Rheum* 1988;31:745–9.
- Joomaye Z, Sotto A, Jourdan J. Toux isolée prolongée due à la maladie de Horton. *Rev Mal Respir* 1997;14:59–60.
- Rischmueller M, Davies RP, Smith MD. Three year follow-up of a case of giant cell arteritis presenting with a chronic cough and upper limb ischaemic symptoms. *Br J Rheumatol* 1996;35:800–2.
- Le Thi Huong D, de Gennes C, Papo T, Wechsler B, Bletry O, Piette JC, et al. Manifestations pleuropulmonaires des vascularites systémiques. *Rev Med Interne* 1996;17:640–52.
- Blockmans D, Knockaert D, Bobbaers H. Giant cell arteritis can be associated with T4-lymphocytic alveolitis. *Clin Rheumatol* 1999;18:330–3.
- Herry I, Cadranet J, Antoine M, Meharzi J, Michelson S, Parrot A, et al. Cytomegalovirus-induced alveolar hemorrhage in patients with AIDS: a new clinical entity? *Clin Infect Dis* 1996;22:616–20.
- Kaplan MH, Klein SW, McPhee J, Harper RG. Group B coxsackievirus infections in infants younger than three months of age: a serious childhood illness. *Rev Infect Dis* 1983;5:1019–32.
- Abbondanzo SL, English CK, Kagan E, McPherson RA. Fatal adenovirus pneumonia in a newborn identified by electron microscopy and in situ hybridization. *Arch Pathol Lab Med* 1989;113:1349–53.
- Ho M, Chen ER, Hsu KH, Twu SJ, Chen KT, Tsai SF, et al. An epidemic of enterovirus 71 infection in Taiwan. Taiwan Enterovirus Epidemic Working Group. *N Engl J Med* 1999;341:929–35.
- Takahashi Y, Teranishi A, Yamada Y, Yoshida Y, Hashimoto K, Sakamoto Y, et al. A case of congenital mumps infection complicated with persistent pulmonary hypertension. *Am J Perinatol* 1998;15:409–12.
- Gomez-Tello V, Onoro-Canaveral JJ, de la Casa Monje RM, Gomez-Casero RB, Moreno Hurtrez JL, Garcia-Montes M, et al. Diffuse recidivant alveolar hemorrhage in a patient with hepatitis C virus-related mixed cryoglobulinemia. *Intensive Care Med* 1999;25:319–22.
- Mitchell BM, Font RL. Detection of varicella zoster virus DNA in some patients with giant cell arteritis. *Invest Ophthalmol Vis Sci* 2001;42:2572–7.
- Gabriel SE, Espy M, Erdman DD, Bjornsson J, Smith TF, Hunder GG. The role of parvovirus B19 in the pathogenesis of giant cell arteritis: a preliminary evaluation. *Arthritis Rheum* 1999;42:1255–8.
- Duhaut P, Bosshard S, Calvet A, Pinede L, Demolombe-Rague S, Dumontet C, et al. Giant cell arteritis, polymyalgia rheumatica, and viral hypotheses: a multicenter, prospective case-control study. Groupe de Recherches sur l'Artérite à Cellules Géantes. *J Rheumatol* 1999;26:361–9.

Circulating soluble CD40 ligand in patients with eosinophilic fasciitis

M Jinnin, H Ihn, N Yazawa, Y Asano, K Yamane, K Tamaki

Ann Rheum Dis 2003;62:190–191

Recently, some reports showed the increased expression of CD40 ligand in autoimmune diseases. CD40 ligand can be expressed in a soluble form.^{1,2} Soluble CD40 ligand (sCD40L) is present in supernatants of in vitro activated T cells in 15 kDa and 18 kDa forms, and these forms are the products of enzymatic cleavage at a metalloproteinase sensitive site in the membrane proximal region of the extracellular domain of the molecule.¹ Their abnormalities have been demonstrated in various kinds of diseases such as chronic lymphocytic leukaemia² or systemic lupus erythematosus.¹ But, there has been no report demonstrating the serum levels of sCD40L in patients with eosinophilic fasciitis (EF). In this study we determined the serum levels of sCD40L in patients with EF, and investigated their clinical significance in this disease, in order to evaluate whether sCD40L might be a useful marker for this disease.

METHODS AND RESULTS

Eleven patients (disease duration 1–8 months) with a classic clinical picture of EF, who had received no treatment, were included in this study. All the patients had a recent history of increased skin induration. Skin biopsies including deep subcutaneous tissue and fascia showed markedly indurated and thickened fascia in all cases. Additionally, the thickened fascia contained accumulation of collagen and intense inflammatory cell infiltrates comprising lymphocytes, macrophages, and eosinophils. Clinical manifestations and labora-

tory findings of each patient were obtained from the medical records. All the laboratory findings were obtained at the time of serum sampling. We also collected control serum samples from 20 healthy volunteers matched for age and sex. Levels of sCD40L were measured with a specific enzyme linked immunosorbent assay (ELISA) kit (Bender MedSystems, Vienna, Austria), according to the manufacturer's instructions. Values greater than the mean plus 2SD for normal control subjects were regarded as raised. Additionally, serum IgG was evaluated by a turbidimetric immunoassay as described previously.³ Statistical analysis was carried out with Student's *t* test for the comparison of means, and Fisher's exact probability test for the analysis of frequency. Values of *p* < 0.05 were considered significant.

Figure 1 shows the serum sCD40L levels in patients with EF and in the healthy control subjects. The serum sCD40L levels in patients with EF were significantly higher than those in the healthy controls (mean (SD) 0.29 (0.16) ng/ml v 0.13 (0.08) ng/ml, *p* < 0.01). When the cut off value was set at 0.29 ng/ml (mean + 2SD for the controls), raised serum sCD40L levels were seen in 5/11 (45%) patients with EF.

Serum sCD40L levels correlated significantly with serum IgG levels (*r* = 0.75, *p* < 0.05). On the other hand, serum sCD40L levels were not significantly correlated with serum gammaglobulin, peripheral cell count of eosinophils, erythrocyte sedimentation rate, or serum levels of aldolase. Additionally, three of the five patients with raised serum

Figure 1 Serum soluble CD40 ligand (sCD40L) levels determined with specific ELISAs in serum samples from patients with EF and healthy control subjects. Bars show means. The horizontal dotted line represents 2SD above the mean value of healthy controls. p Values were determined by Student's *t* test.

Figure 2 Longitudinal study of serum soluble CD40 ligand (sCD40L) levels in patients with EF.

sCD40L levels were examined longitudinally before and after corticosteroid treatment for two months to three years. Their clinical manifestations and laboratory abnormalities improved with treatment. Serum sCD40L levels became normal in all three patients (fig 2).

DISCUSSION

As described above, expression of sCD40L in patients with several connective tissue diseases has already been evaluated and shown to be increased. Berner *et al* reported that increased expression of CD40 ligand on CD4+ T cells in rheumatoid arthritis indicated prolonged and increased activation of CD4+ T lymphocytes and was associated with active disease and, possibly, an unfavourable prognosis.⁴ Valentini *et al* found that expression of CD40 ligand in activated CD4+ T lymphocytes was increased in patients with systemic sclerosis.⁵ On the other hand, Vakkalanka *et al* reported that the mean concentration of serum sCD40L was statistically significantly higher in patients with systemic lupus erythematosus (SLE) than in disease controls or healthy subjects, and segregation of patients with SLE by severe, moderate, or mild extent of disease showed a relationship between disease

severity and sCD40L concentration.¹ These findings suggest that CD40 ligand or sCD40L are associated with clinical features of these diseases. In our study, serum levels of sCD40L in patients with EF were significantly higher than those in healthy controls. sCD40L is present in supernatants of *in vitro* activated T cells.¹ In patients with EF, activated T cells were thought to be increased because of the presence of raised interleukin 5 and interleukin 10.⁶ Thus, our results may reflect such a condition. Additionally, serum levels of sCD40L correlated significantly with serum IgG levels in patients with EF, and serum sCD40L levels normalised after treatment in patients with raised sCD40L levels. As well as peripheral cell counts of eosinophils, erythrocyte sedimentation rate or serum levels of aldolase, hypergammaglobulinaemia is reported to be one of the markers of disease activity,^{7,8} which occurs in 75% of patients and is usually due to a polyclonal increase in IgG.⁹ Thus, our results suggest that sCD40L is also good marker of EF, reflecting the effects of treatment. However, only 5/11 patients showed raised levels of sCD40L. Thus, the usefulness of sCD40L as a marker of disease activity was not completely substantiated in this study. Additionally, serum sCD40L levels did not correlate with gammaglobulin despite significant correlation with IgG, possibly owing to the small number of patients studied. Moreover, we performed the longitudinal study in only three patients with raised sCD40L levels because other serum samples were not available, so the longitudinal data may be incomplete. Additionally, there is a possibility that corticosteroid treatment, independently of disease, can reduce sCD40L levels. Further studies are needed to clarify the significance of the role of sCD40L in this disease.

Author's affiliations

M Jinnin, H Ihn, N Yazawa, Y Asano, K Yamane, K Tamaki, Department of Dermatology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-Ku, Tokyo 113-8655, Japan

Correspondence to: Dr H Ihn; IN-DER@h.u-tokyo.ac.jp

Accepted 7 June 2002

REFERENCES

- Vakkalanka RK, Woo C, Kirou KA, Koshy M, Berger D, Crow MK. Elevated levels and functional capacity of soluble CD40 ligand in systemic lupus erythematosus sera. *Arthritis Rheum* 1999;**42**:871–81.
- Hollenbaugh D, Grosire I, Kullas C, Chalupny NJ, Braesch-Andersen S, Noelle RJ, *et al*. The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell costimulatory activity. *EMBO J* 1992;**11**:4314–21.
- Bergstrom M, Lefvert AK. An automated turbidimetric immunoassay for plasma proteins. *Scand J Clin Lab Invest* 1980;**40**:637–40.
- Berner B, Wolf G, Hummel KM, Muller GA, Reuss-Borst MA. Increased expression of CD40 ligand (CD154) on CD4+ T cells as a marker of disease activity in rheumatoid arthritis. *Ann Rheum Dis* 2000;**59**:190–5.
- Valentini G, Romano MF, Naclerio C, Bisogni R, Lamberti A, Turco MC, *et al*. Increased expression of CD40 ligand in activated CD4+ T lymphocytes of systemic sclerosis patients. *J Autoimmun* 2000;**15**:61–6.
- Viallard JF, Taupin JL, Ranchin V, Leng B, Pellegrin JL, Moreau JF. Analysis of leukemia inhibitory factor, type 1 and type 2 cytokine production in patients with eosinophilic fasciitis. *J Rheumatol* 2001;**28**:75–80.
- Falanga V, Medsger TA. Frequency, levels, and significance of blood eosinophilia in systemic sclerosis, localized scleroderma, and eosinophilic fasciitis. *J Am Acad Dermatol* 1987;**17**:648–56.
- Fujimoto M, Sato S, Ihn H, Kikuchi K, Yamada N, Takehara K. Serum aldolase level is a useful indicator of disease activity in eosinophilic fasciitis. *J Rheumatol* 1995;**22**:563–5.
- Doyle JA, Glinesberg WW. Eosinophilic fasciitis. *Med Clin North Am* 1989;**73**:1157–66.