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CASE REPORT

Waldenstrom Macroglobulinemia Arising During Maintenance Therapy of Plasma Cell Myeloma

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SUMMARY

Background: **Both plasma cell myeloma (PCM) and Waldenstrom's macroglobulinemia (WM) are mature B-cell neoplasms commonly involving bone marrow and usually related to paraproteinemia.**
Methods: **Secondary WM in a patient with PCM during maintenance therapy has not been previously reported. We herein report the first case of WM arising during maintenance therapy of PCM.**
Results: **The diagnosis of secondary WM during maintenance therapy of PCM was based on combination of medical history, morphology, flow cytometry, immunofixation electrophoresis, and molecular genetics.**
Conclusions: **This case highlights the importance of an integrated diagnostic work-up, with an interesting role for morphology and flow immunotyping.**
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KEYWORDS

Waldenstrom's macroglobulinemia, plasma cell myeloma, morphology, flow cytometry, immunofixation electrophoresis

INTRODUCTION

Pasma cell myeloma (PCM) and Waldenstrom's macroglobulinemia (WM) are both mature B-cell neoplasms commonly involving bone marrow and usually related to paraproteinemia [1-2]. So far, an association of PCM with WM has been described in a few cases [3,4], and the evolution of WM into an IgM positive MM in a patient has been reported [5]. However, secondary WM in a patient with PCM during maintenance therapy has not been previously reported. We report the first case of WM arising during maintenance therapy of PCM.

CASE PRESENTATION

A 64-year-old man presented with fatigue for half a year, low back pain for 2 months. Nuclear magnetic examination showed compressional bone fracture and de-

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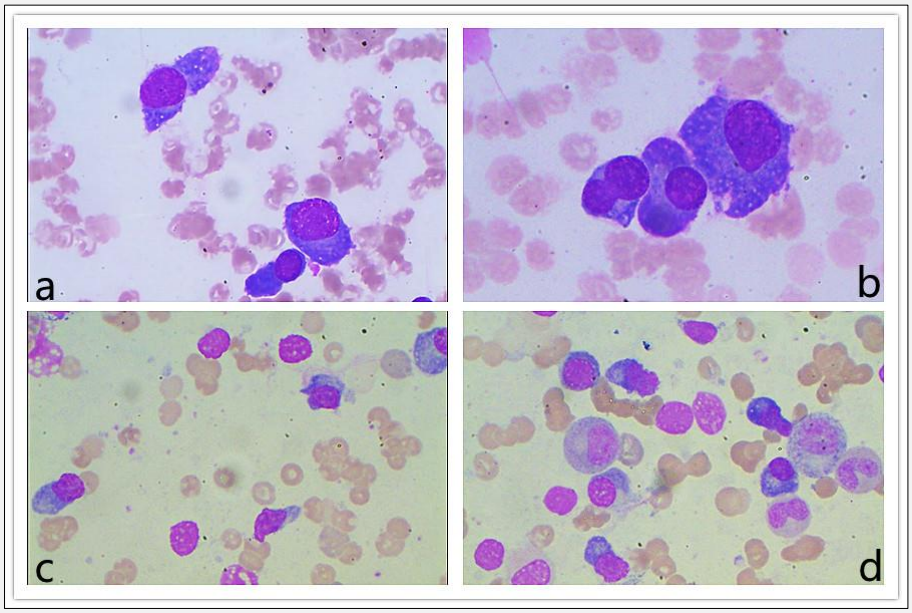

Figure 1. (a, b) Bone marrow aspiration showed diffuse invasion by abnormal plasmocytes. (c, d) During maintenance therapy, 6 months after the initial diagnosis, bone marrow examination indicated obvious infiltration by lymphocytes and lymphoplasmacytoid cells and coexisting plasma cells accounting for 11% of cellularity (Wright-Giemsa, x 1,000).

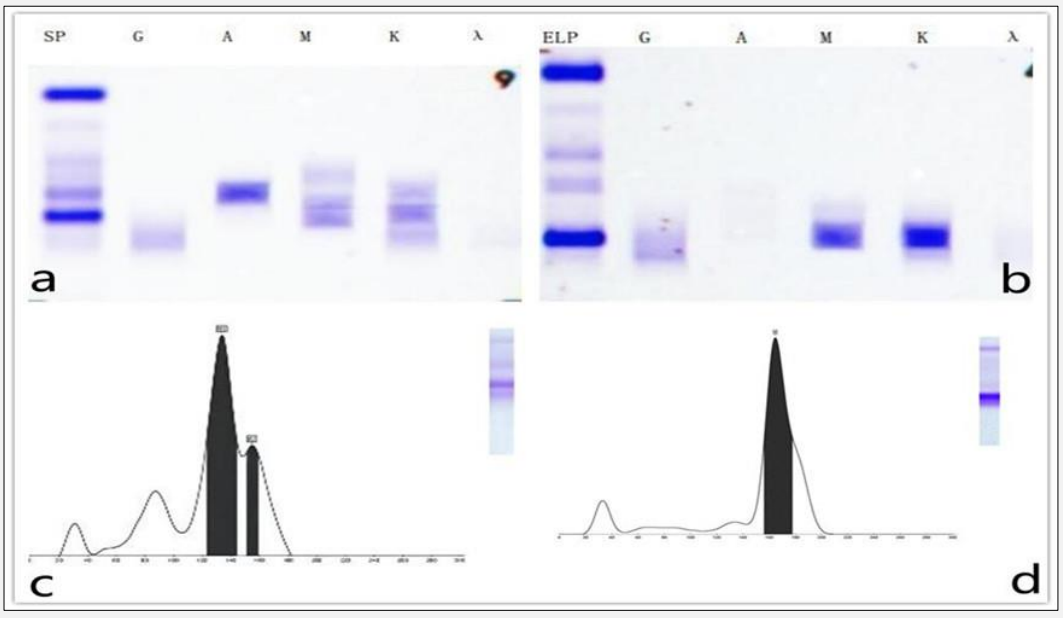

Figure 2. (a, c) Serum/urine protein immunofixation electrophoresis indicated double M-Proteins of IgA-κ and IgM-κ paraproteins. (b, d) During maintenance therapy, 6 months after the initial diagnosis, serum/urine protein immunofixation electrophoresis showed monoclonal M-Protein of IgM-κ paraprotein.

generation of thoracic and lumbar vertebrae. A complete blood count indicated anemia (white blood count: 5.95 x 10^9/L, hemoglobin: 68 g/L, and platelet 218 x 10^9/L). Serum creatinine and calcium were 427.00 µmol /L and 2.30 mmol/L, respectively. Bone marrow aspiration showed diffuse invasion by abnormal plasmocytes, (Figure 1a, b) and flow cytometry immunophenotyping indicated the abnormal plasma cell population (7.5%) was positive for CD38, CD138, and negative for CD45, CD19. Serum/urine protein immunofixation electrophoresis indicated double M-proteins of IgA-κ and IgM-κ paraproteins (Figure 2a, c). Quantitative immunoglobulins and free light chains of serum were as follows: IgA 12.73 g/L, IgM 2.26 g/L, free Kappa light chain 3,352.22 mg/L, and κ/λ 271.65. A diagnosis of PCM was established. After being treated with chemotherapy using BDT regimen (bortezomib, dexamethasone, thalidomide), the proportion of marrow plasma cells returned to normal. During maintenance therapy, 6 months after the initial diagnosis, bone marrow examination indicated obvious infiltration by lymphocytes and lymphoplasmacytoid cells, and coexisting plasma cells accounting for 11% of cellularity (Figure 1c, d). Flow cytometry showed two groups of CD45-positive cells, which were monoclonal plasma cells with positive CD38, CD138, CD19, and mature monoclonal B lymphocytes with negative CD38, CD138 and positive CD19. MYD88 gene mutation was identified using second generation gene sequencing method. Serum/urine protein immunofixation electrophoresis showed monoclonal M-Protein of IgM-κ paraprotein (Figure 2b, d). The diagnosis of second WM during maintenance therapy of PCM was made by combination of medical history, morphology, flow cytometry, immunofixation electrophoresis, and molecular genetics.

DISCUSSION

PCM is a multifocal neoplastic proliferation of abnormal plasma cells, usually related to an M protein in serum and/or urine and organ damage evidence associated with the plasma cell neoplasm. The original site of nearly all PCMs is bone marrow, and in almost all cases there is disseminated involvement of bone marrow. Lymphoplasmacytic lymphoma (LPL) is a kind of small B lymphocyte neoplasm, plasma cells, and plasmacytoid lymphocytes, commonly involving bone marrow, and sometimes spleen and lymph nodes, which can have plasmacytic differentiation, and does not fit the criteria for the other neoplasms of small B cell lymphoid. WM is defined as LPL with an IgM monoclonal immune globulin and bone marrow involvement.

The association of PCM with WM seems to be very rare and only a few cases have been described. Wang E et al. describe a concomitant WM and IgA PCM in a patient with untreated IgM paraproteinemia [3]. Carulli G et al. reported simultaneous presentation of WM and MM [4]. In this rare case, both PCM and WM were restricted to κ light chain. However, the former expressed IgM and IgA, whereas the plasmacytic component of the latter produced IgM.

CONCLUSION

The rare phenomenon has put hematologists into dilemma. The diagnosis was made by integration of medical history, morphology, flow cytometry, immunofixation electrophoresis, and molecular genetics. This case highlights the importance of an integrated diagnostic workup, with an interesting role for morphology and flow immunotyping.

Ethical Approval:
This article does not contain any studies with human participants performed by any of the authors.

Informed Consent:
Informed consent was obtained from all individual participants included in the study.

Declaration of Interest:
All authors declare that they have no conflict of interest.

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