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The acute Charcot foot is characterised by increased proinflammatory cytokines, TNF-alpha and IL-6, which correlate with its pathological bone turnover

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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±2.2mg/l) and diabetic control patients (4.8±4.3mg/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 µg/L) compared with chronic Charcot patients (12.7±4.42 µg/L) and diabetic controls (14.7±5.13 µg/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.