Takayasu's arteritis, and isolated vasculitis of the vasa vasorum.[9] Histopathological analysis often discloses arterial thrombosis associated with non-giant cell, non-necrotising, and non-granulomatous vasculitis. A search for blood coagulation disorders has never been performed until now. Factor V Leiden is a well known risk factor for venous thrombosis but may also play a part in arterial thrombosis, particularly myocardial infarction[10] or ischaemic cerebrovascular disease.[11] Even if we cannot exclude a fortuitous association in our case, factor V Leiden mutation might have played a role in arterial thrombosis. This observation reminds doctors of this rare entity and highlights the need to study blood coagulation in cases of JTA.

Authors' affiliations
B Granel, J Serratrice, N Ene, P Disdier, P-J Weiller, Service de Médecine Interne, Hôpital de la Timone, 264 rue Saint Pierre, 13385 Marseille, cedex 5, France
P E Morange, Laboratoire d'Hématologie, Hôpital de la Timone, 264 rue Saint Pierre, 13385 Marseille, cedex 5, France

Correspondence to: Dr P Disdier; patrick.disdier@ap-hm.fr

Accepted 12 May 2003

REFERENCES

1 **Lie JT**, Gordon LP, Titus JL. Juvenile temporal arteritis. Biopsy study of four cases. *JAMA* 1975;**234**:496–9.
2 **Villalta J**, Estrach T. Temporal arteritis with normal erythrocyte sedimentation rate. *Ann Intern Med* 1985;**103**:808.
3 **Genereau T**, Herson S, Piette JC, Coutellier A, Pelletier S, Wechsler B, *et al.* Temporal arteritis in young subjects. A trial of nosological classification on 6 cases. *Ann Med Interne (Paris)* 1992;**143**:303–8.
4 **Fielding DI**, Brown IG. Temporal arteritis in a young patient with a normal erythrocyte sedimentation rate. *Aust NZ J Med* 1994;**24**:66–7.
5 **Tomlinson FH**, Lie JT, Nienhuis BJ, Konzen KM, Groover RV. Juvenile temporal arteritis revisited. *Mayo Clin Proc* 1994;**69**:445–7.
6 **Lie JT**. Bilateral juvenile temporal arteritis. *J Rheumatol* 1995;**22**:774–6.
7 **Carreiro M**, Margarit-Coll N, Oksman A, Dahan S, Ollier S, Sailler L, *et al.* Juvenile temporal arteritis: a benign disease. *Rev Med Interne* 2003;**24**:138–9.
8 **Olsen TG**, Heing EB. Angiolymphoid hyperplasia with eosinophilia: a clinicopathologic study of 116 patients. *J Am Acad Dermatol* 1985;**12**:781–96.
9 **Disdier P**, Pellissier JF, Harle JR, Figarella-Branger D, Bolla G, Weiller PJ. Significance of isolated vasculitis of the vasa vasorum on temporal artery biopsy. *J Rheumatol* 1994;**21**:258–60.
10 **Doggen CJ**, Cats VM, Bertina RM, Rosendaal FR. Interaction of coagulation defects and cardiovascular risk factors: increased risk of myocardial infarction associated with factor V Leiden or prothrombin 20210A. *Circulation* 1998;**97**:1037–41.
11 **De Lucia D**, Nina P, Papa ML, Belli A, Conte M, Renis V, *et al.* Activated protein C resistance due to a factor V mutation associated with familial ischemic stroke. *J Neurosurg Sci* 1997;**41**:373–8.

Serum osteoprotegerin but not receptor activator of NF-κB ligand correlates with Larsen score in rheumatoid arthritis

M Skoumal, G Kolarz, W Woloszczuk, G Hawa, A Klingler

Ann Rheum Dis 2004;**63**:216–217. doi: 10.1136/ard.2002.004507

Osteoprotegerin (OPG) is a soluble decoy receptor, produced by osteoblastic cells and in the inflamed synovium of RA by dendritic cells, B cells, and other immunocompetent cells.[1 2] It inhibits the differentiation of osteoclast precursor cells and the activation of mature osteoclasts by neutralising the receptor activator of NF-κB ligand (RANKL).[3]

RANKL, a member of the tumour necrosis factor family, is expressed on prae-osteoblasts and T lymphocytes. A soluble RANKL (sRANKL) can be produced by activated T lymphocytes or can be generated from the cell bound form by a protease. RANKL itself activates a receptor activator of NF-κB (RANK).[4]

RANKL, together with monocyte-colony stimulating factor, interleukin 1, and RANK is responsible for osteoclast formation and activation and inhibits osteoclast apoptosis. Thus OPG acts as antagonist to RANKL. An imbalance of this system may play a part in the skeletal complications of rheumatoid arthritis (RA).[5]

Our study aimed at comparing OPG and sRANKL in the serum of patients with RA.

We identified 44 patients with RA (24 female, 20 male, mean age at manifestation of RA 49 years) with 60 measurements. Sixteen patients received low dose steroids, five patients showed generalised osteoporosis (*x* ray and/or osteodensitometry).

The results were analysed by Spearman correlation statistics and Wilcoxon two sample test.

Serum OPG levels were measured in patients with RA using a sandwich-type enzyme linked immunosorbent assay

Table 1 Correlation of OPG and sRANKL with clinical data

				OPG		sRANKL	
Clinical data	**Mean**	**SD**	**No**	r_s	**p Value**	r_s	**p Value**
sRANKL (pmol/l)	0.90	0.85	60	0.21	0.10		
ESR (mm/1st h)	37.3	24.2	60	0.29	0.03	0.004	0.77
CRP (mg/l)	38.2	30.5	60	0.15	0.24	0.09	0.49
RF (U/l)	418.5	1584.8	60	0.02	0.90	0.05	0.71
DAS	3.44	1.09	60	0.21	0.11	0.02	0.86
Larsen score	49.7	44.7	60	0.32	0.01	−0.02	0.85

OPG, osteoprotegerin, sRANKL, soluble receptor activator of NF-κB ligand; ESR, erythrocyte sedimentation rate, CRP, C reactive protein; RF, rheumatoid factor; DAS, disease activity score.

(ELISA) based on two OPG-specific antibody preparations. The mean value of a healthy control group of 170 blood donors[6] is 2.2 pmol/l (2.0 pmol/l for men, 2.4 pmol/l for women).

sRANKL was measured by an enzyme catalysed colour change detectable on a standard ELISA reader. To measure only the biologically active form(s) of sRANKL biosynthetic OPG/Fc was used as capture protein. The mean value of serum sRANKL levels in healthy subjects was calculated as 1.3 pmol/l (median 0.9).

We detected serum levels of OPG with a mean value of 4.2 pmol/l (SD 2.0) and serum levels of RANKL with a mean value of 0.9 pmol/l (SD 0.8). We found a significant correlation between OPG and erythrocyte sedimentation rate (ESR) and OPG and the Larsen score but no correlation between RANKL and OPG or between RANKL and the clinical and radiological measures (table 1).

No significantly different OPG levels were found either in patients receiving steroids or in patients with osteoporosis.

In RA RANKL leads to bone erosions by activation of osteoclasts, and this process is inhibited by OPG.[7] Therefore OPG seems to play an important part in preventing erosions and osteoporosis in patients with RA. Kolarz *et al* suggested that patients with active inflammation may show higher OPG values owing to activation of several other cells.[8] Haynes *et al* showed an increased expression of RANKL in tissues surrounding bone erosions and at the same time OPG was absent in tissues from patients with active RA.[9]

Despite the presence of raised serum OPG levels acting as protection mechanism, the local destructive effect of RANKL by activation of osteoclasts seems not to be fully balanced.

The up regulation of OPG might be a response to the inflammation; in contrast an up regulation of RANKL could not be found in the serum of patients with RA.

Haynes *et al* reported that OPG and RANKL behave differently depending on the cells which produce them.[10] A further explanation may be the different strategies of both assays: the OPG assay measures free and bound OPG, the sRANKL assay only free sRANKL; complexes formed from OPG and sRANKL would therefore be detected only with the OPG, but not with the sRANKL assay.

Authors' affiliations
M Skoumal, G Kolarz, Institut für Rheumatologie der Kurstadt Baden in Kooperation mit der Donauuniversität Krems, Rheumasonderkrankenanstalt der SVA der gewerblichen Wirtschaft, Baden, Austria
W Woloszczuk, Ludwig Boltzmann Institut für experimentelle Endokrinologie, Vienna, Austria
G Hawa, Biomedica Medizinprodukte GmbH & Co KG, Austria
A Klingler, Theoretical Surgery Unit, Department of General and Transplant Surgery, University Hospital, Innsbruck, Austria

Correspondence to: Dr M Skoumal, Rheumasonderkrankenanstalt der SVA der gewerblichen Wirtschaft, Adolfine Malchergasse 1, 2500 Baden, Austria; martin.skoumal@a1.net

Accepted 28 April 2003

REFERENCES

1 **Simonet WS**, Lacey DL, Dunstan CR, Kelley M, Chang MS, Luthy R, *et al*. Osteoprotegerin: A novel secreted protein involved in the regulation of bone density. *Cell* 1997;**89**:309–19.
2 **Itonaga I**, Fujikawa Y, Sabokar A, Murray DW, Athanasou NA. Rheumatoid arthritis synovial macrophage–osteoclast differentiation is osteoprotegerin ligand-dependent. *J Pathol* 2000;**192**:97–104.
3 **Burgess TL**, Qian Y, Kaufman S, Ring BD, Van G, Capparelli C, *et al*. The ligand for osteoprotegerin (OPGL) directly activates mature osteoclasts. *J Cell Biol* 1999;**145**:527–38.
4 **Hofbauer LC**, Heufelder AC. Role of receptor activator of nuclear factor -κB ligand and osteoprotegerin in bone cell biology. *J Mol Med* 2001;**79**:243–53.
5 **Takayanagi H**, Iizuka H, Juji T, Nakagawa T, Yamamoto A, Miyazaki T, *et al*. Involvement of receptor activator of nuclear factor-κB ligand osteoclast differentiation factor in osteoclastogenesis from synoviocytes in rheumatoid arthritis. *Arthritis Rheum* 2000;**43**:259–69.
6 **Kudlacek S**, Schneider B, Woloszczuk W, Pietschmann P, Willvonseder R. Serum levels of osteoprotegerin increase with age in healthy adult population. *Bone* 2003;**32**:681–6.
7 **Gravallese EM**, Manning C, Tsay A, *et al*. Synovial tissue in rheumatoid arthritis is a source of osteoclast differentiation factor. *Arthritis Rheum* 2000;**43**:250–8.
8 **Kolarz G**, Schödl CH, Skoumal M, Woloszczuk W, Wottawa A. Osteoprotegerin serum levels in rheumatoid arthritis: *J Mineralstoffwechsel*, (in press).
9 **Haynes DR**, Crotti TN, Loric M, Bain GI, Atkins GJ, Findlay DM. Osteoprotegerin and receptor activator of nuclear factor-κB ligand (RANKL) regulate osteoclast formation by cells in the human rheumatoid arthritic joint. *Rheumatology (Oxford)* 2001;**40**:623–30.
10 **Haynes DR**, Barg E, Crotti TN, Holding C, Weedon H, Atkins GJ, *et al*. Osteoprotegerin expression in synovial tissue from patients with rheumatoid arthritis, spondylarthropathies and osteoarthritis and normal controls. 2003;**42**:123–34.

Successful management of neonatal cryoglobulinaemia after a gemellar pregnancy in a woman with symptomatic type I cryoglobulinaemia

J Sibilia, O Feugeas, V Laugel, A Dreval, J Messer, J Goetz

Ann Rheum Dis 2004;**63**:217–218. doi: 10.1136/ard.2002.000174

CASE REPORT

Since 1996 a 32 year old woman had had cold-induced clinical manifestations: Raynaud's phenomenon, livedo reticularis, necrotic and purpuric lesions on the legs, and acrocyanosis on the ears and fingers. She had no family history of cold intolerance, autoimmune disease, or recurrent thrombosis. In 1998 these symptoms were traced to a monoclonal IgG1λ cryoglobulin (type I) present at 1.5 g/l and precipitating at 27°C. Cold agglutinin and cryofibrinogen were absent while total complement (CH_{50}) and C4 fraction were low. There were no antinuclear, anti-dsDNA, anti-neutrophil, anticardiolipin, or anti-β2-glycoprotein I antibodies, and viral serology was negative for hepatitis B and C and cytomegalovirus. A skin biopsy showed leucocytoclastic vasculitis and thrombosis of the capillaries related to the cryoglobulin. There were no renal, gastrointestinal, or neurological manifestations, but the patient had intermittent distal polyarthritis and was treated with pentoxifylline accompanied by protective measures against cold.

This mother had born a first healthy child in 1996 and had experienced no previous miscarriage. In 2000, during a second dichorionic gestation of twins, the lesions were progressive while the cryoglobulin persisted at 1.10 g/l. Because the IgG1λ chain can cross the placenta and the initial temperature of cryoprecipitation was 27°C, clinical manifestations could be expected in the newborns at room