hyperuricemia, but without hepatic metastasis [4]; our patient also showed identical results. Therefore, it cannot be precisely stated that the typical STLS in SCLC shows hepatic metastasis at diagnosis, and further studies are required to confirm the previous concept.

In conclusion, we report here a case of STLS associated with BM metastatic SCLC without hepatic metastasis at diagnosis, and to our best knowledge, this is the first case report of STLS associated with BM metastatic SCLC in Korea.

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Characteristics and survival of patients with atypical chronic myeloid leukemia

TO THE EDITOR: BCR/ABL-negative or atypical chronic myeloid leukemia (CML; aCML) is a rare hematologic malignancy with an estimated incidence of 1–2% among all BCR/ABL-positive CML cases [1, 2]. Due to its rarity, no prospective study has been conducted to optimize a treatment strategy for BCR/ABL-negative CML; consequently, BCR/ABL-negative CML is managed with palliative therapy. A population-based study on aCML outcome is rare. Thus, aCML characteristics and outcomes were analyzed using the National Health Information Database (NHID) [3, 4].

Patients diagnosed with aCML (International Classification of Diseases, Tenth Revision, C922) between 2004 and 2015 were included. Patients 1) aged <20 years, 2) who received chemotherapy before the aCML diagnosis, and 3) for whom C922 was recorded just once during the follow-up period were excluded. Data on age, sex, insurance premiums imposed on patients proportionate to their income, location of the medical institution, transfusion history, prescription

Table 1. Characteristics of atypical chronic myeloid leukemia patients.

	N=54
Median age at diagnosis, yr (range)	73 (26–90)
≤65, N (%)	15 (27.8)
>65, N (%)	39 (72.2)
Sex, male, N (%)	35 (64.8)
Income	
High, N (%)	35 (64.8)
Low, N (%)	19 (35.2)
Location of the institution	
Capital (Seoul), N (%)	20 (37.0)
Other, N (%)	34 (63.0)
Transfusion, N (%)	49 (90.7)
RBC transfusion only, N (%)	17 (31.5)
Platelet transfusion only, N (%)	0 (0.0)
RBC and platelet transfusions, N (%)	32 (59.3)
Median number of transfused packed RBC per mo, (range)	2.6 (0.2–8.5)
Medication	
Hydroxyurea, N (%)	50 (92.6)
Azacitidine, N (%)	0 (0.0)
Decitabine, N (%)	7 (13.0)
Cytarabine, N (%)	8 (14.8)
Hematopoietic stem cell transplantation, N (%)	0
Progression to acute myeloid leukemia, N (%)	5 (9.3)
Median time to acute myeloid leukemia progression, mo (range)	5 (1–30)
Death, N (%)	47 (87.0)

Abbreviation: RBC, red blood cell.

list, and date of death were collected. The cut-off date was December 31, 2017. Overall survival (OS) was calculated using the Kaplan–Meier method. The Cox proportional hazard regression model was utilized to determine OS predictors. Statistical analyses were conducted using the SAS version 9.2 (SAS Institute, Cary, NC, USA). The institutional review board of Wonju Severance Christian Hospital waived the need for informed consent because of the retrospective design of the study.

Over 11 years, only 54 patients with aCML were identified (Table 1). The median age at diagnosis was 73 (26–90) years. The age distribution was as follows: ≤65 years, 15 (27.8%) patients, and >65 years, 39 (72.2%) patients. About 65% (N=35) of patients were men. Thirty-five patients (64.8%) were paying high insurance premiums, and 20 (37%) were treated at a medical institution located in Seoul (Capital). Most patients received transfusions (91%), 59% (N=32) needed both red blood cell (RBC) and platelet transfusion, and 31.5% (N=17) received RBC transfusion only. The median 2.6 (0.2–8.5) pack of RBCs were transfused every month. Hydroxyurea was administered to 93% of patients. Seven patients (13%) received decitabine, and 8 (14.8%) received cytarabine. No patients received azacitidine or underwent hematopoietic stem cell transplantation (HSCT). Five patients (9.3%) progressed to acute myeloid leukemia (AML) after a median of 5 (1–30) months after the diagnosis. Characteristics (age, sex, income, institution location, transfusion, and medication) of patients who progressed to AML were not different from those of patients who did not progress to AML (data not shown).

Over a median of 10 (1–135) months of follow-up, 47 patients died. The median survival was 10 months with a 95% confidence interval of 6–14 months, and the estimated 1- and 2-year OS rates were 38.9% and 27.8%, respectively. The estimated 1-, 2-, and 3-year OS rates of patients who progressed to AML were 40%, 40%, and 20%, respectively. This was not significantly different from the OS of patients who did not progress to AML, who showed 1-, 2-, and

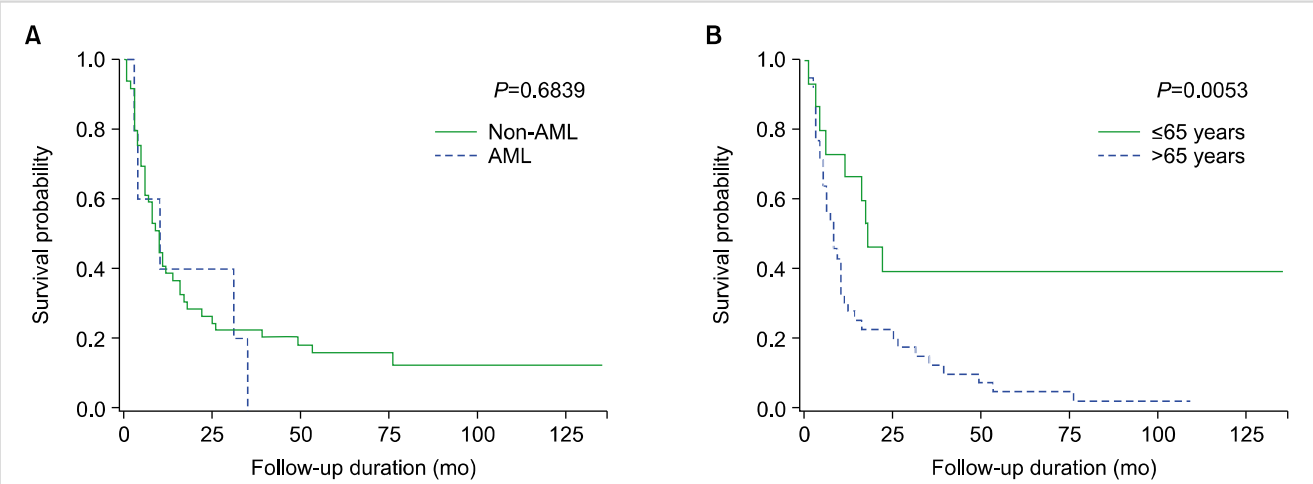

Fig. 1. Kaplan–Meier plot of 52 patients with atypical chronic myeloid leukemia. **(A)** The OS of 5 patients who progressed to AML (dotted line) was not different from that of those who did not progress to AML (solid line, N=49, $P=0.6839$). **(B)** Patients aged ≤65 years (dotted line) showed better OS than those aged >65 years (solid line, $P=0.0053$).
Abbreviations: AML, acute myeloid leukemia; OS, overall survival.

Table 2. Univariate and multivariate analyses of overall survival.

Variable		Median survival (mo)	Death (%)	Crude HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
Sex	Male	11 (6–18)	30/35 (85.7)	1.00 (reference)	0.4642	1.00 (reference)	0.519
	Female	7 (3–16)	17/19 (89.5)	1.24 (0.69–2.27)		1.22 (0.67–2.23)	
Age (yr)	≤65	NR	9/15 (60.0)	1.00 (reference)	0.0088	1.00 (reference)	0.008
	>65	8 (5–10)	38/39 (97.4)	2.68 (1.28–5.60)		2.72 (1.30–5.72)	
Income	High	10 (6–18)	31/36 (88.6)	1.00 (reference)	0.762	1.00 (reference)	0.882
	Low	8 (4–31)	16/19 (84.2)	0.91 (0.50–1.67)		0.96 (0.52–1.76)	
Location of the institution	Seoul	10 (5–17)	29/34 (85.3)	1.00 (reference)	0.630	1.00 (reference)	0.503
	Others	8 (4–22)	18/20 (90.0)	1.16 (0.64–2.09)		1.20 (0.66–2.19)	

Abbreviations: CI, confidence interval; HR, hazard ratio; NR, not reached.

3-year OS rates of 38.8%, 26.5%, and 22.5%, respectively (P=0.68) (Fig 1A).

Prognostic factors of OS were analyzed using Cox proportional hazard ratios with the following variables: sex, age, income, and location of the medical institution. Only age was a significant predictor of OS in both univariate and multivariate analyses. Patients aged >65 years were at 2.68-times higher risk of death than those aged ≤65 years (P=0.0088) (Table 2, Fig 1B).

Although it was unknown whether all patients met the World Health Organization classification criteria, the following data were compatible with those in previous reports: the median age was 73 years [2, 5-10], more men were affected than women [6-10], and the median OS was 10 months [8-11]. However, some other reports indicated better OS than these rates, showing that the median OS ranged from 2 to 3 years [5, 7, 10, 12].

Age >65 years, female sex, hemoglobin levels of <10 g/dL, and leukocyte count of $>50\times10^9$/L have been described as negative predictive factors of OS [5, 7]. As shown in Table 2, the median survival in women was worse than that in men (7 vs. 11 mo). However, this was not significant in both univariate and multivariate analyses in this study. Only old age (>65 yr) was consistently associated with poor OS in this analysis. The natural history of aCML is characterized by increases in leukemic cell burden, organomegaly, anemia, and bone marrow failure with AML transformation in 30–40% of cases [5, 7-9]. In this study, few patients progressed to AML (9.3%). Similarly, Patnaik *et al.* reported a leukemic transformation rate of 8% [10]. Although no long-term survivor was observed in patients who progressed to AML, AML progression did not affect OS. We could not find any predictive factor for AML progression, which may be due to the small number of patients.

Because of poor prognosis, allogeneic HSCT is considered as the only curative treatment to improve OS. Koldehoff *et al.* described favorable outcomes, with a 5-year OS of >80%, in 24 patients who underwent allogeneic HSCT [13]. Conversely, Mittal *et al.* described worse outcomes because of high transplant-related mortality due to graft-versus-host disease, sepsis, and other causes [14]. In this study, no patients underwent allogeneic HSCT. Patients were mainly treated with hydroxyurea and blood product transfusion. Recent studies have suggested potential therapies to target different genetic alterations, such as ruxolitinib for *JAK2* mutations and dasatinib (SRC kinase inhibitor) for *CSFR* truncation mutations, in which downstream signaling is predominantly operated through SRC kinase [15]. Thus, identification of new targets, development of novel therapies, improvement in transplant techniques, and selection of appropriate candidates for allogeneic HSCT will help in improving aCML outcomes.

This study had limitations because blood counts, bone marrow aspiration findings, and cytogenetic or genetic alterations were not available. Therapeutic effects or differences in clinical feature at presentation were unknown. However, a relatively large number of patients with this rare disease could be included using the NHID. Our results may provide background information for clinical trials in the future.

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Successful treatment of non-IgM lymphoplasmacytic lymphoma by bortezomib-containing regimen: case reports and review of literature

TO THE EDITOR: Lymphoplasmacytic lymphoma (LPL) with non-immunoglobulin M (IgM) paraproteinemia is a rare subtype of LPL [1]. Furthermore, the clinicopathological features and appropriate treatment regimen for non-IgM LPL have not been clarified. Non-IgM LPL reportedly has a higher rate of extramedullary involvement and poorer overall survival than IgM LPL-Waldenström macroglobulinemia (WM) [2]. Herein, we report two cases of successful treatment of non-IgM LPL using bortezomib (Bor)-containing regimen, in addition to a literature review.

Case 1

A 71-year-old man was referred to our hospital with fever and abdominal pain for one month. The laboratory findings were as follows: white blood cells (WBC), 6.6×10^9/L; hemoglobin (Hb), 9.8 g/dL; platelet (PLT), 500×10^9/L; total protein (TP), 7.5 g/dL; albumin (Alb), 2.8 g/dL; lactate dehydrogenase (LDH), 195 IU/L; compensated Ca, 9.9 mg/dL; C-reactive protein (CRP), 6.28 mg/dL; IgG, 2363 mg/dL (normal range, 861–1,747 mg/dL); IgA, 147 mg/dL; and IgM, 41 mg/dL. Serum protein electrophoresis demonstrated an M-spike in the gamma fraction, and the serum immunofixation test revealed monoclonal bands of IgG and kappa. A soft tissue mass in the mesenteric lymph nodes was observed on computed tomography (CT) (Fig. 1A). Bone marrow (BM) aspiration revealed abnormal increases in atypical small lymphocytes, lymphoplasmacytes, and plasmacytes. The biopsy specimen of the BM exhibited diffuse infiltration of atypical small lymphocytes, lymphoplasmacytes, and plasmacytes (Fig. 2A). On immunohistochemical staining, the atypical lymphoplasmacytes and plasmacytes were positive for CD138 (Fig. 2B); however, CD79a, IgG-kappa, and CD20 expression was weak (Fig. 2C). Conventional cytogenetic analysis of the BM aspirate demonstrated a normal karyotype, and fluorescence *in-situ* hybridization (FISH) analyses for translocations involving immunoglobulin heavy chain, including IgH-BCL1, chromosome (chr) 13q deletion (del), and chr 6q del, were negative. Thus, the patient was diagnosed with LPL with IgG-kappa M protein, accompanying B symptoms and a mesenteric mass. The patient was categorized as having an intermediate risk according to the international prognostic scoring system for WM [3]. He was treated using BDR therapy [4], which was modified for the Japanese health insurance system: one cycle of subcutaneous injection of Bor (1.3 mg/m^2); oral dexamethasone (Dex, 20 mg) on days 1, 2, 4, 5, 8, 9, 11, and 12; and rituximab (R, 375 mg/m^2) on day 11. For induction therapy, four cycles were repeated every three weeks, followed by four more cycles for maintenance therapy three months

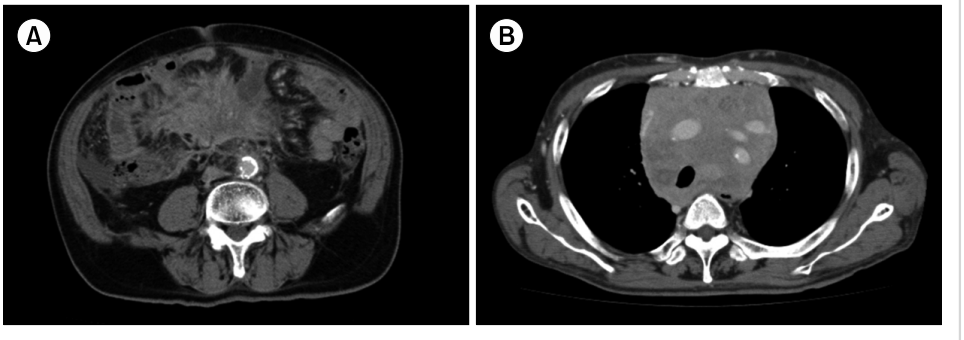

Fig. 1. Computed tomography at diagnosis. **(A)** A soft tissue mass in the mesenteric lymph nodes in Case 1. **(B)** A bulky mass in the mediastinum in Case 2.