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CASE REPORT

A Case of Multiple Myeloma-Associated Systemic Amyloidosis with Multiple Skin Manifestations as the First Symptom

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Abstract: An 81-year-old woman presented with purpura, petechiae, ecchymoses, flesh or brown-colored waxy, smooth, papules, warty plaque, nail dystrophy and palmodigital erythematous swelling for more than 6 years. She was diagnosed as multiple myeloma-associated systemic amyloidosis after skin subcutaneous histopathological examinations and relevant examinations such as blood and bone marrow. Systemic amyloidosis is closely related with multiple myeloma (MM). Multiple and pleomorphic skin lesions are not usual among patients with multiple myeloma or systemic amyloidosis.

Keywords: multiple myeloma, primary systemic amyloidosis, monoclonal immunoglobulin

Case Report

An 81-year-old woman initially presented to a dermatology clinic with recurrent petechiae, ecchymoses, sometimes hemorrhagic blisters which were not easily ruptured, all over the body for 6 years, without pain or itching. Almost at the same time, the patient found nail abnormality, erythematous, swollen palms, buttocks papules, and progressively relaxation of the skin. She had no recent significant weight change.

Physical examination showed multiple petechia, ecchymosis with negative Nissl sign all over the body, abnormal skin wrinkling and laxity, symmetrical periorbital edema accompanied with purpura, and multiple flesh or brown-colored waxy, smooth, papules on the face and the anterior cervical region (Figures 1–4), hard warty plaque and papules on the left buttock (Figure 5), multiple fingernails dystrophy, palmodigital erythematous swelling.

Blood tests showed serum IgG 3.73g/L(8.60–17.40g/L), IgA 34.40g/L(1.00–4.20g/L), IgM 0.08g/L(0.50–2.80g/L), kappa light chain 3.45g/L(6.29–13.50g/L), lambda light chain 22.90 g/L(3.13–7.23g/L), κ/λ 0.15(1.53–3.29), coagulation factor X 48.70%(77–131%).

Protein electrophoresis and immunofixation electrophoresis showed albumin 48.2%(54.0–65.7%), β2-globulin 32.3% (8.2–13.8%), γ-globulin 1.9%(10.6–23.5%), monoclonal IgA-α and monoclonal λ light chain. M protein was positive which was IgA-λ type. The serum free light chains showed κ 6.2mg/L(3.30–19.40 mg/L), λ 307.5mg/L(5.71–26.3mg/L), Fκ/Fλ 0.020(0.26–1.65), and dFLC 301.3mg/L/L. Urine examination showed that protein quantitation 0.32g/L, albumin

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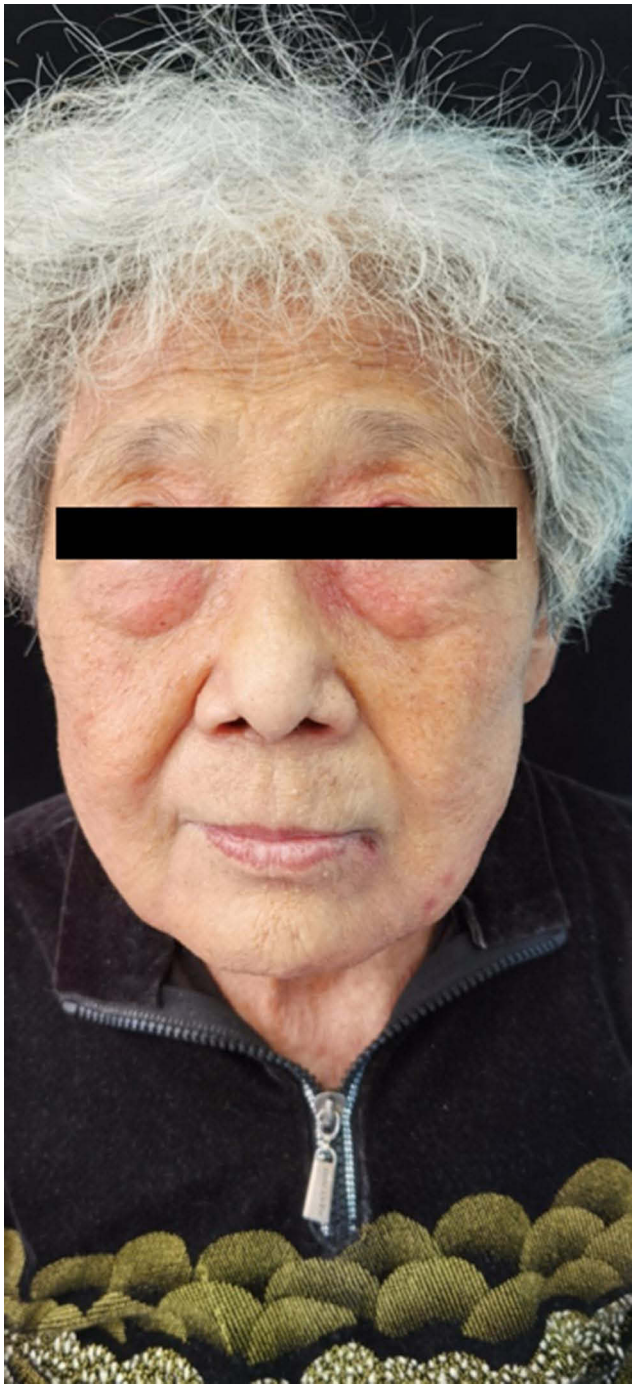

Figure 1 Symmetrical periorbital edema accompanied with purpura, and multiple flesh or brown-colored waxy, smooth, papules were on the patient's face.

98.3%, positive monoclonal IgA-α, monoclonal λ, λ type Bence–Jones protein, λ light chain 7.44mg/dl(0.00–5.00mg/dl) and 24h urine total λ light chains quantification 130mg.

X-ray examination showed no abnormality in bilateral femur and humerus. CT scanning showed no obvious puncture-like bone destruction in the skull, no obvious bone destruction in the whole spine, ribs, sternum and pelvic bones, but cervical and lumbar degeneration.

Bone marrow biopsy showed hyper-cellularity with plasma-cell hyperplasia, which was consistent with multiple myeloma.

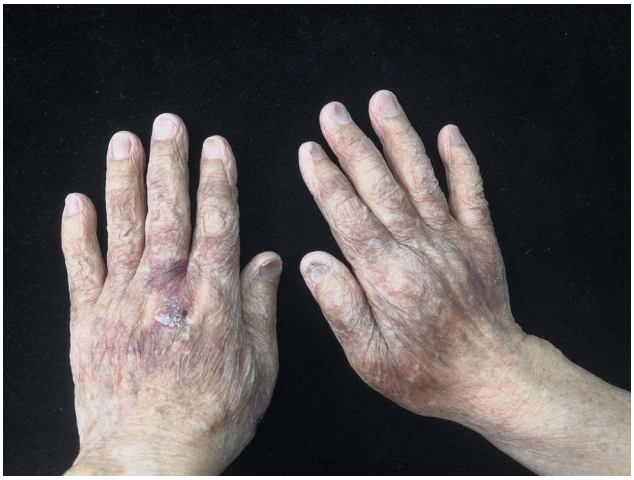

Figure 2 Purpura, petechiae and ecchymoses of the skin and fingernails dystrophy.

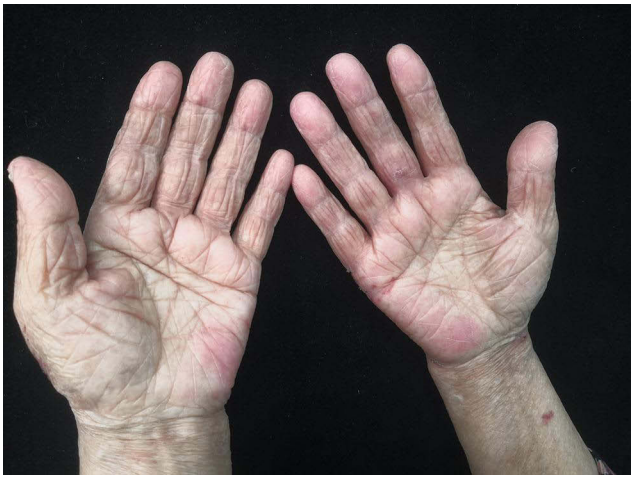

Figure 3 Palmodigital erythematous swelling.

The histopathological features of abdominal skin showed that the eosinophilic, morphous, fissured material was present in the dermis which was positive for Congo red stain (Figures 6 and 7). Electron microscopy showed that sheets of fine fibers 10nm in diameter were disorderly distributed in the dermis (Figure 8). The features were consistent with amyloidosis.

The patient was diagnosed as multiple myeloma and multiple myeloma-associated systemic amyloidosis. After treatment with BD regimen (a regimen of bortezomib in combination with dexamethasone), no significant improvement of skin lesions was observed. The patient refused further treatment due to financial reasons.

Discussion

Immunoglobulin light chain (AL) amyloidosis (known as primary amyloidosis in history) is an uncommon disease, and the exact incidence is still unknown. In the US, the incidence seems to be stable at about 9 to 14 cases per million person-years.[1–3] Olders are more susceptible to AL amyloidosis. As with other plasma cell dyscrasias, the age-specific incidence rates increase in each decade of life after age 40 years.[1] AL amyloidosis in which the fibrils are composed of fragments of monoclonal light chains. Affected patients may suffer from amyloidosis alone, or may be accompanied by other plasma cell dyscrasias (multiple myeloma, Waldenström macroglobulinemia). This portion of AL amyloidosis is related to multiple myeloma, in which the deposited light chains come from plasma

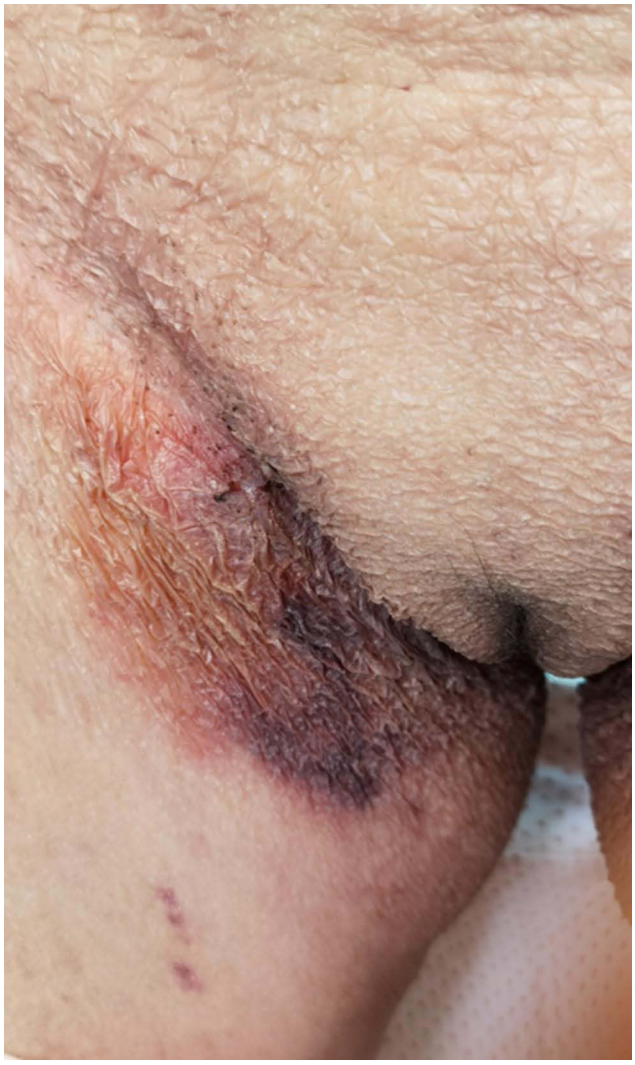

Figure 4 The patient's right groin showed ecchymosis without obvious cause.

cells in the bone marrow, leading to extensive organ deposition and dysfunction.[4–6] There exist complex interactions between immunoglobulin-derived proteins, including light and heavy chains, and elastic tissue components, leading to different types of impairment of the latter.[7] Therefore, AL amyloidosis could have various clinical manifestations of dermatology, including purpura, waxy thickening, ecchymosis and cutis laxa.[7,8]

Amyloid purpura is suspected to be associated with reduction of coagulation factor X, but this connection is not made. It has been observed that in 36 patients, low levels of factor X activity were observed in about 1 out of 4 samples.[9] Because AL amyloidosis is a clonal plasma cell disorder, it is treated with chemotherapy to eradicate the underlying clone. AL amyloidosis must be differentiated from other forms of amyloidosis (eg, AA amyloidosis, ATTRmt amyloidosis, and ATTRwt amyloidosis) since the latter are non-neoplastic and will not benefit from chemotherapy. Compared with normal conditions, MM cells can express lower or higher levels of microRNAs (miRs), which are used as tumor suppressors or oncogenes. Since the expression of tumor suppressor miRs is low in cancer, it may provide therapeutic benefits to restore their normal levels through miRs replacement strategy.[10]

Conclusion

Our patient presented with purpura, flesh or brown-colored waxy, smooth, papules, warty plaque, hemorrhagic blisters, and nail dystrophy in at least five different forms of skin lesions at the same time. We confirmed the presence of amyloid

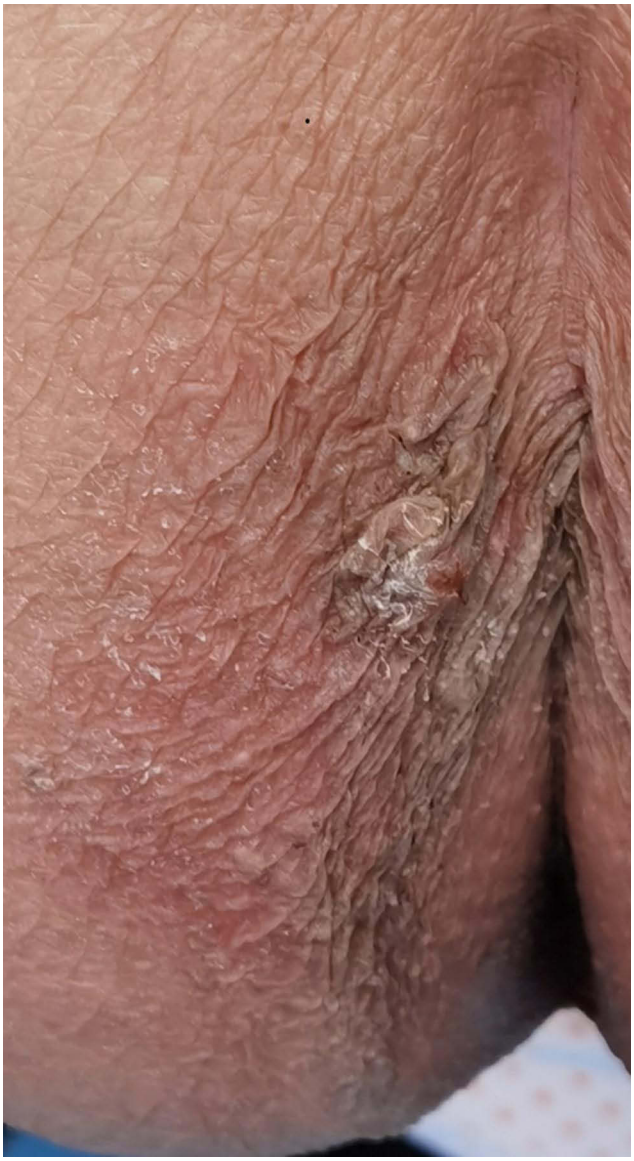

Figure 5 There was a hard warty plaque on the left buttock at 3 o'clock. Bleeding could occur after crushing.

fibrils using Congo red staining for identity. We also observed under the electron microscope, and found sheets of fine fibers with a diameter of about 10nm distributed disorderly in the dermis, consistent with amyloid fibrils. Multiple myeloma was diagnosed through bone marrow biopsy, according to the updated criteria for the diagnosis of multiple myeloma by the International Myeloma Working Group, so the final diagnosis of this patient was multiple myeloma-associated systemic amyloidosis.

We report a case of multiple myeloma-associated systemic amyloidosis, in which the simultaneous presentation of multiple skin lesions at different sites in one patient is clinically rare. It is difficult to identify the same skin disease due to the diverse morphology of the skin lesions. Regarding the skin manifestations, since the morphology of the rash depends on the site of amyloid deposition, if it is deposited in small vessels of the skin, the skin lesions present as petechiae, ecchymosis and purpura; if it is deposited in the superficial layer of dermis, it will present with waxy papules; and if it is deposited in the dermal elastic tissue, it will present with cutis laxa.Initial skin manifestations included multiple skin manifestations in addition to the typical signs of amyloidosis. Petechiae and ecchymoses were the first symptoms in our patient.

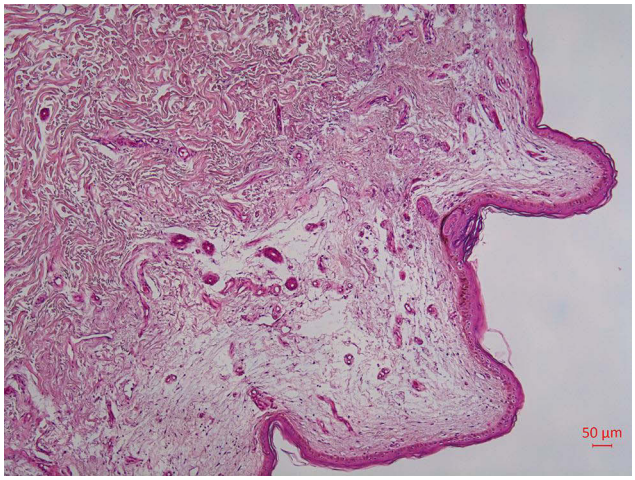

Figure 6 Histological features.

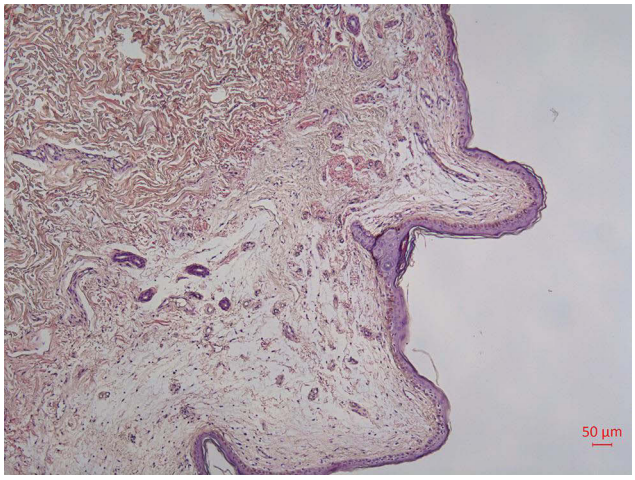

Figure 7 Congo red staining (+).

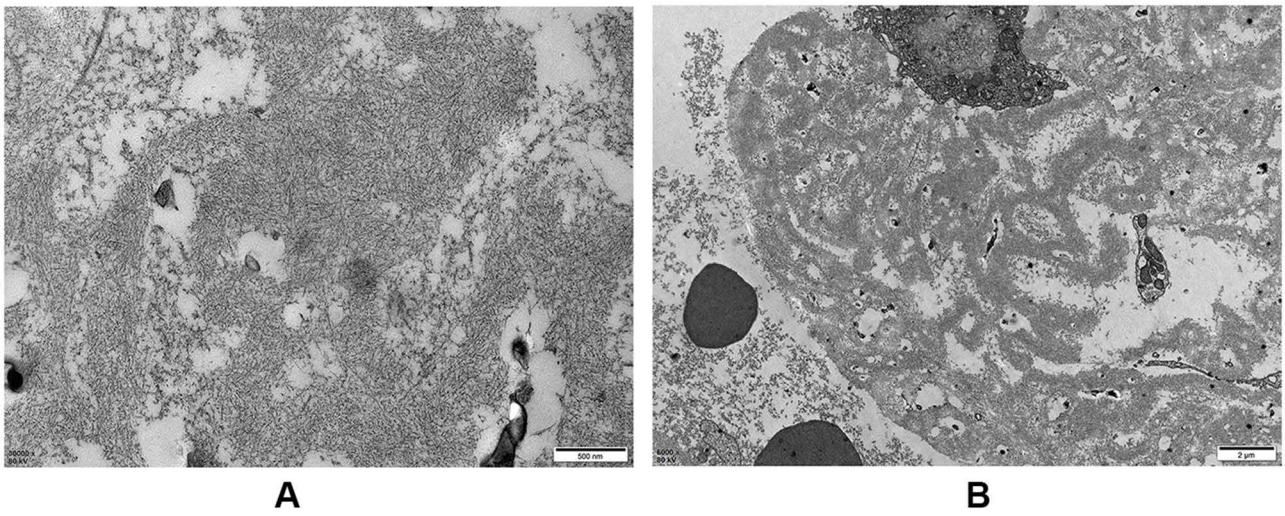

Figure 8 (**A** and **B**) Electron microscopy showed that sheets of fine fibers with a diameter of about 10 nm were disorderly distributed in the dermis, which is in accord with amyloidosis.

Ethics Statements

Written informed consent for publication of their clinical details and clinical images was obtained from the patient. No institutional approval was required. This case report was prepared following the CARE Guidelines.[11]

Disclosure

The authors report no conflicts of interest in this work.

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