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Multiorgan Involvement of Light Chain Deposition Disease

— Report of an Autopsy Case —

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ABSTRACT. An autopsy case of light chain deposition disease is reported here. A 60-year-old female with plasmacytosis of the bone marrow was disclosed to have amorphous eosinophilic deposits in the kidneys and lungs. Glomerular deposits in kidneys were reminiscent of diabetic nodular glomerulosclerosis. Immunohistochemistry disclosed that they were composed of κ-light chain. Systemic deposition of κ-light chain may occur and should be kept in mind whenever eosinophilic amorphous substance is found in the background of plasma cell dyscrasias.

Key words : light chain deposition — light chain nephropathy — κ-light chain — plasmacytosis

Systemic deposition of light chain immunoglobulin components is rarely seen in cases of plasma cell dyscrasia. The amorphous substance deposited in various organs may be identified immunohistochemically as either κ- or λ-light chains. The amount of the light chain deposition is not usually so much as to cause severe functional abnormalities in any organs except for the kidney which is the most common site of involvement and is an organ most severely damaged. Recently, we experienced an autopsy case of light chain deposition disease in association with plasmacytosis. κ-Light chains were deposited in the kidneys and the lungs. Herein, we describe our case and review the literature on this subject.

CASE REPORT

A 60-year-old female was well until 2 years prior to admission when she was found to have hypertension and had been treated with antihypertensive drugs. One year and five months before admission, proteinuria and hematuria were detected. Five months later she was found to have anemia and was given iron. She was hospitalized to the Kawasaki Medical School Hospital because of general fatigue, vomiting, cough and renal dysfunction on December 1, 1986. Laboratory examination showed Ht 26.9%, CCr 65, BUN 46 mg/dl, Ca 4.7 mEq/l. Urine contained 130 mg/dl protein, 80-100/HPF RBC, 1-2/HPF WBC and Bence-Jones protein. Histology of the renal biopsy suggested myeloma kidney, but bone marrow aspirate was not diagnostic of multiple myeloma. Although plasma cells with lobulated nuclei comprised for 40% of the aspirate,

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immature plasma cells or so-called myeloma cells were not present. Immunohistochemically plasma cells in bone marrow biopsy sample were polyclonal. There was no evidence of M-protein in serum and urine or clear-cut punched out lesions of the bone on x-ray examination. Renal function was progressively deteriorated requiring hemodialysis. Soon after hemodialysis was started, she developed sick sinus syndrome, for which a pace-maker was inserted. Although hemodialysis was effective and pace-maker worked well initially, the cardiac response to the pace-maker was gradually decreased and the patient died of cardiac failure on August 8, 1987.

PATHOLOGICAL FINDINGS

Macroscopic examination : Both kidneys were atrophic, weighing 70 g each. They were normal in consistency with smooth yellow brown surface. The cut surfaces also showed the same color with distinct cortico-medullary junction. The lungs, 700 g in combined weight, showed a few millimeter diameter whitish nodules in subpleural region. The heart weighed 470 g. Though a pace-maker wire was inserted both in the right appendage and right ventricle through superior vena cava, it appeared normal.

Light microscopy : The kidney showed parenchymal atrophy and about a half of glomeruli were completely sclerotic with eosinophilic amorphous substance. Other glomeruli showed variable changes from diffuse to nodular widening of mesangium by the similar amorphous substance (Fig. 1). Mesangial cells were either displaced to the periphery or disappeared in some segments. No dilatation of peripheral capillaries was observed. The eosinophilic substance was negative for congo red stain but positive for periodic acid-Schiff reaction. It stained green for Masson trichrome stain. No lamellation of reticulin fibers were detected

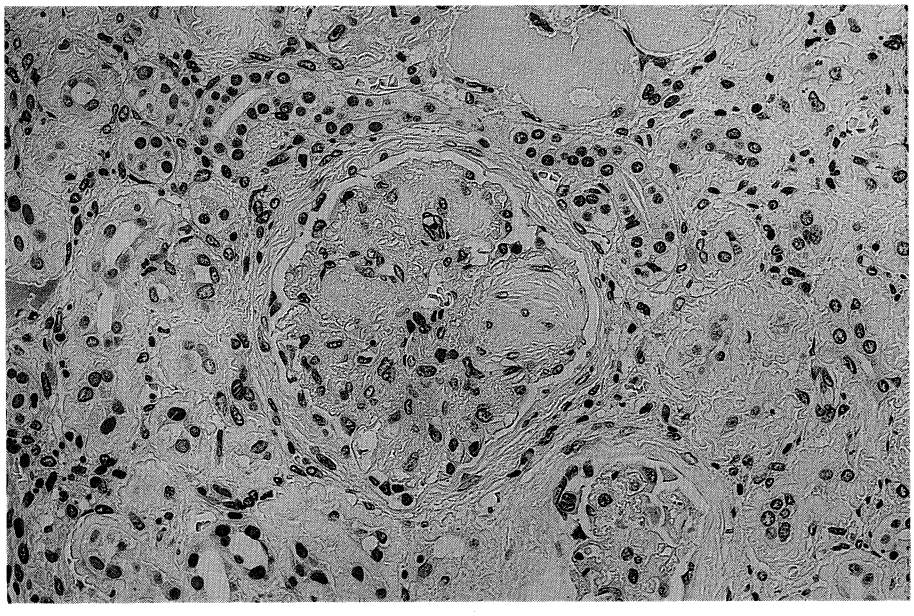

Fig. 1. Nodular change of glomerulus with the deposition of amorphous substance.

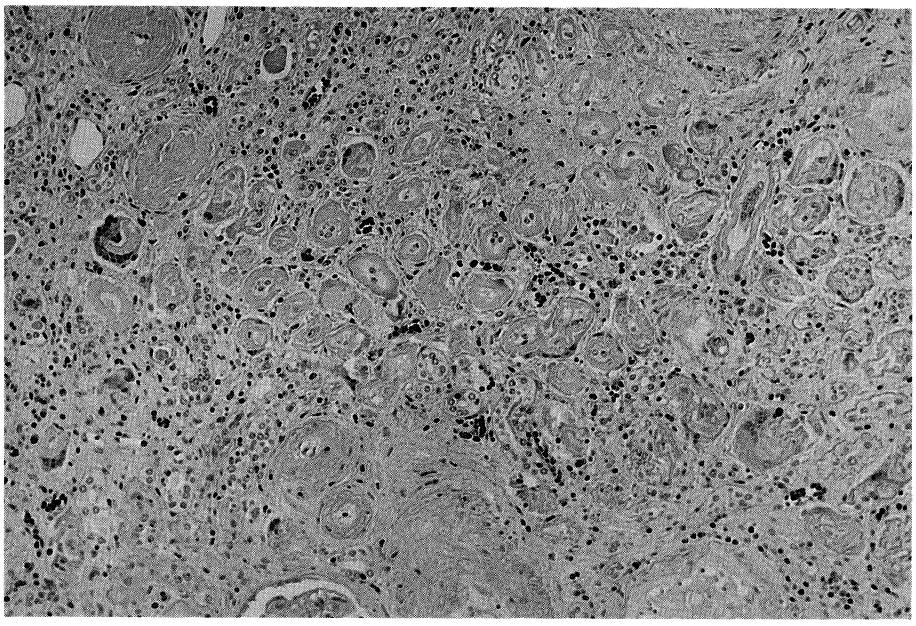

Fig. 2. Atrophy of the tubules. Marked thickenings of the basement membrane by the amorphous substance are seen.

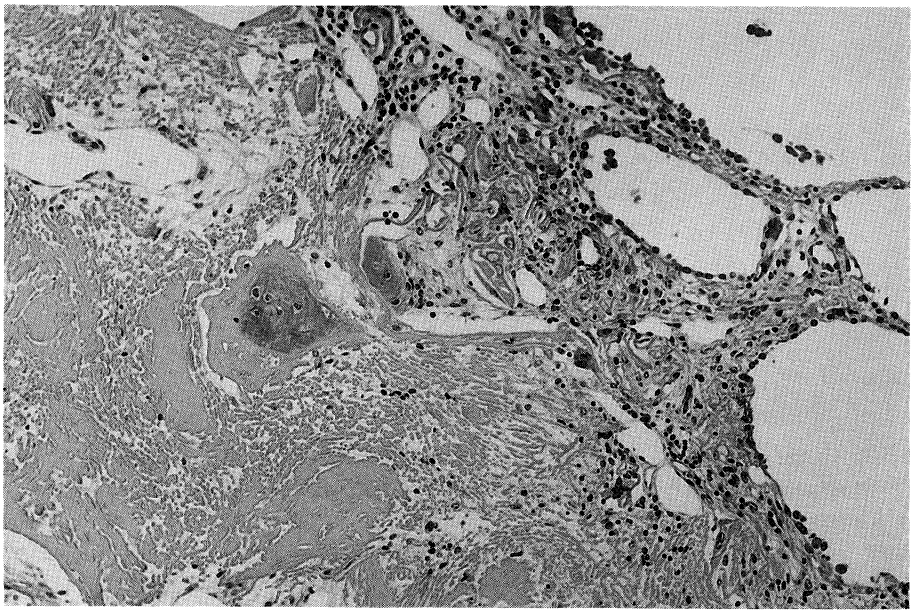

Fig. 3. Amorphous substance in the alveolar wall with focal ossification and giant cell reaction.

with periodic acid methenamin silver (PAM) stain. Tubular basement membranes were markedly thickened and tubules showed atrophy by these substance (Fig. 2). The walls of the blood vessels were also thickened with these amorphous eosinophilic substance. Similar vascular changes were also seen in the liver but not in the heart. Whitish nodules grossly observed in the lung were composed

of the eosinophilic amorphous substance microscopically. They existed in the alveolar wall forming small nodules, with foreign body type giant cells (Fig. 3). These substances in the lungs as well as in the kidneys reacted with anti-κ-light chain antibody but, the one in the liver did not. They were all negative for the anti-λ light chain antibody. Although bone marrow was normal in gross appearance, a large number of plasma cells, having lobulated nuclei, were seen scattered among the erythroid and myeloid precursor cells (Fig. 4). They showed neither nodularity nor osteolytic change. Nuclei of them, slightly larger than the erythroid precursor cells, had obscure small nucleoli. These plasma cells, however, showed monoclonarity with IgG and κ-light chain by immunohistochemical staining.

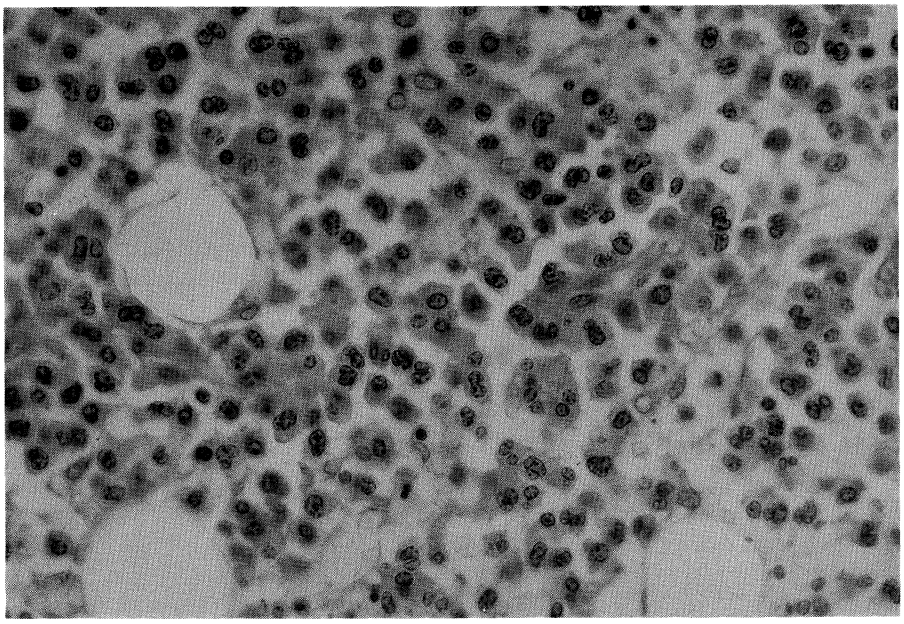

Fig. 4. Proliferation of plasma cells having lobulated nuclei.

DISCUSSION

A variety of renal lesions have been reported in association with plasma cell dyscrasias; namely 1) dysfunction due to neoplastic cellular infiltration to the kidney, 2) functional disorder in which no apparent organic changes are found 3) amyloidosis 4) accumulation of peculiar casts in the renal tubules with foreign body giant cell reaction (myeloma kidney or cast nephropathy) and 5) monoclonal light chain deposition in the glomeruli, tubules and blood vessel walls.[1] The last type is referred to as light chain nephropathy or light chain glomerulosclerosis, and only a small number of such examples have been reported sporadically to date.[2–9] Its exact incidence still remains unknown. Although the term light chain nephropathy was first used in 1976 by Smithline *et al.*,[10] nodular changes of glomeruli associated with multiple myeloma had been already reported in 1957 by Kobernich *et al.*[11] The participation of monoclonal light chain in these glomerular lesions was elucidated by Antonovych *et al.*[12] Although

κ-light chain was implicated as a main component of the deposit in most cases, a few cases with λ-light chain deposition were also observed.[1,13] Glomerular lesions with mesangial proliferation varied in their degree of deposition from minimum to severe. Nodular and/or lobular configuration of such lesions may give some difficulties in differentiating it from diabetic glomerulosclerosis. Whereas nodules of diabetic glomerulosclerosis show argyrophilia with lamination, those of light chain nephropathy are usually nonargyrophilic in PAM stain.[14] Immunohistochemical method, of course, provides a good tool for the differentiaton of these two lesions.

Bone marrow in our case contained many plasma cells. Some of them had small-irregular and/or lobulated nuclei. They neither formed nodular aggregates nor showed osteolytic changes which are commonly seen in cases of multiple myeloma. Clinical settings were also inconsistent with multiple myeloma. The plasma cells present at autopsy, however, disclosed monoclonarity on immunohistochemical basis, which suggests neoplastic proliferation in the light of present oncology. They might have been in the initial or very early stage of multiple myeloma, and small and overt myelomatous proliferation might have been over-looked during the early clinical course. We are not sure, however, whether such a monoclonarity alone substantiates its neoplastic nature without having a neoplastic nodular growth with bony destruction, and/or cellular atypism. Semantically, therefore, we prefer to call this abnormal plasmacytic proliferation as monoclonal plasmacytosis rather than multiple myeloma, as Preud'homme pointed out.[15]

Systemic deposition of the light chain is a rare occurrence; however, multiorgan involvement does occur like Randall *et al.* described.[4] Sites of extrarenal deposition were the blood vessels, the liver, the heart and the spleen in descending order.[16] In our case, extrarenal deposition was mainly seen in the lung where a few millimeter white nodules were present in the subpleural region and in the liver where similar amorphous substance was found in the blood vessel wall of the portal area. The deposits of the lung reacted with anti κ-light chain antibody, while the ones in the liver did not. This discrepancy is inexplicable. Several speculations may be entertained. First, deposits in the liver might not have been made of light chain itself but other unknown substance might have been produced synchronously or asynchronously by plasma cells in bone marrow or elsewhere and was deposited in the liver. Second, the deposits might have been composed of variable region fragments which cannot be detected by the usual antisera which detect the constant region determinants.[1] Third, they may be abnormal immunoglobulin fragment different in its amino acid sequence and antigenicity.

The amount of the deposits in both lungs and liver was rather too small to impair the organ function in our case. Previous reports, however, indicates that strict correlation does not always exist between the severity of the functional abnormality and the amount of the deposits.[7] In our case, severe sick sinus syndrome was clinically observed after hemodialysis, but postmortem examination of the heart disclosed no abnormality in the myocardium, coronary arteries as well as conduction system. It may be, therefore, rather functional than organic.

At any rate, pathologists should always bear in mind of the possibility of the light chain deposition disease when amorphous substance with no reaction to congo red staining is seen in either biopsy or autopsy samples from a patient

with plasma cell dyscrasia, and immunohistochemical examination should always be done in such cases.

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