Received: 11 January 2023 | Revised: 19 April 2023 | Accepted: 1 May 2023

DOI: 10.1002/ccr3.7346

CASE REPORT

Clinical Case Reports Open Access WILEY

A case of systemic amyloidosis showing papular/nodular lesions due to Waldenström's macroglobulinemia

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Key Clinical Message

This case report provides evidence that Waldenström's macroglobulinemia may cause cutaneous manifestations represented as papules/nodules through the development of light chain amyloidosis. Here, we report a case of a 67-year-old man.

KEYWORDS

amyloidosis, cutaneous manifestation, lymphoplasma cell, non-Hodgkin lymphoma, Waldenström's macroglobulinemia

1 | 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 by 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.

2 | 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 (Figure 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: 0.8–1.8) and high immunoglobulin M level of 2928 mg/dL (33–190), represented as a monoclonal peak by electrophoresis. The examination also disclosed mild abnormalities of the coagulation/fibrinolysis system including factor X, 40% (70–130); fibrin/fibrinogen degradation products, 9 μg/mL (0–5); and plasmin-α2 plasmin inhibitor complex, 2.8 μg/mL (0–0.8). 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 (Figure 1B,C), which was highlighted in an orange color (Figure 1D) and apple-green birefringence (Figure 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 (Figure 1F,G), and the presence of CD20-positive cells (Figure 1H). Based on them, a diagnosis of AL amyloidosis due to WM was made.

3 | DISCUSSION

WM is a type of lymphoma clinically similar to indolent non-Hodgkin lymphoma characterized by the invasion of lymphoplasma cells into bone marrow and

IgM-monoclonal proteinemia. The incidence rate of WM is three to four cases per million persons per year, accounting for only 1% of lymphomas.[1] Only 3% of WM cases causes AL amyloidosis.[2] Knowledge 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 due to the following mechanisms: (i) abnormalities of factors controlling coagulation and fibrinolysis were not severe

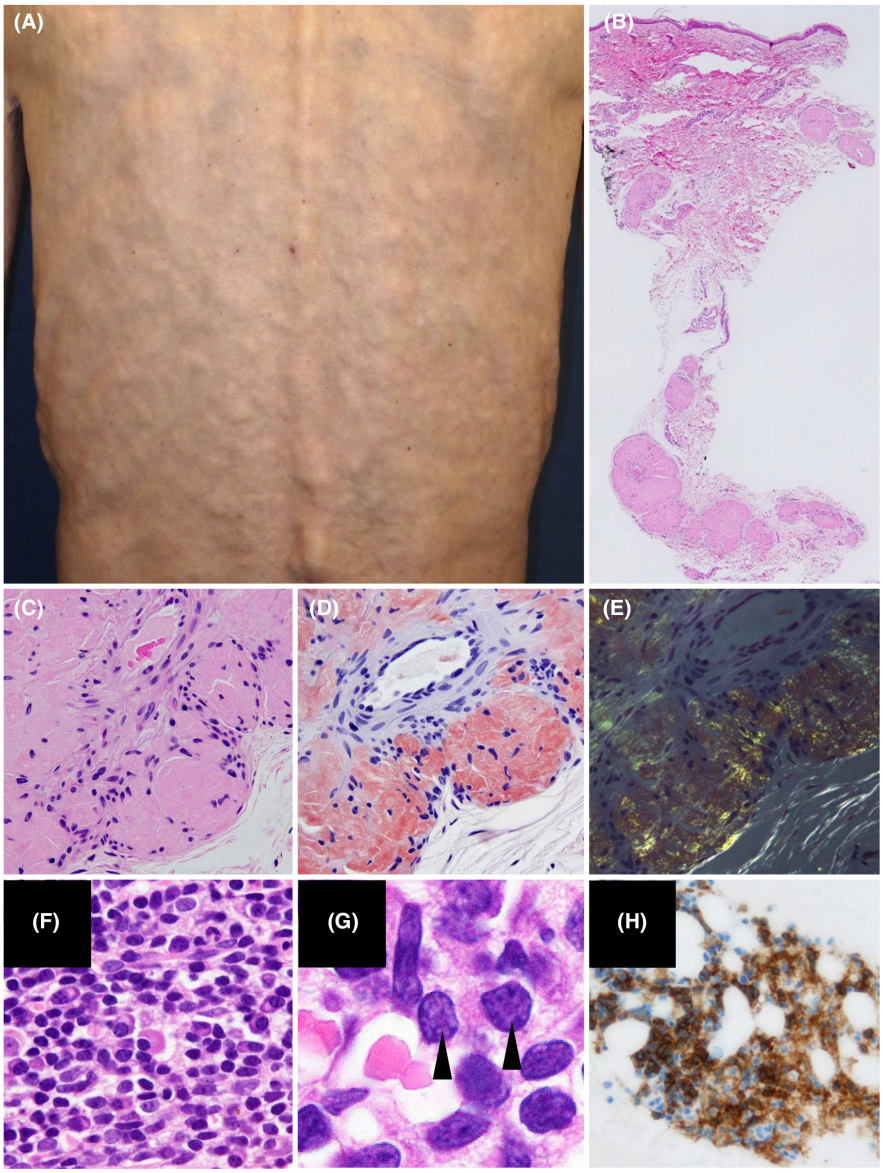

FIGURE 1 (A) Clinical findings. Numerous papules and nodules on the trunk and extremities are evident. (B) Histopathological findings of the skin (hematoxylin–eosin stain, ×20). Amorphous eosinophilic nodular lesions can be noted in the dermis and subcutis. (C) Histopathological findings of the skin (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).

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.

AUTHOR CONTRIBUTIONS

Yumeno Toma: Resources. **Yoshimasa Nobeyama:** Project administration; writing – original draft; writing – review and editing. **Hiroyuki Matsuzaki:** Resources. **Ken-ichi Yasuda:** Resources. **Akihiko Asahina:** Supervision.

ACKNOWLEDGMENTS

None.

FUNDING INFORMATION

The authors received no financial support for this study.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Additional data sharing is not applicable to this article due to ethical restrictions.

ETHICS STATEMENT

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

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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How to cite this article: Toma Y, Nobeyama Y, Matsuzaki H, Yasuda K-i, Asahina A. A case of systemic amyloidosis showing papular/nodular lesions due to Waldenström's macroglobulinemia. *Clin Case Rep*. 2023;11:e7346. doi:10.1002/ccr3.7346