

HEPATITIS C-ASSOCIATED OSTEOSCLEROSIS (HCAO): REPORT OF A NEW CASE WITH INVOLVEMENT OF THE OPG/RANKL SYSTEM

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Hepatitis C virus (HCV) is predominantly hepatotropic virus. The morbidity and mortality associated with HCV infection, however, are not only dependent on the consequences of liver disease, but also on extra-hepatic manifestations. A syndrome was characterized a few years ago in patients infected with hepatitis C virus that featured acquired, severe, generalized osteosclerosis and hyperostosis. To date, 11 cases have been reported which appeared to have acquired HCV infection from blood transfusion or by i.v. drug abuse. We report a new case of hepatitis C-associated osteosclerosis (HCAO) in Europe, whose viral infection was not acquired from blood transfusion or i.v. drug abuse. The clinical presentation of the patient, 65 years old, was an acquired deep severe bone pain with increased serum ALP activity (up to 1.2 times the upper limit of normal, with 92% of bone isoform and 8% liver isoform), and generalized bone sclerosis (documented by spine, humerus, pelvis, hips and tibia X-Ray) temporally related to the hepatitis C-virus (HCV) infection. No fractures were present in the past medical history. Serum calcium, phosphorus, 25-hydroxy-vitamin D, serum acid phosphatase activity and creatinine were normal. Serum PTH was elevated, perhaps secondary to avoid net bone formation or in some cases to mild hyperparathyroidism. Urinary indicator of bone resorption were also normal. Bone biopsy of an iliac crest showed dense cortical bone with no defective bone remodelling. The HCAO pathogenesis is still unknown. Recently, the receptor activator of nuclear factor- κ (RANK) its ligand (RANKL) and soluble receptor osteoprotegerin (OPG) have been identified as a cytokine system in the bone remodelling control. We documented in this patient an increase of circulating osteoprotegerin (OPG = 7.6 pmol/l) (normal range: 3.4±1.05 pmol/l), and a concentration of circulating receptor activator for RANKL below the lower limit of the reference range, to may reflect the lack of a compensatory response to enhanced osteoblast activity. The observed abnormalities of the OPG/RANKL system may contribute to the maintenance of the positive balance of bone remodelling that characterizes patients with HCAO. Since hepatitis C virus induces overexpression of the proto-oncogene c-fos and of other oncogenes (involved in increased bone formation, osteosclerosis and osteopetrosis) it would be interesting to evaluate whether the osteosclerosis observed in HCV-infected patients is dependent on up-regulation of these factors.