Letter to the Editor

A Case of Hepatitis C-associated Osteosclerosis in an Elderly Man. Comment on the Article by Tanaka *et al.*

Dear Sir;

We read with interest the article by Tanaka *et al.* [1], in which the Authors described a new case of hepatitis C-associated osteosclerosis (HCAO), an impressive and rare bone disorder characterized by acquired diffuse osteosclerosis in adulthood occurring in patients infected with hepatitis C virus (HCV). They affirmed that since 1992 twelve cases of HCAO have been reported, nine from the United States, two from Japan, one from Australia and one from Italy, whose age ranged from 27 to 73, so they stated that their 68-year-old Japanese patient is the 13th reported case with HCAO [1].

Actually, we recently described a 74-year-old Italian man affected by HCAO [2] that Tanaka *et al.* did not report. Our patient, the oldest one with HCAO, presented a long lasting history of skeletal pain, starting nearly simultaneously to the HCV infection, and a dramatic increase of bone mass [2]. Of note, in our HCAO patient we studied the receptor activator of nuclear factor- κ B (RANK), its ligand (RANKL), and soluble decoy receptor osteoprotegerin (OPG) system, whose

role in the control of bone remodelling has been recently highlighted [3]. The patient's bone tissue was characterized by a high number of OPG-positive osteoblasts, a moderate increase of RANKL-positive stromal cells, and a severe reduction of the osteoclasts [2]. Moreover, OPG serum levels were enhanced. Interestingly, HCV-infected controls, in the absence of bone alterations, presented a similar ratio between OPG-positive osteoblasts and RANKL-positive stromal cells compared with the HCAO patient, suggesting that even a reduced sensitivity by the osteoclast progenitors may occur in this condition, further contributing to the blunted osteoclastogenesis [2]. These findings are consistent with a pathogenetic role of the OPG/RANKL system imbalance in HCAO. The involvement of the OPG/RANKL network has been also underlined by Fiore *et al.*, reporting on another Italian HCAO patient [4].

We think that this new pathogenetic perspective may contribute to the understanding of such a rare and amazing bone disorder, and we hope that further studies will elucidate these interesting aspects.

References

1. Tanaka T, Oki S, Muro S, Tanaka K, Hashimoto J (2006) A case of hepatitis C-associated osteosclerosis in an elderly man. *Endocrine J* 53: 393–399.
2. Manganelli P, Giuliani N, Fietta P, *et al.* (2005) OPG/RANKL system imbalance in a case of hepatitis C-associated osteosclerosis: the pathogenetic key? *Clin Rheumatol* 24: 296–300.
3. Hofbauer LC, Heufelder AE (2001) Role of receptor activator of nuclear factor- κ B ligand and osteoprotegerin in bone cell biology. *J Mol Med* 79: 243–253.
4. Fiore CE, Riccobene S, Mangiafico R, Santoro F, Pennisi P (2005) Hepatitis C-associated osteosclerosis (HCAO): report of a new case with involvement of the OPG/RANKL system. *Osteoporosis Int* 16: 2180–2184.

PIERANNA Fietta and PAOLO Manganelli

Osteo-Articular Department, Rheumatic Disease and Internal Medicine Unit, Hospital and University of Parma, Via Gramsci, 14, 43100 Parma, Italy

Correspondence to: Pieranna FIETTA, M.D., Osteo-Articular Department, Rheumatic Disease and Internal Medicine Unit, Hospital and University of Parma, Via Gramsci, 14, 43100 Parma, Italy