Clinical Case Report

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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 slivery 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, CR = 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.[1] 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.[3,4] The psoriatic skin lesion is an inflammatory reaction initiated by infiltrating of T cells and neutrophils in epidermis and dermis.[5] T cells play an important role in the pathogenesis of psoriasis, bone marrow transplantation may alter the course of the disease.[6] 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

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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 (2.83 g/24 h), mild hypoalbuminemia (albumin 32.4 g/L) and normal serum creatinine (0.53 mg/dl). The λ FLC level was 316.73 mg/L and the κ FLC level was 44.74 mg/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, 10–15 nm 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 1.5 g/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 (200 mg/m^2 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.

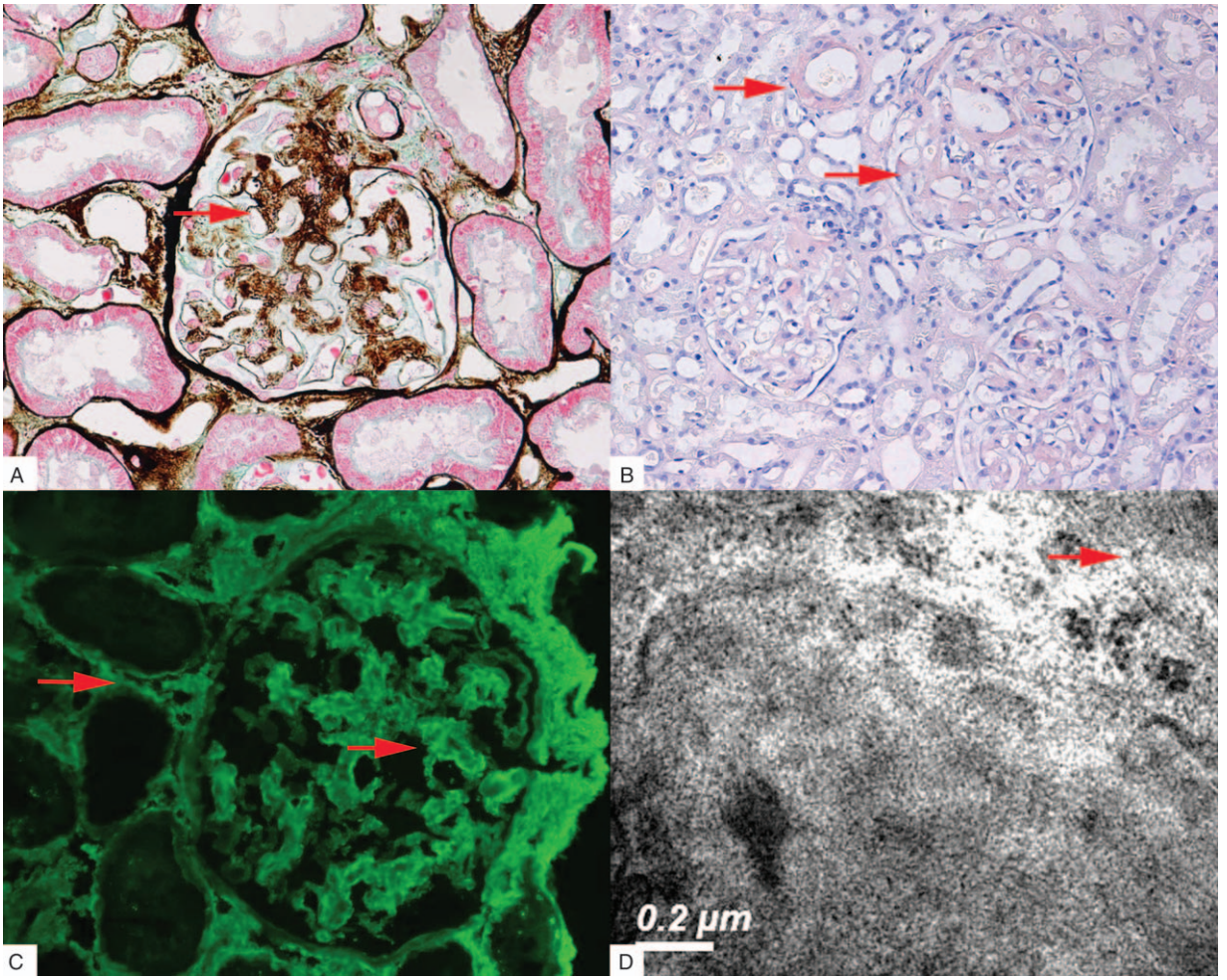

Figure 1. Pathological examination of renal biopsy. A, PASM revealed argyrophilic deposits in the mesangium, capillary loops (arrow) (PASM × 400). B, Congo red positive material deposited in mesangium, capillary loops and interstitial vascular walls (arrows) (Congo red × 200). C, Immunofluorescence staining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

Table 1

Reported cases of psoriasis undergoing autologous hematopoietic stem cell transplantation.

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	PCL	BU+ MEL	13	Before collection	8	8
Mohren et al[15]	2004	34	M	36	MGUS	CTX+ATG	16	3 days after CTX	16	16
Masszi et al[16]	2006	50	M	27	NHL	BEAM	20	After ASCT	21	120
Braiteh 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	Unknown	20 days after ASCT	None	15
Sung et al[19]	2015	48	F	Moderate to severe	MM	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, PCL = plasma cell leukemia.

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] 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] 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%.[11] 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 value in AIDs are unclear.[14] The depletion of pre-existing auto-reactive lymphocytes by the conditioning therapy before ASCT might be an important mechanism of disease regression, ASCT can then be associated with the generation of a new T cell pool that may be tolerant to self-antigens.[15] There is growing evidence that ASCT can also re-establish immunological tolerance. These changes in the repopulated immune cell repertoire, also fundamental post-transplant modifications of the adaptive immune system can contribute to the long-standing effects of ASCT.[16]

Table 1 summarizes 10 patients (including present study) of psoriasis with a median age of 44 years old (range from 9 to 58 years old) that have underwent ASCT.[17–22] There were 8 males and 2 females and the most common reason of performing ASCT was plasma cell diseases (6 cases). Psoriasis completely subsided in all patients, 7 after ASCT and 3 before ASCT. Within a median follow-up of 17.5 months (range from 8 to 204 months), 6 cases had recurred and the median time to recurrence was 17.5 months (range from 8 to 156 months). The longest remission maintained 156 months, although eventually relapsed. The four patients without recurrence all pretreated with melphalan before ASCT. Based on a limited number of patients, psoriasis is likely to remit after allogeneic HSCT, but it is likely to recur after autologous HSCT.[18,23] Although allogeneic HSCT appears more effective, for the high morbidity and mortality of this procedure, it should not be recommended for AIDs unless concurrent with high-risk hematologic malignancy.

In our case, psoriasis occurred 30 years before AL amyloidosis 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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References

[1] Sungur CI. Molecular mechanisms of amyloidosis. N Engl J Med 2003;349:1872–3. author reply 1872-1873.
[2] Palladini G, Merlini G. Current treatment of AL amyloidosis. Haematologica 2009;94:1044–8.
[3] Raschle J, Banz Y, Suter T, et al. A single-centre cohort of patients with systemic light chain AL-amyloidosis treated with conventional chemotherapy or with high-dose chemotherapy and autologous stem cell transplantation. Swiss Med Wkly 2014;144:w13922.
[4] Palladini G, Perfetti V, Obici L, et al. Association of melphalan and high-dose dexamethasone is effective and well tolerated in patients with AL (primary) amyloidosis who are ineligible for stem cell transplantation. Blood 2004;103:2936–8.
[5] Nickoloff BJ, Nestle FO. Recent insights into the immunopathogenesis of psoriasis provide new therapeutic opportunities. J Clin Invest 2004;113:1664–75.

[6] Sullivan KM. Bone marrow transplantation for non-malignant disease. Int J Hematol 2002;76(Suppl 1):169–70.
[7] Leung N, Nasr SH, Sethi S. How I treat amyloidosis: the importance of accurate diagnosis and amyloid typing. Blood 2012;120:3206–13.
[8] Cohen AD, Comenzo RL. Systemic light-chain amyloidosis: advances in diagnosis, prognosis, and therapy. Hematology Am Soc Hematol Educ Program 2010;2010:287–94.
[9] Kagan A, Husza'r M, Frumkin A, et al. Reversal of nephrotic syndrome due to AA amyloidosis in psoriatic patients on long-term colchicine treatment. Case report and review of the literature. Nephron 1999;82:348–53.
[10] Merlini G, Seldin DC, Gertz MA. Amyloidosis: pathogenesis and new therapeutic options. J Clin Oncol 2011;29:1924–33.
[11] Villasenor-Park J, Wheeler D, Grandinetti L. Psoriasis: evolving treatment for a complex disease. Cleve Clin J Med 2012;79:413–23.
[12] Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med 2009;361:496–509.
[13] Hugle T, Daikeler T. Stem cell transplantation for autoimmune diseases. Haematologica 2010;95:185–8.
[14] Li HW, Sykes M. Emerging concepts in haematopoietic cell transplantation. Nat Rev Immunol 2012;12:403–16.
[15] Muraro PA, Douek DC, Packer A, et al. Thymic output generates a new and diverse TCR repertoire after autologous stem cell transplantation in multiple sclerosis patients. J Exp Med 2005;201:805–16.
[16] Zeher M, Papp G, Szodoray P. Autologous haemopoietic stem cell transplantation for autoimmune diseases. Expert Opin Biol Ther 2011;11:1193–201.
[17] Cooley HM, Snowden JA, Grigg AP, et al. Outcome of rheumatoid arthritis and psoriasis following autologous stem cell transplantation for hematologic malignancy. Arthritis Rheum 1997;40:1712–5.
[18] Masszi T, Farkas A, Remenyi P, et al. Ten-year remission of psoriasis after allogeneic but not autologous bone marrow transplantation. Dermatology 2006;212:88–9.
[19] Braiteh F, Hymes SR, Giralt SA, et al. Complete remission of psoriasis after autologous hematopoietic stem-cell transplantation for multiple myeloma. J Clin Oncol 2008;26:4511–3.
[20] Held K, Rahmetulla R, Loew TW, et al. Complete resolution of guttate psoriasis following autologous SCT for Ewing's sarcoma in a pediatric patient. Bone Marrow Transplant 2012;47:1585–6.
[21] Sung SM, Kimball AB. Remission of psoriasis 13 years after autologous stem cell transplant. Cutis 2015;95:E7–8.
[22] Azevedo A, Goncalves C, Selores M, et al. Remission of psoriasis after autologous stem cell transplantation—until when? Eur J Dermatol 2017;27:74–5.
[23] Kaffenberger BH, Wong HK, Jarjour W, et al. Remission of psoriasis after allogeneic, but not autologous, hematopoietic stem-cell transplantation. J Am Acad Dermatol 2013;68:489–92.