We presented our experience with a patient who was diagnosed with MM and CML simultaneously. Evaluation of other cases is required to shed light on clinical characteristics of the disease states, as well as to explore potential evaluable treatments.

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## Sequential heart and autologous stem cell transplantation for light-chain cardiac amyloidosis

**TO THE EDITOR:** Primary cardiac amyloidosis accompanying heart failure, angina, and/or arrhythmia is very serious and has a poor prognosis [1]. Sequential heart and autologous stem cell transplantation has resulted in some promising outcomes in a few series [2-4]. We present a case of primary amyloidosis with cardiac involvement that was successfully managed with these combined approaches.

### Case

A 62-year-old woman was referred to our clinic with 3 months of dyspnea on exertion; she was categorized in New York Heart Association class III, and had abnormal echocardiographic findings. She had no other medical history of note. On initial physical examination, her vital signs were as follows: blood pressure, 88/45 mmHg; pulse rate, 79 beats/min; and body temperature, 36.6°C. Neck vein engorgement and pretibial pitting edema were noted. Heart and lung sounds on auscultation were normal. Initial laboratory tests were as follows: white blood cell count, 5,600/μL; hemoglobin, 12.4 g/dL; platelet count, 150,000/μL; protein, 6.0 g/dL; albumin, 3.6 g/dL, blood urea nitrogen, 21 mg/dL; serum creatinine, 1.33 mg/dL; aspartate aminotransferase, 19 IU/L; alanine aminotransferase, 20 IU/L; alkaline phosphatase, 128 IU/L; troponin I, 0.041 ng/mL; and brain natriuretic peptide (BNP), 629 pg/mL. There were no abnormal findings on urinalysis.

A chest radiograph revealed cardiomegaly with a cardiothoracic ratio of 0.7 and increased interstitial markings suggesting pulmonary edema. Both costophrenic angles were blunted with bilateral pleural effusion. Electrocardiography displayed low voltage in leads I, II, and III and T-wave inversion in leads V5 and V6. Transthoracic echocardiography revealed thickened ventricle walls with minimal pericardial effusion and impaired diastolic function. Left ventricle (LV) filling pressure was high, with an E/E' of 37. No regional wall motion abnormality was observed and the LV ejection fraction was 59%. Cardiac magnetic resonance imaging indicated diffuse transmural or subendocardial enhancement at both ventricular walls on a delayed enhancement image, which were consistent with cardiac amyloidosis (Fig. 1A). Endomyocardial biopsy with a femoral venous approach was performed to confirm this diagnosis. On pathologic examination, amyloid deposits were confirmed by Congo-red staining. Immunohistochemical staining results were as follows: prealbumin (+); kappa chain (++); lambda chain (-); and amyloid A (-) (Fig. 1B, C). Although paraproteinemia or Bence-Jones proteinuria were not evident by electrophoresis and immunofixation, the patient's serum free light-chain ratio was increased to 114 (kappa, 2,040.0 mg/L; lambda, 17.9 mg/L). A bone mar-

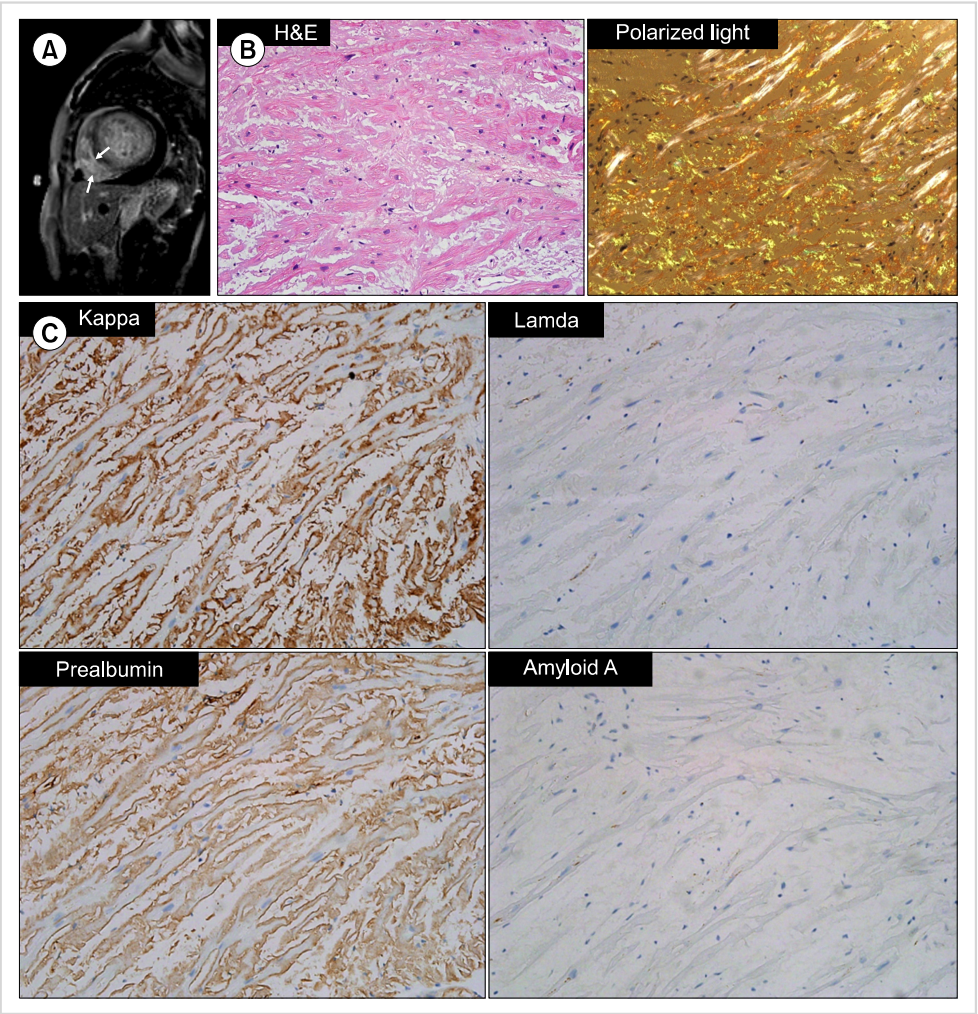


**Fig. 1.** Cardiac magnetic resonance image of the study patient at the time of diagnosis. The delayed enhancement image displays subendocardial enhancement at both the left and right ventricle walls **(A)**. Pathology of the initial endomyocardial biopsy **(B, C)**. Congo-red stain showing positivity for amyloid deposits. Under polarized light, amorphous materials showing an apple-green birefringence were evident **(B)**. Immunohistochemical staining results: prealbumin (+); kappa chain (++); lambda chain (-); amyloid A (-) (C).

row biopsy revealed mild plasmacytosis of 3.6% without infiltration of neoplastic plasma cells or amyloid deposits. There was no evidence of light chain deposition in other organs including the gastrointestinal tract. The patient had no symptoms suggestive of neuropathy. Computed tomography of her chest, abdomen, and pelvis also revealed no abnormal findings other than benign-appearing hepatic cysts. From these aforementioned findings, the patient was diagnosed with immunoglobulin light chain (AL) amyloidosis with cardiac involvement.

Heart transplantation followed by high-dose chemotherapy (HDC) with autologous stem cell transplantation (ASCT) was the planned treatment in this case. While the patient was waiting for her heart transplant, she received high-dose dexamethasone to control her monoclonal gammopathy, as no other novel anti-myeloma therapies were covered by National Health Insurance in Korea at that time. After 2 cycles of treatment, the patient's intraventricular septal thickness and ejection fraction were unchanged on follow-up echocardiography and her BNP level had actually increased (Fig. 2). However, the difference between the kappa and lambda serum free light chain decreased from

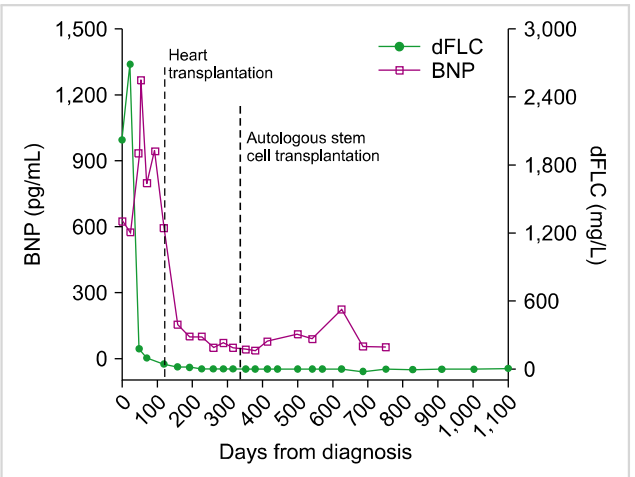


**Fig. 2.** Changes in the free light-chain profile and levels of brain natriuretic peptide in the study patient.
Abbreviations: BNP, brain natriuretic peptide; dFLC, free light-chain difference.

2,022.1 to 8.2 after 4 cycles of high-dose dexamethasone.

Four months after her diagnosis, the patient underwent

**Table 1.** Previously reported outcomes in patients with AL amyloidosis and cardiac involvement who underwent heart transplantation followed by autologous stem-cell transplantation and/or chemotherapy.

| References | Time | HT/ASCT (N) | TRM (%) | Relapse in graft/serum | Alive (%, median FU mo) |
|---|---|---|---|---|---|
| Gillmore *et al.* [2] | 1992 to 2005 | 5/5 | 0 (0) | NA/2 of all | 3 (60%, 95.5) |
| Lacy *et al.* [11] | 1994 to 2005 | 11/11 | 2 (18.2) | 5/2 of 6 survivors | 6 (54.5%, 24) |
| Dey *et al.* [3] | 2000 to 2008 | 9/8 | 1 (12.5) | 1/2 of 7 evaluable patients | 5 (62.5%, 56) |
| Davis *et al.* [4] | 2008 to 2013 | 10/5 | 0 (0) | 1/NA | 10 (100%, 12.6) |

Abbreviations: ASCT, autologous stem cell transplantation; FU, follow-up; HT, heart transplantation; NA, not available; TRM, treatment related-mortality.

heart transplantation. Subsequent echocardiography and cardiac computed tomography revealed no abnormal findings. The level of BNP decreased to within normal range. The patient then received immunosuppressive therapy including tacrolimus, mycophenolic acid, and methylprednisolone. Mycophenolic acid was tapered after 8 months. Eleven months after transplantation, the patient underwent high-dose chemotherapy (melphalan 200 mg/m$^2$), supported by ASCT with a well-functioning transplanted heart. She experienced grade 3 diarrhea and grade 3 esophageal ulcers during ASCT, which resolved without sequelae. Neutrophil engraftment (absolute neutrophil count $>$500/μL) was achieved on day 9. The patient was in complete remission with normal heart function at 21 months after ASCT at the time of last follow-up.

## Discussion

Deposits of amyloid fibrils from the monoclonal protein induced-impairment of organ function can cause disease-related morbidity and/or mortality in patients with systemic AL amyloidosis. Cardiac involvement is reported in up to 50% of amyloidosis cases and is associated with poorer clinical outcomes compared with amyloidosis cases involving other organs [5]. HDC with ASCT has been a main therapeutic approach for amyloidosis and has dramatically improved overall survival outcomes from 12–21 months to 4.6 years [6-8]. However, a substantial degree of treatment-related mortality due to heart failure and/or arrhythmia is associated with this therapy in cases of cardiac amyloidosis, and this has resulted in a much shorter median survival of 1.6 years compared with amyloidosis involving other organs [6, 9]. In addition, advanced stage cardiac amyloidosis is notorious for having a dismal prognosis with a median overall survival of only 5 months [10].

Accordingly, heart transplantation prior to HDC and ASCT has emerged as a treatment strategy for cardiac amyloidosis. In 2006, Gillmore *et al.* [2] reported that of 5 AL amyloidosis patients with cardiac involvement who underwent heart transplantation prior to ASCT, 3 had long-term survival with no evidence of amyloid deposits. Subsequent promising outcomes have been documented, but mostly from studies in the USA (Table 1) [3, 4, 11]. To the best of our knowledge, the present study is the first Asian case report of a cardiac amyloidosis patient treated with heart transplantation followed by ASCT. Given the poor prognosis associated with cardiac amyloidosis, this combined treatment modality is likely to be the best available therapeutic option for long-term survival in appropriately selected patients.

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## An unusual case of metachronous NK/T cell lymphoma and interdigitating dendritic cell sarcoma

**TO THE EDITOR:** Interdigitating dendritic cell sarcoma (IDCS) is a very rare disease entity characterized by neoplastic proliferation of spindle-shaped cells with phenotypic features similar to those of interdigitating dendritic cell (IDC). To date, only about 100 cases of IDCS have been reported in English literature [1], and because of its rarity, the pathophysiology is not fully understood. Interestingly, IDCS has been reported to be associated with other malignancies, in particular lymphoid malignancies [2, 3]. Traditionally, IDC has been recognized as a myeloid lineage due to its functional similarities to macrophages. Therefore, IDCS frequently occurring in patients with B-cell lymphoid malignancies is difficult to explain through the usual hematopoietic process, which is uni-directional and has irreversible lineage commitment. In this paper, we present a rare case of a patient who was diagnosed as NK/T cell lymphoma 19 months after achieving complete remission of IDCS with literature review.

A 77-year-old female presented to our institution with palpable left lower quadrant abdominal mass in September 2015. Abdominal computed tomography (CT) scan showed a soft tissue mass near the left external iliac nodal area (Fig. 1A). Subsequent $^{18}$fluorodeoxyglucose-positron emission tomography (18 FDG PET)-CT showed high FDG uptake only on the same lesion (Fig. 1B). A core needle biopsy of the lesion revealed atypical T-cell proliferation with angiodestructive pattern (Fig. 2). Neoplastic cells were strongly positive for CD4, granzyme B, CD3, and CD8 but negative for CD20, CD1a, S-100, and CD56a. Fluorescent in situ hybridization of the biopsy specimen was positive for Epstein-Barr virus (EBV). These findings were consistent with NK/T cell lymphoma. Considering limited lesion, old age, and poor general condition of the patient, we performed radiation therapy for the abdominal mass. However, 1 month after completion of treatment, she complained of aggravated general condition with a febrile sensation. On sequentially performed PET-CT (Fig. 1C, D), disseminated FDG-avid masses were identified on the nasopharynx, lymph nodes in multiple areas, spleen, and both lungs, whereas the radiated abdominal mass regressed. Biopsy on the nasopharynx also revealed NK/T cell lymphoma. Despite Aspa-Met-Dex chemotherapy (dexamethasone 40 mg on days 1–4; high-dose methotrexate 3 g/m$^2$ on day 1; and L-asparaginase 6,000 U/m$^2$ on days 2, 4, 6, and 8 every 21 days), her condition drastically deteriorated only after the first cycle of chemotherapy, and she died of disease progression and pneumonia. Interestingly, 2 years earlier, she was diagnosed with IDCS after pathologic evaluation of newly developed cervical lymphadenopathy (Fig. 3). At that time, biopsy of the cervical lymph node showed S-100 and CD68 staining spindle- to ovoid-shaped cells intermingled with reactive T lymphocytes that are distinctively different from the pathologic finding of abdominal mass in this time. She received 6 cycles of ABVD chemotherapy (doxorubicin 25 mg/m$^2$, bleomycin 10 mg/m$^2$, vinblastine 6 mg/m$^2$, and dacarbazine 375 mg/m$^2$ on days 1 and 15 every 28 days) for IDCS and achieved complete remission. She has remained well for 19 months (Fig. 2B).

The World Health Organization classifies dendritic cells (DCs) into 4 types: follicular, interdigitating, Langerhans cell, and fibroblastic cells. DC neoplasms are classified based on those 4 types of normal counterpart. Among them, IDCs are primarily distributed in the thymus or T-cell zones of lymphoid organs where they are responsible for presenting various antigens on the cell surface to the T-cells of the immune system. As mentioned earlier, IDCS cases have been frequently reported to be accompanied by synchronous or metachronous lymphoid malignancies. To elucidate this unique phenomenon, a few putative mechanisms have been proposed. The cross-lineage "trans-differentiation" theory is among the most convincing concepts. In particular, several recent studies demonstrated a clonal relationship between a few indolent B cell lymphoma and IDCS that occurred synchronously or metachronously in the same patient by showing the presence of identical clonal immunoglobulin (Ig) gene rearrangement or showing that the Ig gene harbors the same molecular or cytogenetic abnormalities in 2 different malignancies [4, 5]. Moreover, some studies supported the lineage plasticity of DC by showing an inheritance of B-cell or T-cell genotype in patients with histiocytic/DC malignancies [6]. Although we did not perform comparative molecular study including assessment of T-cell receptor gene rearrangement, the 2 different hematologic malignant cells in our case are less likely clonally related with each other