

Editorial: Amyloid arthropathy

Amyloidosis is a condition in which extracellular deposition of characteristic abnormal protein material occurs. This protein is predominantly in the form of fibrils, and the unique conformation of the polypeptide chains in the fibrils is thought to account for the relative insolubility and resistance to proteolytic digestion of the fibrils and for their characteristic staining properties.¹⁻³ The peptide subunits of the amyloid fibril proteins are of different composition in different forms of amyloidosis, and chemical composition is used as the basis of current classification.⁴⁻⁵ Many of the fibril proteins are known to be similar or identical to serum proteins, from which, under certain circumstances, they may be derived. In addition to the fibrillar proteins a minor constituent of all forms of amyloid deposit so far investigated (with the possible exception of the amyloid in the cerebral neuritic plaques in Alzheimer's disease⁶⁻⁷) is amyloid P component (AP) which is apparently identical to the normal serum protein, serum amyloid P component.⁸⁻⁹

Amyloidosis may present clinically with systemic or localised deposits.²⁻³ Systemic amyloidosis may occur in association with plasma cell dyscrasia (AL amyloid) when the fibrils are derived from immunoglobulin light chains. AL amyloid deposits in joints may occur in about 5% of patients with multiple myeloma, and the clinical picture can resemble rheumatoid arthritis with symmetrical arthritis of the wrists and small joints of the hands.¹⁰⁻¹¹ There may also be median nerve compression in the carpal tunnel; subcutaneous nodules are present in many patients, and amyloid infiltration around the glenohumeral articulation produces the characteristic 'shoulder-pad' sign.¹² Staining of centrifuged deposits of synovial fluid from affected joints may show fragments of amyloid.¹³ Reactive systemic amyloidosis (AA amyloid) is associated with chronic inflammatory or infectious disease, and the fibrils are thought to be derived from the acute phase protein, serum amyloid A protein (SAA). Although this type of amyloid may occur as a complication of various forms of arthritis, including rheumatoid arthritis, juvenile chronic arthritis, ankylosing spondylitis, and psoriatic arthropathy, amyloid deposits rarely occur in the joints in these conditions. Heredofamilial systemic amyloidosis occurs in many forms,¹⁴ including rare neuropathic amyloidosis syndromes in which the fibril protein is

related to prealbumin. Some of the families involved have an associated erosive arthritis, but this does not appear to be due to amyloid deposition.¹⁵

A variety of forms of amyloidosis have been recognised which are localised to particular organs or tissues or distributed focally within one or more tissues, for example amyloid localised to the heart and cerebral vasculature (in which the fibril protein may be related to prealbumin) and endocrine organs (in which the fibril protein may be related to the appropriate hormone or its precursors). Localised amyloid deposition occurs in joints and has been demonstrated in the joint capsule and articular cartilage of most osteoarthritic joints examined at autopsy or surgery,¹⁶⁻¹⁷ and the amyloid appears closely related to calcium pyrophosphate deposits. Localised amyloid has also been described in the fibrocartilaginous disc of the sternoclavicular joint.¹⁸ The biochemical nature of these amyloid deposits in joints or their clinical significance are not known, but in common with the other forms of localised amyloid mentioned above their presence appears to be age related and may possibly be a normal accompaniment of the aging process.

In this issue Muñoz-Gómez and colleagues report a form of amyloid arthropathy occurring in patients undergoing regular haemodialysis.¹⁹ Amyloid deposits were found in synovial biopsy specimens, sediments of synovial fluids, and also in tissue removed during surgery for carpal tunnel syndrome, but in no case was there evidence of generalised amyloidosis. Interestingly, two reports of amyloid deposits in tissue removed during surgical decompression of the carpal tunnel in long-term haemodialysis patients have recently been presented as abstracts at the XXIst Congress of the European Dialysis and Transplant Association. One group found that 95% of their patients with such amyloid also complained of shoulder pain,²⁰ the other group found that two of their patients also had polyarthralgia, intermittent synovial effusions, and amyloid deposits in synovial biopsy specimens.²¹ In none of these studies was there any apparent underlying condition predisposing to the development of amyloidosis and in no patients was amyloidosis the cause of the renal failure. In the patients studied by Muñoz-Gómez *et al.*¹⁹ the results of staining with Congo red after prior treatment with potassium permanganate argue against the amyloid being of AA type.

The aetiology of this form of amyloid is not known, and it has not been established whether the fibrils in the deposits are of the same type as in some previously investigated forms of amyloid. It is possible therefore that the fibrils contain polypeptide chains which have not been previously shown in amyloid deposits, thus representing a 'new' type of amyloidosis. It may be speculated that perhaps the complex metabolic changes associated with chronic renal impairment predispose to the deposition of a serum protein, not previously thought to be associated with amyloid, as a precursor of the amyloid fibrils. It would be of interest therefore to perform immunohistochemical studies on these amyloid deposits with specific antisera to known fibril constituents such as AA and prealbumin to determine whether these proteins may be present (and also to establish whether the deposits contain AP). Studies may also be required to isolate the amyloid fibrils and to study their amino acid composition and sequence and to compare these with data on known serum proteins.

Characterisation of the nature of the fibrils in this form of amyloid may be of practical as well as academic interest. There is no established effective medical treatment for amyloidosis, however, identification of the likely serum precursor may allow specific treatment to be aimed at reducing its circulating concentrations and thereby possibly reduce the risk of these patients developing amyloidosis.

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