

The acute Charcot foot is characterised by increased proinflammatory cytokines, TNF-alpha and IL-6, which correlate with its pathological bone turnoverM Edmonds¹, T Dew², R Musto², S Thompson², R Sherwood², C Moniz², N Petrova¹¹Diabetic Foot Clinic, ²Dept of Biochemistry, King's College Hospital, London, UK

The Charcot foot is characterised by acute inflammation but its role in the pathogenesis is poorly understood. This study shows that the proinflammatory cytokines, tumour necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6), as well as high sensitive C-reactive protein (hsCRP)- an acute phase protein, are raised in acute Charcot osteoarthropathy and are significantly associated with serum C-telopeptide of type I collagen (CTX), a marker of bone resorption. We studied 3 groups of patients: 27 presenting with acute Charcot osteoarthropathy; 14 with chronic Charcot osteoarthropathy and 24 diabetic control patients. In acute Charcot patients, there was a significant increase in the serum levels of IL-6 (3.84 ± 3.55 pg/ml) compared with chronic Charcot patients (1.73 ± 1.23 pg/ml) and diabetic controls (1.86 ± 1.52 pg/ml), $p=0.025$. Furthermore, there was a significant rise in serum TNF-alpha in acute Charcot patients (1.74 ± 0.94 pg/ml) compared with chronic Charcot patients (1.25 ± 0.38) and diabetic control patients (1.12 ± 0.38 pg/ml), $p=0.008$. Similarly, serum levels of hsCRP were significantly increased in acute Charcot patients (10.1 ± 13.4 mg/l) compared with chronic Charcot patients (2.6 ± 2.2 mg/l) and diabetic control patients (4.8 ± 4.3 mg/l), $p=0.013$. Serum CTx, a breakdown product of type 1 collagen, was significantly raised in patients with acute Charcot foot (0.409 ± 0.395 ng/ml), compared with patients with chronic Charcot foot (0.095 ± 0.042 ng/ml) and diabetic patients (0.107 ± 0.68 ng/ml), $p=0.001$. Serum bone specific alkaline phosphatase (BAP), a marker of bone formation, was also significantly raised in acute Charcot patients (18.5 ± 9.2 μ g/L) compared with chronic Charcot patients (12.7 ± 4.42 μ g/L) and diabetic controls (14.7 ± 5.13 μ g/L), $p=0.041$. Serum osteoprotegerin (OPG), a cytokine that modulates bone resorption and osteoclastic activity, was significantly raised in acute Charcot patients (5.52 ± 1.74 pmol/l) compared with chronic Charcot patients (4.86 ± 1.42 pmol/l) and diabetic patients (4.37 ± 1.38 pmol/l), $p=0.048$. Serum IL-6 ($r=0.472$, $p<0.001$) and TNF-alpha levels ($r=0.556$, $p<0.001$) were significantly associated with serum CTx. Similarly, serum hsCRP levels were significantly correlated with serum CTx ($r=0.561$, $p<0.001$). This study indicates that inflammation, as reflected by the proinflammatory markers TNF-alpha and IL-6, and hsCRP plays an important role in the pathological bone resorption of the acute Charcot foot.