Systemic amyloidosis of β_2 microglobulin type

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Abstract

A patient receiving haemodialysis for 15 years developed systemic amyloidosis of β_2 microglobulin type. Noticeable deposits of amyloid were present in the myocardium, intervertebral discs, joint cartilages and tendons. Less conspicuous amounts were present in blood vessel walls in the lungs, liver, adrenal glands and brain, and within the stroma of the prostate, testis and kidney, often with foci of calcification.

Many of the bone, joint, and connective tissue disorders experienced by patients receiving long term haemodialysis are due to the deposition of β_2 microglobulin amyloid in the affected sites.¹ Most reported cases describe localised amyloid deposits and the carpal ligament is a common site.² There have been a few cases of more extensive deposition.³

Case report

A 59 year old man had had chronic renal failure treated by haemodialysis for 15 years. At various points during this time he had sustained a failed cadaveric renal transplantation, tertiary hyperparathyroidism treated by

parathyroidectomy, a myocardial infarct and a transitional cell carcinoma of the urinary bladder. His last illness was septicaemia (*Staphylococcus aureus*) and he died suddenly.

At necropsy the heart weighed 794 g. There was extensive calcification of the mitral valve ring and the mitral valve cusps with evident mitral incompetence. There was bilateral pulmonary oedema and prominent passive venous congestion of the spleen and liver. In addition to the visceral organs, the vertebral column, iliac bone, both knee joints, both shoulder joints and the right carpus were removed, examined macroscopically, and sampled for histological examination.

All tissue samples were fixed in 10% formalin, embedded in paraffin wax, stained with either haematoxylin and eosin or alkaline Congo red, or alkaline Congo red after pre-treatment with potassium permanganate. Those samples considered positive for amyloid deposits were studied by a standard indirect immunoperoxidase technique with the following: anti-AA, anti-P-component, anti- κ and anti- λ light chains, anti-prealbumin and anti-fibrin antibodies.

Histologically, in the myocardium there was extensive fibrosis with calcification. Eosinophilic material with the staining characteristics of amyloid of β_2 microglobulin type was present in some areas (fig 1). A recent myocardial infarct with a related microscopic abscess was also present.

Large deposits of amyloid were present in different joint cartilages and menisci, intervertebral discs, and adjacent bone. In the latter site there was a prominent multinucleated giant cell reaction (fig 2). Small amounts of amyloid were further found in blood vessel walls of the lungs, liver, adrenal glands and brain and within the stroma of the prostate, testis, and kidney, often together with foci of calcification, which were discovered almost in each organ examined.

The immunostaining results showed that only β_2 microglobulin and P-component were present in the amyloid deposits. None of the other molecules sought was found in these deposits.

Discussion

Amyloids of prealbumin, light chain, or amyloid A type are capable of systemic deposition. β_2 microglobulin amyloid is usually considered to be localised to articular and juxta-articular structures, and it was initially assumed that any deposition in extra-articular sites was low in

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Figure 1 Deposits of amyloid showing positive reactions for the presence of β_2 microglobulin (arrowed) (AB-PAP).

Figure 2 Deposit of amyloid (A) in vertebral body adjacent to intervertebral disc (C). The amyloid exhibits a positive reaction for the presence of β_2 microglobulin. Multinucleated giant cells (arrowed) contain β_2 microglobulin amyloid material (AB-PAP).

incidence and small in quantity and, as such, unlikely to lead to serious complications.⁴

In 1987 Theaker *et al* described the first immunohistochemically verified case of systemic amyloidosis of β_2 microglobulin type.³ The amyloid deposits were found within the wall of the blood vessels of parenchymatous organs, and large amounts of amyloid could be shown in the broad ligament, kidney, and lymph nodes. Closely associated with the latter were areas of acute and granulomatous inflammation with occasional necrotising granulomata. Some of the vessels with heavy amyloid deposition showed evidence of vasculitis, with both acute and granulomatous inflammation.

This inflammatory reaction is striking because amyloid is generally considered to be a relatively inert substance. β_2 microglobulin amyloidosis is a relatively newly recognised condition, so that all its characteristics are not known, but experience with localised disease has tended to show only mild degrees of

inflammatory response.⁵⁻⁷ In contrast, as in this case, systemic disease is associated with granulomatous inflammation.

In four other cases of reported systemic β_2 microglobulin amyloidosis⁸⁻¹⁰ found at necropsy in subjects with chronic renal failure, treated with haemodialysis, there were deposits of the amyloid in blood vessel walls and, to a variable extent, round the blood vessel. Clinically relevant myocardial pathology with superimposed calcification was a feature of one case. In the present case there had been previous tertiary hyperparathyroidism treated by parathyroidectomy. The associated hypercalcaemia was probably responsible for the observed ectopic calcification.

In conclusion, systemic β_2 microglobulin amyloidosis is a distinct entity, although osteoarticular disease remains dominant: why this should be is an intriguing question. Systemic visceral disease entails depositions in and around blood vessel walls. The precise effects will depend on site and quantity, but single and multiple organ failure does not yet seem to be a particular risk in this condition.

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