

The role of the proinflammatory cytokine TNF- α in acute Charcot osteoarthropathyNL Petrova¹, C Moniz², G Mabileau³, A Sabokbar³, ME Edmonds¹¹Diabetic Foot Clinic, King's College Hospital, London, UK²Department of Clinical Biochemistry, King's College Hospital, London, UK³Botnar Research Centre, Nuffield Department of Orthopaedic Surgery, University of Oxford, Oxford, UK

Background and aims: The proinflammatory cytokine tumour necrosis factor-alpha (TNF- α) can stimulate osteoclastogenesis independently of receptor activator of nuclear factor kappa/beta ligand (RANKL). The aim was to investigate a possible association between TNF- α and osteoclastic bone resorption in acute Charcot osteoarthropathy, measured in vivo and in vitro. **Methods:** We studied 9 patients with acute Charcot osteoarthropathy and 8 diabetic controls, matched for age, duration, type of diabetes and degree of neuropathy. We measured serum levels of C-Terminal Telopeptide (CTx), an osteoclastic resorption marker, as well as serum levels of high sensitivity TNF- α (hsTNF- α). Osteoclast formation and resorption were measured in vitro. Peripheral blood mononuclear cells (PBMCs) were cultured with macrophage-colony stimulating factor (M-CSF) and RANKL and also after the addition of osteoprotegerin (OPG) **Results:** Serum levels of CTx were significantly higher in patients with acute Charcot osteoarthropathy compared with diabetic patients (0.68 ng/ml \pm 0.47 versus 0.24 ng/ml \pm 0.13, p=0.021; mean \pm SD). There was significant correlation between CTx and hsTNF- α (r= 0.535, p=0.033). Although hsTNF- α levels were increased in acute Charcot osteoarthropathy, this did not reach significance (1.62 \pm 1.11 pg/ml versus 0.95 \pm 0.28 pg/ml, p=0.351). However, hsTNF-levels were significantly associated with the osteoclast formation (r=0.489, p=0.046) and resorption in cultures with M-CSF+sRANKL (r=0.605, p=0.013) and similarly with osteoclast formation (r=0.813, p<0.001) and resorption in cultures with M-CSF+RANKL+OPG (r=0.537, p=0.032). **Conclusions:** TNF- α may be important as an osteoclastic activator in acute Charcot osteoarthropathy and its inhibition may lead to future therapies.

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