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CAPSULAR SYNOVIAL AND BONE AMYLOIDOSIS: COMPLICATIONS OF LONG-TERM HAEMODIALYSIS

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Introduction

In 1980 Assenat et al [1] demonstrated amyloid infiltration in the synovium of a large number of haemodialysis patients with carpal tunnel syndrome. The fact that none of these patients suffered from amyloid disease led to the suggestion that long-term haemodialysis may cause amyloid deposition. In the present report we further demonstrate the accumulation of amyloid in synovium and bone outside the carpal tunnel in patients undergoing haemodialysis for more than seven years.

Results

Case report

A 66-year-old man was dialysed at home with $1m^2$ cuprophan membrane since 1976 as a result of biopsy proven extracapillary glomerulonephritis. In 1979 the patient complained of pain in the right hip joint and both knee joints. Non-steroidal inflammatory drugs were successfully prescribed. In March 1982 neurolysis of the left median nerve was performed for carpal tunnel syndrome detected three months earlier. No amyloid deposits were disclosed on histological examination. In 1983, a bilateral scapulo humeral peri-arthritis required two local steroid infiltrations.

In 1984, the carpal tunnel syndrome recurred on the right side. For the first time mild signs of subperiostal resorption were observed in the fingers. An extensive X-ray examination performed to evaluate the cause of shoulder pain disclosed a thickening of the synovium and soft tissues at the shoulder and cavities in the neck of the left humerus. Needle biopsy of the synovium of the left shoulder revealed amyloid material. Further radiological investigations showed fracture of the sixth left rib with widening suggesting a brown tumour, fractures of the third and fourth dorsal vertebral plates and multiple bone cavities on the third, fourth, fifth and ninth dorsal vertebras. Immunoelectrophoresis showed no monoclonal peak. C-reactive protein 25.2mg/dl compared with 1.5mg/dl one year earlier.

The pain required a Harrington instrumentation. Pathological examination of the vertebral plates revealed adenocarcinoma cells.

The patient died a few days later and post-mortem examination revealed a renal cell carcinoma with metastases in the spine and the ribs. Amyloid deposits were detected in the synovium and the cavities of the humeral head. No parenchymal amyloid deposits were discovered.

Other observations

A few months earlier we had observed two patients who had developed bone defects of the femoral heads after seven and 13 years of chronic haemodialysis treatment. One of these cases has been recently reported in detail [2]. The bone defects were initially interpreted as a brown tumour leading, in one case, to subtotal parathyroidectomy. In both patients, spontaneous fracture of a femoral neck necessitated subsequently a total hip replacement. Pathological study of the femoral heads revealed amyloid deposits in the 'cysts' and in the synovium. In the two patients a carpal tunnel syndrome developed after six and 16 years of haemodialysis respectively. Amyloid deposits were demonstrated in the perineural tissue. Both presented carpal bone defects. A search for multiple myeloma proved negative but amyloid was disclosed in a rectal biopsy in one case.

Discussion

Since Assenat's original publication [1], amyloid deposits in the carpal tunnel syndrome are increasingly recognized as a complication of long-term haemodialysis. Our three patients illustrate the extension of this complication to the joints. In each case central or marginal bone defects develop either in the humerus, femoral head or in the carpal bones. The erosive marginal bone defect involves the site of synovial insertion and is associated with peri-articular soft tissue swelling. Cytological study with congo red staining of synovial fluid collected by needle aspiration, and examination of bone specimen after surgery demonstrate the amyloid deposits. Interestingly, this complication developed after the appearance of a carpal tunnel syndrome which, in two cases, was associated with amyloid deposits. The three patients had undergone haemodialysis for more than seven years.

Kuntz and Bardin [3] have recently provided suggestive evidence that amyloid deposits may contribute to the development of osteoarthritic changes in patients undergoing chronic haemodialysis. They pointed to the similarities of their X-ray findings with those of myelomatous patients with AL amyloidosis. They suggest that amyloid deposits in the peri-articular tissues and their extension in bones results from chronic synovial irritation by hydroxyapatite crystals. The observed association between amyloid osteo-arthritis and amyloid deposits in the carpal tunnel syndrome in two of our patients raises an alternative hypothesis: if these two facts are linked, amyloid deposits might be part of a generalized reaction to long-term chronic haemodialysis. Within this context, it is of interest to draw attention to two recent case reports of generalized amyloidosis in

long-term dialysis patients [4,5]. These patients may represent the extreme end of a spectrum of amyloid deposits initiated by haemodialysis.

The cause of a tendency to form amyloid is not evident. It might be related to repeated stimulus of immune reaction from poorly biocompatible membranes. In this context we were interested to find that our three patients had been treated with cuprophan membranes for more than seven years whereas in a similar group of patients treated for more than seven years with polyacrylonitrile, a much more biocompatible membrane, we failed to observe similar X-ray lesions.

In conclusion, peri-articular bone defects with synovial and peri-articular swelling in patients undergoing dialysis for more than seven years and with a previous history of surgical intervention for carpal tunnel syndrome, should suggest the existence of amyloid deposit. Needle aspiration of the involved joint may provide enough material to confirm the diagnosis. This still unrecognized complication of long-term haemodialysis, is probably more common than hitherto reported. It may be related to a chronic stimulation of the immune system with production of altered proteins. Initially involved tissues are the perineural median nerve synovium, followed by the synovia and the adjacent bones, and eventually, perhaps, organs such as the heart and liver.

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