Complete remission of both immunoglobulin light chain amyloidosis and psoriasis after autologous hematopoietic stem cell transplantation
A case report

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Abstract
Rationale: Immunoglobulin light chain amyloidosis (AL amyloidosis) is characterized by the deposition of abnormal amyloid protein produced by a pathological plasma cell clone in various organs and soft tissues. Hematopoietic stem cell transplantation (HSCT) is an effective way to treat AL amyloidosis. Psoriasis is a common autoimmune disease (AID) and HSCT is a potential treatment for severe AIDs. We report a rare case of AL amyloidosis coincidence with psoriasis obtained continuous complete remission of the 2 diseases by autologous hematopoietic stem cell transplantation (ASCT).

Patient concerns: A 58-year-old man with a 30-year history of psoriasis complaining of edema and hypotension for 2 weeks was referred to our institution. His urine protein was quantified 2.83 g/day, without hematuria and decrease of glomerular filtration rate.

Diagnosis: Renal biopsy confirmed AL amyloidosis and multiple myeloma was excluded by bone marrow cytomorphologic examination.

Interventions: Chemotherapy regimen based on bortezomib and thalidomide had achieved hematologic partial remission, but the kidney had no response and psoriasis was still active. Furthermore, he received a standard myeloablative conditioning with high dose melphalan followed by ASCT.

Outcomes: The erythema with silvery scales of psoriasis vulgaris gradually improved and almost disappeared after granulocyte implantation. He obtained persistent hematological complete remission, organ response and recovery of psoriasis.

Lessons: We report a rare case of AL amyloidosis coincidence with psoriasis treated by ASCT. The outcome of this patient indicated that ASCT has therapeutic values both in AL amyloidosis and AIDs.

Abbreviations: AID(s) = autoimmune disease(s), AL amyloidosis = immunoglobulin light chain amyloidosis, ASCT = autologous hematopoietic stem cell transplantation, OR = complete remission, FLC = free light chain, HDM = high dose melphalan, HSCT = hematopoietic stem cell transplantation, PR = partial remission.

Keywords: autologous hematopoietic stem cell transplantation, high dose melphalan, immunoglobulin light chain amyloidosis, psoriasis

1. Introduction
Immunoglobulin light chain amyloidosis (AL amyloidosis) is the most common form of systemic amyloidosis associated with underlying plasma cell dyscrasia, which is characterized by the deposition of aberrant amyloid protein derived from monoclonal immunoglobulin light chains.[11] Treatment is aimed at reducing the free light chain (FLC) levels by eliminating the abnormal monoclonal plasma cells.[2] Compared with conventional chemotherapy, the introduction of high dose melphalan (HDM) followed by autologous hematopoietic stem cell transplantation (ASCT) has improved the outcome of AL amyloidosis.[1,4] The psoriatic skin lesion is an inflammatory reaction initiated by infiltrating of T cells and neutrophils in epidermis and dermis.[1] T cells play an important role in the pathogenesis of psoriasis, bone marrow transplantation may alter the course of the disease.[16] Here we report a case diagnosed as AL amyloidosis with psoriasis received HDM/ASCT and has achieved continuous remission of both diseases.

2. Case report
A 58-year-old male with a 30-year history of psoriasis vulgaris presented with hypotension and edema for 2 weeks was referred
to our institution in June 2010. He also complained of dizziness especially in posture change. On physical examination, no abnormalities were noted in his breath or cardiac sounds except mild depressions of both lower limbs. The erythema with slivery scales of psoriasis vulgaris covered more than 50% of the body-surface area, involving mainly the head, extremities, thorax, abdomen and back. The electrocardiogram revealed low voltages in the limb lead, but no obvious abnormalities were found in cardiac ultrasound. The laboratory data showed moderate proteinuria (2.83g/24h), mild hypoalbuminemia (albumin 32.4g/L) and normal serum creatinine (0.53mg/dl). The λ FLC level was 316.73mg/L and the κ FLC level was 44.74mg/L. However, no monoclonal protein was found in serum and urine immunofixation electrophoresis. There was no hypercalcemia, bone pain and osteolytic lesions. Bone marrow cytological examination showed that the proportion of bone marrow plasma cells was 5%, which excluded multiple myeloma. Renal biopsy showed argyrophilic deposits in the mesangium, capillary loops and interstitial vascular walls, which demonstrated positive of Congo red-stained sections (Fig. 1A, B). Immunofluorescence staining for λ light chain was positive in the above mentioned parts (Fig. 1C), and electron microscopy showed the presence of characteristic, 10–15nm diameter, linear, nonbranching, amyloid fibrils (Fig. 1D), which confirmed the diagnosis of AL amyloidosis.

After 2 cycles of bortezomib and dexamethasone treatment, the disease achieved hematologic partial remission (PR), but the kidney had no response. Then the treatment regimen was switched to thalidomide and dexamethasone for ten cycles. He maintained hematologic PR and proteinuria decreased to 1.5g/day. The psoriasis care during the chemotherapy period was limited to topical corticosteroids for avoiding the additional adverse effect of systemic immunosuppressive agents without a tendency to get better. For further organ remission, he underwent HDM/ASCT. After successful harvest of the stem cells, he received a standard myeloablative conditioning with intravenous melphalan (200mg/m² on day -2) followed by ASCT (on day 0). No special treatment was used for psoriasis vulgaris during ASCT. The psoriasic lesions improved gradually and almost disappeared after neutrophil implantation.

He achieved hematologic complete remission (CR) 3 months after ASCT and the proteinuria became negative 23 months later. Postural hypotension and edema improved significantly. During the follow-up of more than 7 years, he acquired persistent hematologic and organic CR accompanied by complete regression of his skin lesions without any treatment.

![Figure 1](image_url). Pathological examination of renal biopsy. A, PASM revealed argyrophilic deposits in the mesangium, capillary loops (arrow) (PASM × 400). B, Congo red positive material deposited in mesangium, capillary loops and interstitial vascular walls (arrows) (Congo red × 200). C, Immunofluorescence staining for λ light chain was strong positive in the mesangium, capillary loops and interstitium (arrows). D, Electron microscope demonstrated 10–15nm diameter, linear, nonbranching, amyloid fibrils (arrow).
3. Discussion

Amyloidosis is a heterogeneous group of diseases characteristic by the deposition of amyloid fibrils in soft tissues.\[7\] The most common type of systemic amyloidosis is AL amyloidosis.\[8,9\] The type of amyloidosis in association with psoriasis is usually AA type,\[9\] especially in patients with renal involvement. The long history of psoriasis may not lead to AL amyloidosis, so the AL amyloidosis was coincidence with psoriasis of this patient. The AL amyloidosis is a fatal disease which can affect most vital organs. Chemotherapy and/or ASCT are aimed at eliminating the clonal plasma cells producing the toxic precursor protein, and can improve the outcomes of AL amyloidosis.\[10,11\] This patient had good response for ASCT, and also got the remission of psoriasis.

Psoriasis is a common AID, with a reported prevalence ranging from approximately 2% to 4.7%.\[12,13\] The cycle of keratinocytes activating dendritic cells, dendritic cells activating T cells, and T cells activating keratinocytes appears to be the main force maintaining the disease.\[12\] Clinical data show that ASCT can be effective against severe AIDs, including Crohn’s disease, systemic sclerosis, systemic lupus erythematosus, multiple sclerosis and juvenile idiopathic arthritis.\[13\] The mechanisms by which ASCT have therapeutic values both in AL amyloidosis and AIDs and the relationship between them is not clear. However, the treatment results of this patient indicated that ASCT have therapeutic values both in AL amyloidosis and AIDs.

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Table 1

| Study     | Year | Age (years) | Gender | BSA%/severity | Reason | Conditioning regimen | Course of psoriasis (years) | Psoriasis CR | Recurrence (mo) | Follow-up (mo) |
|-----------|------|-------------|--------|---------------|--------|----------------------|----------------------------|--------------|-----------------|----------------|
| Cooley et al\[15\] | 1997 | 35 | M | Mild | BL | BU+ CTX | 15 | Before chemotherapy | 19 | 19 |
| Cooley et al\[15\] | 1997 | 53 | M | Unknown | APL | BU+ CTX | Long (unknown) | After ASCT | 14 | 14 |
| Cooley et al\[15\] | 1997 | 40 | F | Severe | BL | BU+ CTX | 15 | Before collection | 8 | 8 |
| Mohren et al\[16\] | 2004 | 34 | M | 36 | MGUS | CTX+ATG | 16 | 3 days after CTX | 16 | 16 |
| Massoc et al\[16\] | 2006 | 50 | M | 27 | NHL | BEAM | 20 | After ASCT | 21 | 120 |
| Bottthe et al\[17\] | 2008 | 35 | M | 50 | MM | MEL | 15 | After ASCT | None | 15 |
| Held et al\[18\] | 2012 | 9 | M | Severe | ES | BU+MEL | Unkown | 20 days after ASCT | None | 15 |
| Sung et al\[19\] | 2015 | 48 | F | Moderate to severe | MM | BU+MEL | Unknown | 20 | After ASCT | 156 | 204 |
| Azevedo et al\[20\] | 2017 | 54 | M | Severe | MM | MEL | 25 | 3 months after ASCT | None | 39 |
| Present study | 2018 | 58 | M | 50 | AL | MEL | 30 | 1 month after ASCT | None | 82 |

AL = immunoglobulin light chain amyloidosis, APL = acute promyelocytic leukemia, ASCT = autologous hematopoietic stem cell transplantation, ATG = antithymocyte globulin, BEAM = BCNU + etoposide + cytosine arabinoside + MEL, BL = Burkitt’s lymphoma, BSA = body surface area, BU = Busulfan, CR = complete remission, CTX = cyclophosphamide, ES = Ewing’s sarcoma, F = female, M = male, MEL = melphalan, MGUS = monoclonal gammopathy of unknown significance, MM = multiple myeloma, mo = months, NHL = non-Hodgkin lymphoma, PGL = plasma cell leukemia.
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