

LETTER TO THE EDITOR

Long-term remission after autologous peripheral blood stem cell transplantation for relapsed intravascular lymphoma

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Intravascular lymphoma (IVL), previously described as ‘angiotropic lymphoma’, is a rare lymphoma, classified as a subtype of diffuse large B-cell lymphoma (DLBCL) in the World Health Organization classification.¹ It is pathologically characterized by the presence of lymphoma cells only in the lumina of small vessels, particularly the capillaries, and by the absence of overt lymphadenopathy and tumor formation. Its clinical manifestations are nonspecific and result from the occlusion of vessels by lymphoma cells.^{2,3} Case studies of IVL in Europe have indicated that IVL most commonly presents as skin lesions with plaques and nodules or with neurological abnormalities, including dementia and focal symptoms. Recently, IVL in the absence of cutaneous lesions or neurological abnormalities has been reported, mostly in East Asia.^{4,5} The clinical manifestations of IVL are highly variable. Thus, it is difficult to determine the definite diagnosis in many cases.

Owing to the difficulty of antemortem diagnosis, little information is available about the treatment of IVL. Upfront or salvage autologous peripheral stem cell transplantation (auto-PBSCT) is an attractive therapeutic option in malignant lymphoma. Auto-PBSCT probably improves IVL patient outcomes, but only a small number of case reports with short-term follow-up have been reported.^{6,7}

We describe the long-term follow-up of a case we have previously reported as having angiotropic large-cell lymphoma which presented as nephrotic syndrome.⁸ To our knowledge, this is the first report dealing with long-term follow-up of an IVL patient following auto-PBSCT.

A 63-year-old woman with relapsed IVL was referred to Toyohashi Municipal Hospital in March 2000 to receive salvage therapy and auto-PBSCT. She had been diagnosed as having ‘angiotropic lymphoma’ based on a renal biopsy done in September 1989. At the time of the initial diagnosis, she presented with fever and nephrotic syndrome. No lymphadenopathy, organomegaly, skin lesions or neurological abnormalities were found. Renal biopsy revealed that the glomeruli were filled with lymphoma cells. These cells occupied the capillary lumina and invaded the mesangial area. The precise clinical and pathological findings have been previously reported.⁸ Bone marrow examination revealed a normal distribution of cells. She achieved a complete remission (CR) after five courses of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) therapy.

In October 1999, she had a renal biopsy due to persistent fever and proteinuria. The pathological examination confirmed relapsed IVL. Her disease was refractory to three courses of CHOP therapy, but she achieved a second CR after five courses of dose-modified CHASE therapy (cytarabine 130 mg/m² × 3 days, cyclophosphamide 800 mg/m² × 1 day, etoposide 70 mg/m² × 3 days and dexamethasone 25 mg × 3 days).⁹ G-CSF-mobilized peripheral blood stem cells (PBSCs) were collected after the fifth course of modified CHASE therapy.

The patient underwent auto-PBSCT after receiving a conditioning regimen of carboplatin 300 mg/m² × 4 days, etoposide 400 mg/m² × 4 days and cyclophosphamide 1200 mg/m² × 4 days in June 2000. Neutrophil engraftment was achieved on day 10. Currently, 62 months after auto-PBSCT, she is doing well with no evidence of relapse.

This case suggests that auto-PBSCT could be a therapeutic option for IVL patients with a chemosensitive relapse. Reports of auto-PBSCT in relapsed IVL patients are limited.^{6,7} This strategy is feasible in only a small population of IVL, since ante-mortem diagnosis is difficult,^{2,3,5} their median age is 70 years, and their performance status is usually poor.⁷ Yamaguchi *et al.* have also reported successful auto-PBSCT in relapsed patients; their patients, as well as ours, achieved a second CR after salvage therapy. *In vivo* purging by salvage chemotherapy is probably an important part of achieving success, since intravascular lymphoma cells might easily contaminate the PBSC product. The population of IVL patients in whom auto-PBSCT would be feasible would increase if chemotherapy could be initiated early. Therefore, earlier ante-mortem diagnosis is needed to improve patient survival. Thus, carefully designed clinical studies are needed to investigate the feasibility and usefulness of this strategy.

Interestingly, this patient relapsed more than 10 years after her first CR, even though most patients with aggressive lymphoma rarely relapse 5 years after CR. There have been no previous reports of such a long-term follow-up of an IVL patient. Nevertheless, there are several possible reasons for this patient’s relapse. First, patients can develop IVL as a secondary malignancy 10 years after receiving chemotherapy. However, it is unlikely that our patient developed an identical rare malignant lymphoma at the same sight for both the primary and the secondary malignancy. Second, the clinical characteristics of IVL are different from those of other aggressive lymphomas. The characteristics associated with IVL relapse are not known, as there have been no long-term follow-up studies of IVL patients. Thus, further research is warranted.

We report a case of long-term remission following auto-PBSCT in a relapsed IVL patient. Our report suggests that auto-PBSCT could be a therapeutic option in chemosensitive patients with relapsed IVL. Due to her atypical clinical course, further careful long-term follow-up of our patient is needed.

A Sawamoto¹, H Narimatsu¹, T Suzuki², S Kurahashi¹,
T Sugimoto¹ and I Sugiura¹

¹Department of Hematology, Toyohashi Municipal Hospital,
Toyohashi, Japan and

²Department of Nephrology, Gamagori City Hospital,
Gamagori, Japan

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