Is There a Systemic Inflammatory Response in the Acute Charcot Foot?

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Although patients with acute Charcot osteoarthropathy exhibit a marked local inflammatory response to trauma by the classical presentation of a red, hot swollen foot, the systemic acute phase response has not been fully investigated. The aim of this study was to measure the systemic serologic markers of inflammation in acute Charcot osteoarthropathy.

RESEARCH DESIGN AND METHODS

— We studied 36 consecutive patients who presented to the Diabetic Foot Clinic over the last 5 years with a red, hot swollen foot and a skin temperature >2°C compared with the same site on the contralateral foot and who had no previous treatment. There was no evidence of any skin breakdown or ulceration. Foot skin temperatures were measured by Dermatemp 1001 (Exergen, Watertown, MA). The diagnosis of Charcot osteoarthropathy was confirmed in 25 cases by evidence of subluxation, dislocation, or fragmentation of bone on standard foot radiographs and in 11 cases by the presence of an increased focal uptake on the bony (third) phase of the triphasic Technetium-Diphosphonate bone scan (Tyco Healthcare) even though the radiographs at presentation were normal. In the patients with radiological abnormalities, the patterns of involvement were described using Sanders and Frykberg's classification (1). Four patients presented with pattern I (metatarsal-phalangeal joints), seven with pattern II (tarsometatarsal joints), four with pattern III (tarsal joints), one with pattern IV (ankle joint), and two with pattern V (calcaneum). Seven patients presented with multiple sites of involvement: six had a combination of patterns II and III, and one had patterns I and II. In the remaining 11 patients who presented with normal radiographs, there was increased focal uptake on the bony (third) phase of the triphasic Technetium Diphosphonate bone scan: 10 in the midfoot and 1 in the forefoot. These patients were similar to the Charcot foot stage 0 with normal radiograph and abnormal bone scan as described in Sella and Barrette's staging of Charcot osteoarthropathy (2).

Serum C-reactive protein (CRP), white cell count (WCC), erythrocyte sedimentation rate (ESR), Hb, and GHb were measured at presentation. Data on liver synthesis function including liver enzymes (aspartate transminase, alkaline phosphatase, and γ-glutamyl tranferase) and serum proteins (albumin and globulin) were also recorded. Renal function was assessed by serum creatinine levels.

Statistical analyses

Data are presented as median (25th–75th percentile). The limit for detection of the CRP assay was 5 mg/l, and therefore levels ≤5 mg/l were taken as 5 mg/l for the purpose of the analysis.

RESULTS

— There were 21 type 1 (11 male and 10 female) and 15 type 2 (7 male and 8 female) diabetic patients. Median age was 51 years (41–62), and median duration of diabetes was 20 years (13–26.5). Skin foot temperature was 3.1°C (2.4–4.2) greater in the Charcot foot compared with the contralateral foot. Median CRP level was 5.8 mg/l (5–11) and ≤5 mg/l in 47.2% of patients presenting with acute Charcot osteoarthropathy. Median ESR was 21 mm/h (13–36); WCC was 7.0 10\S\9/l (5.8–8.1), reference range 4–11; GHb was 8.5% (7.3–10.3), reference range <6; and Hb was 13.1 g/dl (11.7–14.7). Patients had preserved synthesis liver function as indicated by normal liver enzymes (median aspartate transminase 25 units/l [19–29], reference range 10–50; alkaline phosphatase 105 units/l [76–136], reference range 30–130; γ-glutamyl tranferase 26 units/l [18–43], reference range 1–55) and normal protein synthesis (median serum albumin 44 g/l [40–46], reference range 35–50, and serum globulin 29 g/l [27–31], reference range 25–35). The median creatinine level was 88 μmol/l (79–109), reference range 45–120, and only one patient had renal failure and was on hemodyalisis treatment.

CONCLUSIONS

— This report has shown that in the acute stage of Charcot osteoarthropathy, there is dissociation between the presence of local signs of inflammation, as demonstrated by increased skin temperature in the Charcot foot, and the lack of systemic response, as shown by a normal to slight increase in CRP levels, normal WCC, and mild increase in ESR. CRP is one of the well-established sensitive markers of inflammation widely used in clinical practice as a direct serological measure of acute phase response to injury and infection. The local inflammatory response seen in our patients may be related to increased expression of proinflammatory cytokines (3), but this did not lead to a classical systemic acute phase response. Lack of rise of CRP levels in our patients with acute Charcot osteoarthropathy cannot be related to abnormal hepatic synthesis, as both liver enzymes and albumin levels were within the reference range. Although there is evidence that CRP levels are markedly raised in patients with diabetic foot infection and osteomyelitis, some reports have suggested that it might be normal in patients with Charcot osteo-

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Abbreviations: CRP; C-reactive protein; ESR, erythrocyte sedimentation rate; WCC, white cell count.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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arthropathy (4,5). Indeed, in a small series of patients, serum CRP was significantly lower in patients with Charcot osteoarthropathy compared with patients with osteomyelitis (6). The WCC was normal in our patients with acute Charcot osteoarthropathy. Although the ESR was mildly raised in our patients, this was not related to anemia, as our patients had normal Hb levels. However, ESR has a high sensitivity but a low specificity, and there are many conditions that can lead to a rise in ESR in diabetic patients, including diabetic nephropathy per se. Thus, a moderate rise in ESR may not necessarily indicate the presence of acute Charcot osteoarthropathy (4).

Thus, there is dissociation between the local and systemic inflammatory response in acute Charcot osteoarthropathy. When patients present with a hot red foot, with no obvious skin breakdown and a CRP level that is normal or only slightly raised, acute Charcot osteoarthropathy should be firmly suspected.

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