

A Case of Nodular Amyloidosis

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A 65-year-old female patient visited our clinic complaining of multiple skin lesions since one year ago. There were yellowish to brownish colored, bean to walnut-sized nodules on both lower extremities. Dylon stain with polarizing microscopy, immunohistochemical stain to amyloid-P and immunoglobulin-kappa chain showed positive reactivities but keratin stain was negative.

According to histopathologic and immunohistochemical findings, she was diagnosed as nodular amyloidosis. (Ann Dermatol 4:(2) 113-116, 1992)

Key Words: Nodular amyloidosis

Primary localized cutaneous amyloidosis may be classified into three major types. They are lichen amyloidosis, macular amyloidosis, nodular or tumefactive amyloidosis. Nodular amyloidosis is a rare form of cutaneous amyloidosis characterized clinically by single or multiple pink to yellowish nodules or plaques on the trunk, extremities, genitals, face, or scalps, which may have an atrophic or anetodermic appearance and may contain superficial telangiectasias. Histologically, it is characterized by extensive deposits of amyloid in the papillary dermis and reticular dermis^{1,2}. It affects mostly middle-aged women, and may occasionally be associated with Sjogren's syndrome³. The origin of this type of amyloid fibrils has not been clarified yet, but it is suggested to have an immunoglobulin light chain derivation^{1, 4, 7}. Recently, the association of nodular amyloidosis with systemic amyloidosis has been reported and some authors regard it as one manifestation of systemic amyloidosis^{2, 5}.

We report herein a case of nodular amyloidosis together with all the results from immunohistochemical evaluation.

REPORT OF A CASE

A 65-year-old female visited our clinic complaining multiple skin lesions present for a year. No subjective symptom except mild itching sensation was accompanied. There was no history of previous treatment. She had the past medical history of hypertension and anterior uveitis.

Cutaneous examination revealed multiple well demarcated yellowish to brownish bean to walnut-sized papules and nodules on both lower extremities, especially on the shins and the buttocks (Fig. 1).

A biopsy was performed from right shin. The epidermis showed atrophic change. There were relatively ill-demarcated pale eosinophilic, amorphous materials on both papillary dermis and reticular dermis. At the periphery of the lesion, there was a perivascular infiltration of plasma cells and lymphocytes (Fig. 2). Dylon stain for amyloid fibrils showed positive results in both the papillary dermis and reticular dermis (Fig. 3). Under the polarizing microscope with Dylon stain, there was apple-green birefringence (Fig. 4). Immunohistochemical stain with the antiepidermal keratin antiserum showed positive reactivity in the epidermis, but no reactivity in dermal deposits, indicating that the dermal amyloid protein was not derived from keratinocytes. Amyloid-P stain brought positive results in light brown color. Immunoperoxidase stain with the use of antibodies

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Fig. 1. Well-demarcated yellowish to brownish bean to walnut sized papules and nodules on right shin.

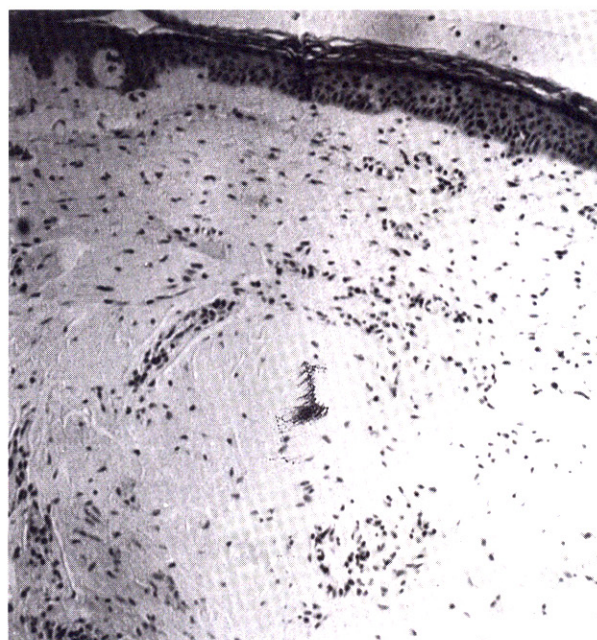


Fig. 2. Pale eosinophilic amorphous amyloid deposits in papillary and reticular dermis (H&E stain, ×40).

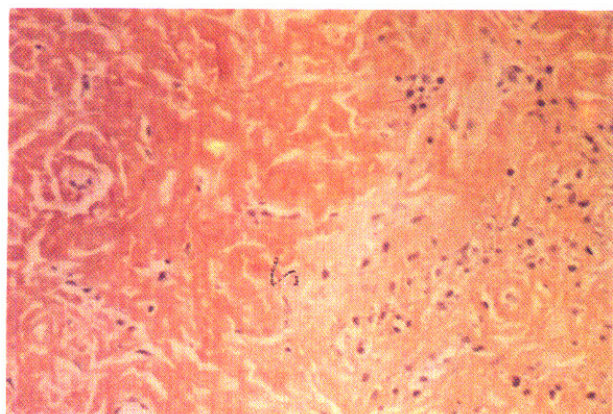


Fig. 3. Amyloid showing salmon-pink color (Dylon stain, ×100).

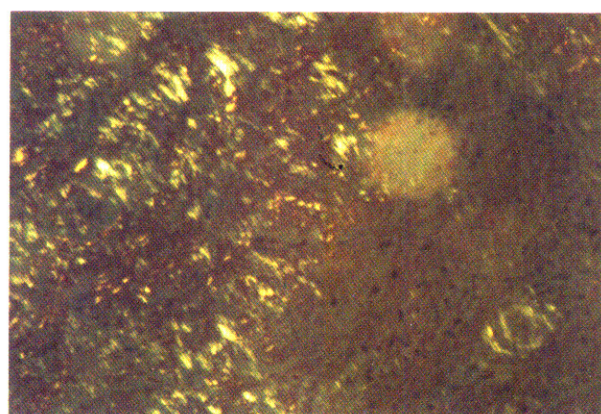


Fig. 4. Amyloid showing yellow-green birefringence under a polarizing microscope (Dylon stain, ×100).

to kappa and lambda light chains of the immunoglobulins showed positive reaction with kappa light chain in both amyloid materials and the surrounding plasma cells (Fig. 5).

Under the diagnosis of cutaneous amyloidosis, we performed systemic work-up to rule out the primary systemic amyloidosis. Complete blood count showed mild anemia with hemoglobin level of 11.0g/dl and differential cell count showed increase of lymphocytes and eosinophils. Erythrocyte sedimentation rate was elevated to 50mm/hr.

Liver function tests and lipid battery were within normal limits, but albumin/globulin ratio was reversed, and the levels of blood urea nitrogen and serum creatinine were elevated to 30mg/dl and 2.3mg/dl respectively. On urine analysis, there was albuminuria of 2+, but Bence-Jones proteins were not found in the urine. Chest roentgenogram showed no abnormality. Electrocardiogram showed left ventricular hypertrophy. Antinuclear antibody was negative. Serum IgG level was elevated to 2290mg/ml, but serum IgA and IgM

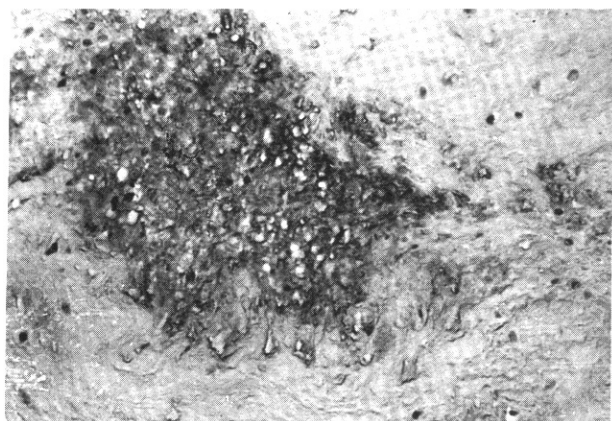


Fig. 5. Amyloid stained with anti-kappa light-chain amyloid antibody (peroxidase-antiperoxidase method, $\times 100$).

levels were within normal limits. Serum protein electrophoresis revealed increased amount of total protein and diffusely increased gammaglobulin, suggesting of polyclonal gammopathy. Lipoprotein electrophoresis showed increase of pre- β fraction.

DISCUSSION

Nodular amyloidosis was first reported in 1950 by Gottron⁶, referred to as amyloidosis cutis nodularis atrophicans diabetica, and is also called amyloid tumor formation of the skin, primary localized amyloidosis cutis-tumefactive type, nodular primary localized cutaneous amyloidosis, as well as nodular primary cutaneous amyloidosis⁷. To our knowledge, about 60 cases of nodular amyloidoses have been reported in the literatures, but there has been no case report in Korea.

The origin of nodular amyloidosis is still controversial. MacDonald et al⁸ demonstrated deposits of IgM and C3 in the dermis and vessel walls of three patients with primary nodular cutaneous amyloidosis studied by immunofluorescence. Two of these patients also showed extensive deposits for Kappa and Lambda light chains. In an article by Eto et al⁹, a series of five monoclonal antibodies to keratin failed to react with biopsy specimens from four cases of nodular cutaneous amyloidosis. Using immunofluorescence and immunoperoxidase techniques, Northcutt and Vanover² demonstrated positive reactions with anti-IgG, IgM, IgA, Kappa and

Lambda light chain immunoglobulins in both the amyloid materials and the surrounding plasma cells. Kitajima et al¹ found that the amyloid deposits of nodular cutaneous amyloidosis stained with anti-Lambda light chain amyloid antibody. From the above findings, it was hypothesized that the plasma cells secreted light chain immunoglobulins, which were further processed in an abnormal fashion by macrophage enzymes to produce the partially degraded light chains of amyloid fibrils and then accumulated as nodules^{10, 11, 12}. In our case, Kappa light chain and amyloid-P were demonstrated by immunoperoxidase method. Immunohistochemical stain with the anti-epidermal keratin antisera showed negative response for amyloid materials, suggesting that amyloid of the former had a different origin from lichen amyloidosis and macular amyloidosis.

Nodular amyloidosis may either occur primarily in the skin or as a manifestation of systemic amyloidosis^{2, 5, 13}. Brownstein and Helwig⁵ pointed out that long-term follow-up is necessary in the patients with nodular amyloidosis, because five of ten patients in their reports who were originally believed to have the localized form later developed systemic amyloidosis. In our case, no evidence of multiple myeloma was found. Laboratory studies revealed abnormal findings suggesting nephropathy such as proteinuria, elevated BUN/Cr. In addition, gammaglobulinemia and left ventricular hypertrophy were detected. Therefore systemic amyloidosis must be included in differential diagnosis. Rectal biopsy, abdominal subcutaneous fat pad aspiration or renal biopsy may be helpful to rule out the systemic involvement.

There is no consistently effective treatment of nodular primary localized cutaneous amyloidosis. Variable success has been reported with surgical excision, cryotherapy, electrodesiccation and curettage, and shave removal with the use of cutting current⁵. Truhan et al¹¹ reported a good cosmetic result in a patient using carbon dioxide laser. No specific treatment has been done to our patient because of her old age and poor compliance.

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