Light Chain Amyloidosis due to Waldenström's Macroglobulinemia Showing Papular/Nodular Lesions

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Abstract

A 67-year-old Japanese man was referred to us with numerous papules and nodules. Examination revealed i) IgM-monoclonal proteinemia, ii) amyloid protein deposition around vessels in the dermis and subcutis, and iii) lymphoplasma cells into bone marrow. This report shows that Waldenström's macroglobulinemia causes papules/nodules through the development of amyloidosis.

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Short title: Amyloidosis in WM

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Key Clinical Message

Waldenström's macroglobulinemia may cause cutaneous manifestations represented as papules/nodules through the development of light chain amyloidosis. This report potentially provides novel findings in Waldenström's macroglobulinemia.

Introduction

Light chain (AL) amyloidosis is a disease characterized by the deposition of AL amyloid protein in each tissue/organ, typically followed by lymphoproliferative disorder accompanied with globulinemia. Although monoclonal gammopathy of undetermined significance and multiple myeloma are well-known causes of AL amyloidosis, AL amyloidosis due to Waldenström's macroglobulinemia (WM) has rarely been reported. Here, we report a case of AL amyloidosis developing during the course of WM.

Case Reports

A 67-year-old Japanese man was referred to our department with numerous papules and nodules on the trunk and extremities, without any subjective symptoms (**Fig. 1a**). The patient did not experience fever, hepatosplenomegaly, or systemic lymphadenopathy. The complete blood cell count indicated mild anemia and no atypical lymphocyte in the peripheral blood. A biochemical blood test revealed a high β2-microglobulin level of 4.2 mg/L (normal range: 0.8 to 1.8) and high immunoglobulin M level of 2,928 mg/dL (33 to 190), represented as a monoclonal peak by electrophoresis. The examination also disclosed mild abnormalities of the coagulation/fibrinolysis system including factor X, 40% (70 to 130); fibrin/fibrinogen degradation products, 9 μg/mL (0 to 5); and plasmin-α2 plasmin inhibitor complex, 2.8 μg/mL (0 to 0.8). Flow cytometric analysis of bone marrow showed T-cell dominants. Histopathological examination of the skin revealed an amorphous substance around vessels in the dermis and subcutis (**Fig. 1b and 1c**), which was highlighted in an orange color (**Fig. 1d**) and apple-green-birefringence (**Fig. 1e**) by direct fast scarlet staining and polarization, respectively. Histopathological examination of the bone marrow revealed mild proliferation of lymphocytes, plasmacytes, and lymphoplasma cells with Dutcher's bodies without atypia (**Fig. 1f and 1g**), and the presence of CD20-positive cells (**Fig. 1h**). A diagnosis of AL amyloidosis due to WM was made.

Discussion

WM is a non-Hodgkin lymphoma characterized by the invasion of lymphoplasma cells into bone marrow and IgM-monoclonal proteinemia. The incidence rate of WM is 3–4 cases per million persons per year, accounting for only 1% of lymphomas[1]. WM causes AL amyloidosis in only 3% of WM cases[2]. Information about cutaneous manifestations of WM-related AL amyloidosis is limited.

AL amyloidosis affects various organs/tissues including the kidneys, heart, nerves, and skin[3]. Cutaneous manifestations are dependent on the histological area where amyloid protein deposits; previous literature reported that protein deposition in vessel walls, folliculosebaceous units, and the epidermis/dermis causes purpura, alopecia, and papules/nodules, respectively[4]. Purpura is reportedly caused by vessel fragility due to the deposition and abnormality of the coagulation/fibrinolysis system[5]. Our case, however, presented with papules/nodules and not purpura. The cutaneous manifestation was considered to have developed by the following mechanisms: i) abnormalities of factors controlling coagulation and fibrinolysis were not severe enough to cause the collapse of the coagulation/fibrinolysis system; ii) the vascular endothelial cells were not destroyed by the deposition, compatible with the histopathological findings that vascular endothelial cells were not affected by the deposition; and iii) marked deposition around vessels in the dermis and subcutis caused papules/nodules.

This case report provides evidence that WM may cause cutaneous manifestations represented as papules/nodules through the development of AL amyloidosis.

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Statement of Ethics: This study protocol was approved by The Ethics Committee of The Jikei University School of Medicine and the patient provided written informed consent.

Author Contributions

Yumeno Toma: The author contributed to data curation and resources.

Yoshimasa Nobeyama: The author contributed to conceptualization and project administration.

Hiroyuki Matsuzaki: The author contributed to resources and supervision.

Ken-ichi Yasuda: The author contributed to resources and supervision.

Akihiko Asahina: The author contributed to review and supervision.

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Figure Legends

Fig. 1

a) Clinical findings. Numerous papules and nodules on the trunk and extremities are evident. **b)** Histopathological findings of the skin (hematoxylin-eosin stain, × 20). Amorphous eosinophilic nodular lesions can be noted in the dermis and subcutis. **c**) Histopathological findings of the skin (hematoxylin-eosin stain, ×100). Amorphous eosinophilic nodular lesions are present around vessels.**d**) Histopathological findings of the skin (direct fast scarlet stain, ×100). An amorphous substance around vessels is stained with orange dye. **e**) Histopathological findings of the skin (×100). Apple-green-birefringence with polarization is evident in the amorphous substance around vessels. **f)** Histopathological examination of the bone marrow (hematoxylin-eosin stain, ×400). Proliferation of lymphocytes and plasmacytes without atypia is evident. **g)**Histopathological examination of the bone marrow (hematoxylin-eosin stain, ×1000). Lymphoplasma cells with Dutcher's bodies without atypia are evident. Dutcher's bodies are indicated by arrowheads. **h**) Histopathological examination of the bone marrow (×400). Some lymphocytes react with anti-CD20 antibody (Nichirei Biosciences, Tokyo, Japan).