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Skin Amyloid Deposition in Systemic Amyloidosis in a Patient with IgD M-protein

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A 45-year-old male, with a history of irritation on the exposed skin by handling fine glass-fibers for 10 years, was noted to have swelling and pigmentation of the eyelid. He also had pleural effusion and cardiac arrythmia. The identification of serum IgD M-protein and urinary Bence Jones protein of lambda in this case led to the diagnosis of primary amyloidosis on the basis of amyloid deposits in the skin and in the rectum. Association of AL amyloidosis and IgD M-protein was discussed.

Key Words
Skin amylodosis,
IgD M-protein,
Bence Jones protein (BJP),
Systemic amyloidosis,
AL (Amyloid derived from immunoglobulin light chain).

INTRODUCTION

Amyloidosis is characterized by a large variety of clinical manifestations (1), including skin lesions such as petechiae, papules, lichen, nodules, bullae, xanthoma-lesion and scleroderma-like lesions (2−7).

The present case with pigmentation of the eyelid, pleural effusion and cardiac arrythmia, as the first manifestation of primary amyloidosis remained undiagnosed until the identification of serum IgD M-protein (8−10).

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CASE REPORT

H. Ter., 45-year-old male, visited the local hospital because of the swelling and pigmentation of the bilateral eyelid at the age of 43 (Figure 1). He had the occupational history of handling fine glass-fibres for 10 years, which had irritated the exposed skin associated with frequent erythematous skin rashes. There was no history of dysphagia, sclerodactylia, Raynaud's phenomenon, arthralgia or pulmonary disorders. On examination at the age of 44, he was found to have swelling and pigmentation of the eyelid at Kobe University Hospital. Other findings on physical examination disclosed the enlargement of the heart and moderate right pleural effusion. ECG findings changed from A-V block of first degree to auricular flutter in one year (Fig-

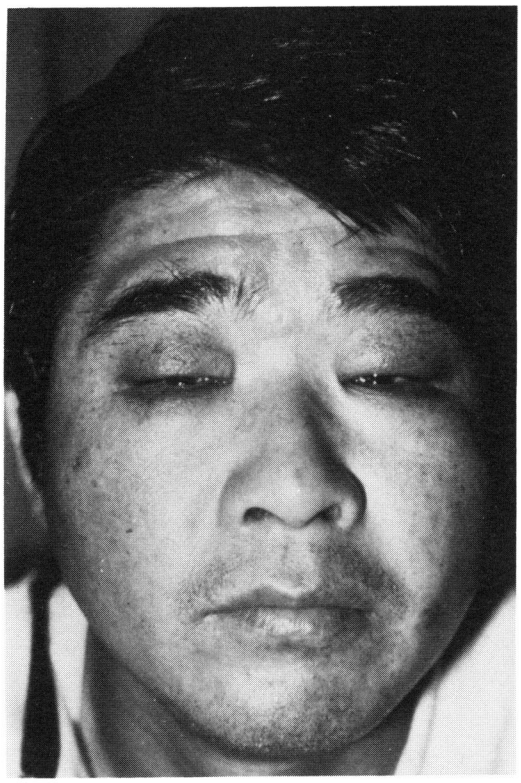

Figure 1. Edematous and pigmented skin, especially upper eyelids and buccal area.

ure 2) during the clinical course at the ward of our Department. He had no evidence of lymphadenopathy or hepato-splenomegaly. Neurological examinations showed nothing particular.

Laboratory examinations included an ESR 5 mm/hr, red blood cells 440 × 10^4/mm^3, hemoglobin 14.3 g/dl, white cells 4900/mm^3 with a normal differential, platelet 17.5 × 10^4/mm^3, normal liver function tests, normal lipid levels and normal plasma electrolytes. Immunologic analyses included negative results for CRP, TPHA, LE test, DNA test, rheumatoid factor, micorsome test and thyroid test.

It is noteworthy that initially urine protein was completely negative for sulfosalicytic acid and the serum protein electrophoresis revealed a normal-looking contour as shown in Figure 3. A serum total protein was 6.3 g/dl, with a differential of albumin 4.4 g/dl, α_1-globulin 0.2, α_2 0.3, β 0.8 and γ 0.6 g/dl. An immunodiffusion Quantiplate showed low immunoglobulin levels in the serum of IgG 518 mg/dl, IgA 52 mg/dl and IgM 32 mg/dl. Further analysis of the serum was positive for anti-delta chain antiserum by agarose Ouchterlony, which prompted the identification of serum IgD(λ) M-protein and Bence Jones protein of lambda type by immunoelectrophoresis, as shown in Figure 3. A bone marrow aspiration showed nucleated cells 3.1 × 10^4/mm^3 with 11 % of plasma cells. These findings of plasma cell dyscrasia suggested a possiblity of amyloidosis. Biopsies of the skin from the left buccal area showed massive amyloid deposits in the dermal layer as shown in Figure 4. Although the relationship between the long-standing cutaneous irritations by glass-fibers and amyloid formation is not clear, the rectal biopsy confirmed the presence of amyloid materials.

In summary, the present case is skin amyloid in systemic amyloidosis associated with serum IgD(λ) M-protein and urinary Bence Jones protein.

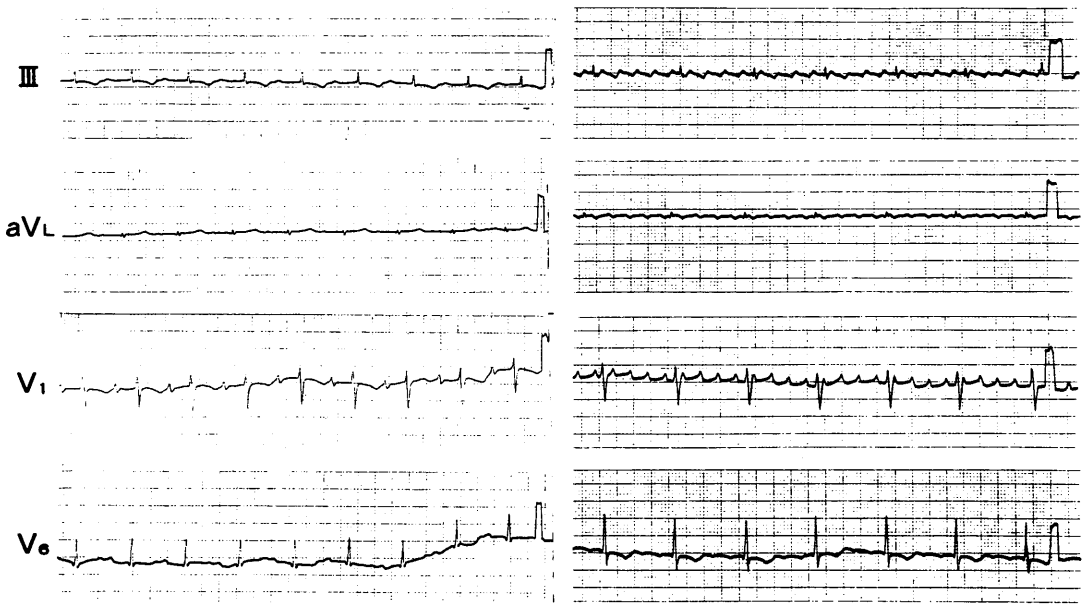

Figure 2. Changes of ECG abnormalities from A－V block of I st degree (left in 1983) to auricular flutter (right in 1984).

DISCUSSION

The nature of amyloidosis has been extensively investigated in the past twenty-five years (1). Several types of amyloid fibril proteins such as AL, AA, AF and AE have been characterized biochemically and immunochemically from amyloid-laden tissues (1). As to skin (cutaneous) amyloidosis (2－5), the involvements of the skin with amyloid deposits can be clinically classified into two types; (1) primary localized skin amyloidosis, as seen in most cases, and (2) infiltrations of amyloid in the skin probably through the small vessels in systemic amyloidosis, as seen less frequently (2－3).

The anthors previously described in a study that the skin amyloidosis in a systemic amyloidosis differed from the primary cutaneous amyloidosis by the simultaneous findings such as the presence of urinary Bence Jones proteins by immunoelectrophoresis in association with the positive perivascular deposits of amyloid fibrils by electron-microscopy, in 10 of total 55 cases (18%) with skin amyloidosis (3). These 10 cases which were initially diagnosed as localized skin amyloidosis at the Department of Dermatology in sev-

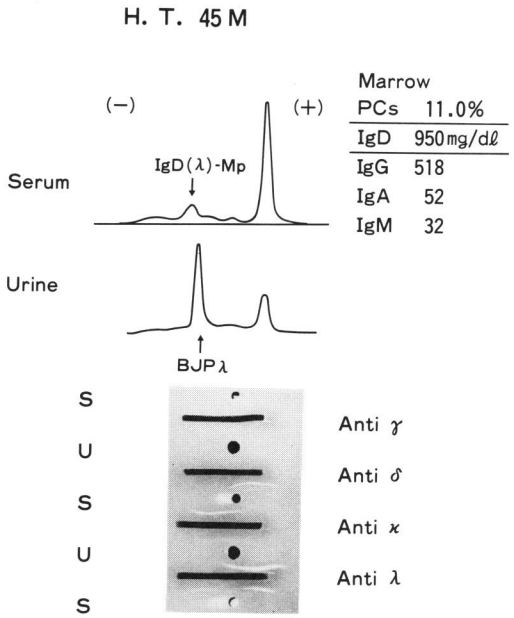

Figure 3. Electrophoretic patterns of the serum and the concentrated urine, demonstrating narrow spikes of serum M−p and urinary BJP, respectively. By immunoelectrophoresis, IgD(λ)-Mp in the serum and BJP λ in the urine.

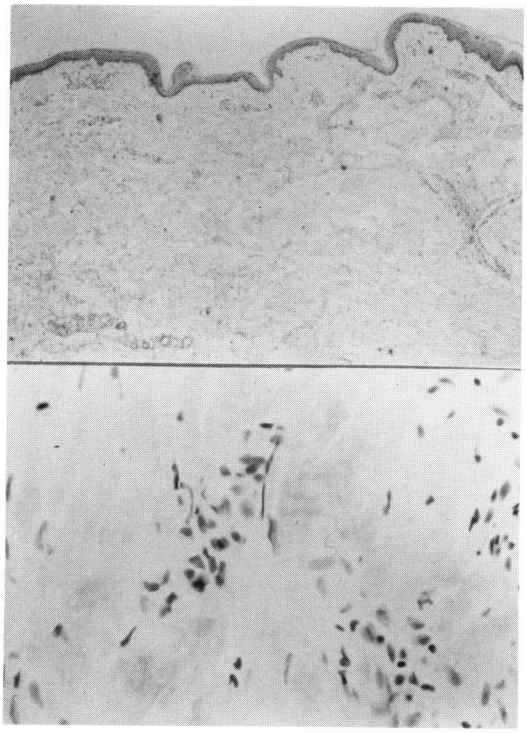

Figure 4. Amyloid deposits in the dermal layer on the biopsied material by Dyron-dye staining. Upper (×100), lower (×400).

eral hospitals, were thus later classified into systemic amyloidosis with the confirmation of amyloid deposits in other tissues of tongue, stomach, kidney liver or rectum, respectively. Incidence of systemic type among cases with skin amyloidosis was reported by Cohen's group (4). They performed a punch or excisional biopsy of the skin in 50 patients with generalized amyloidosis, obtaining a result that amyloid was seen in the skin of 21 of 38 cases with primary or myeloma-associated amyloidosis, and 5 of 12 cases with secondary amyloidosis in the biopsied skin of clinically normal or uninvolved skin. As to progression of cardiac arrythmia and pleural effussion, systemic involvement of AL amyloid may possibly be identified histologically in the heart and in the pleura in the present case.

AL amyloidosis, consisting in most instances of primary systemic amyloidosis and myeloma-associated amyloidosis, cause clinically detectable cutaneous changes in approximately 10 to 40 % of patients (4). In these instances, the analysis of

serum monoclonal protein and/or urinary Bence Jones protein is significantly important. In this regard, the normal-looking contour of the cellulose-acetate electrophoretic pattern of the serum in the present case could not esily suggest the possiblity of IgD M-protein, unless the β-fraction was considered somewhat abnormal in shape. Although it was interesting that sulfosalicylic acid gave negative precipitation for the rountine urine protein analysis, the concentrated urine electrophoresis showed a prominent spike in the γ-region in the present case. Therefore, the careful observation and analysis of monoclonal immunoglobulin is indispensable in establishing the diagnosis of AL amyloidosis, on the basis of high incidence of M-protein in systemic AL amyloidosis (3, 8).

The delta-class heavy chain has been reported to have different features from heavy chains of other classes, such as (1) high contents of carbohydrate, (2) association (more than 90 %) to lambda type light chain in IgD M-protein, (3) frequent association of urinary BJP λ, osteolytic lesions and azotemia in IgD myeloma, (4) extreme susceptibility of IgD to various proteolytic enzymes and (5) a major membrane immunoglobulin on B-lymphocytes. Some of these abnormalities might be related to form amyloid fibrils. Further protein study is currently undertaken in investigating of amyloidogenic λ-chain or more interestingly amyloidogenic δ-chain, since there have been some reports of high incidence of amyloidosis in IgD-myeloma in the past (9−12).

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