Report of 6 Cases of Large Granular Lymphocytic Leukemia and Plasma Cell Dyscrasia

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Clinical Practice Points

- Both large granular lymphocytic leukemia (LGLL) and multiple myeloma (MM) are rare diseases. This report describes 6 cases of concurrent LGLL and MM from a database of 858 patients with LGLL.
- The present results suggest that the association of the 2 disorders is not a mere coincidence. This report also explores the effects of one disease treatment on the other.

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Introduction

Large granular lymphocytic leukemia (LGLL) is a rare lymphocytic malignancy that was discovered in 1985.[1,2] There are 2 types of LGLL: the type with T-cell large granular lymphocytes (LGLs), called T-LGLL (85%), and the type with natural killer−cell LGLs, called NK-LGLL (15%). Clinical features of LGLL include cytopenias and rheumatoid arthritis. The majority of patients have an indolent clinical course.

Chronic B-cell dyscrasia is an important clinical feature of LGLL, including monoclonal gammopathy of undetermined significance (MGUS), chronic lymphocytic leukemia, and B-cell lymphoma.[3] One study reported 15 patients with LGLL and coexisting hairy cell leukemia.[4] In a French registry, 12 of 229 patients with LGLL had associated B-cell lymphoid neoplasms.[5] Moreover, monoclonal B-cell lymphocytosis has been found to be frequently associated with LGLL.[6]

This report describes 6 patients with coexistent LGLL and multiple myeloma (MM). The concomitant presence of the 2 disorders presented the opportunity to retrospectively observe the effect of bortezomib and lenalidomide, 2 novel agents used for the treatment of MM, on the LGLL clone.

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Patients and Methods

The authors screened a clinical database of 629 patients with LGLL followed up at Penn State Hershey Cancer Institute and 229 patients with LGLL at the French LGL Registry between January 2007 and December 2011. This search identified 6 patients with concomitant LGLL and MM, 5 from the Penn State Hershey Cancer Institute Registry (cases 1 to 5) and 1 from the French LGL Registry (case 6). The study was approved by the institutional review boards of both institutes. The authors retrospectively reviewed all available medical records.

Results

The basic clinical characteristics of the 6 patients are summarized in Table 1. The median follow-up of the 6 patients with LGLL and MM was 76 months (range, 30-121). A brief history of each case is given in subsequent sections.

Case 1

A 56-year-old African American man was diagnosed with LGLL after a 5-year history of asymptomatic neutropenia. Marrow biopsy found low-level infiltration by T-cell LGLL. Eleven years later, he developed MGUS, with progression to smoldering MM 1 year later. He remains on close observation, without specific treatment. His LGLL has remained stable.

Case 2

A 71-year-old white woman was diagnosed with MM and LGLL during workup for anemia. Bone marrow biopsy found 90% cellularity, 50% plasma cells, and an increased number of T-cell LGLs. Flow cytometry confirmed the presence of 2 clonal populations, one with kappa-restricted plasma cells (8%) and the other

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Table 1 Patient Summary

Case No.	Plasma Cell Dyscrasia	Age (years)	Sex	Serum M Component	Serum Immunofixation	Bone Marrow Biopsy	CRAB Symptoms[a]	LGLL Phenotype	TCR Gene Clone	Follow-Up (mo)[b]	Treatment	Outcome of Plasma Cell Dyscrasia	Outcome of LGLL
1, JC-908	Smoldering multiple myeloma	56	M	18 g/L	IgG-λ	22% clonal plasma cells	None	$CD3^+/CD57^+$	+	36	None	Stable	Stable
2, BK-137	Multiple myeloma	71	F	58 g/L	IgA-κ	50% clonal plasma cells	Lytic bone lesions	$CD3^+/CD56^+$ and $CD3^+/CD57^+$	+	49	Bortezomib + lenalidomide	Complete remission	Stable
3, BD-470	Multiple myeloma	50	F	34 g/L	IgG-κ	80% clonal plasma cells	Anemia	$CD3^+/CD57^+$	+	30	Lenalidomide	Partial remission	Stable
4, SG-326	Smoldering multiple myeloma	84	M	6 g/L	IgA-κ	20%-30% clonal plasma cells	None	$CD3^+/CD57^+$	+	121	Cladribine, methotrexate, cyclophosphamide	Stable	Progressed
5, SC-045	MGUS evolved to multiple myeloma	56	F	30 g/L	IgG-λ	5.2% clonal plasma cells initially	None, later + anemia	$CD3^+/CD16^+/C56^-/CD57^+$	+	103	Cyclosporin A, cyclophosphamide, methotrexate, bortezomib	Progression	Stable
6, BA-918	MGUS evolved to multiple myeloma	59	F	23 g/L	IgG-κ	NA at initial diagnosis; 9 years later, 25% clonal plasma cells	Lytic bone lesions	$CD3^+/Vbeta^+/CD8^+/CD57^+$	+	119	Melphalan, prednisone, and thalidomide	Partial remission	Stable

Abbreviations: CRAB = calcium level elevation, renal failure, anemia, and bone lesions (limits defined in note); Ig = immunoglobulin; LGLL = large granular lymphocytic leukemia; MGUS = monoclonal gammopathy of undetermined significance; NA = not applicable; TCR = T-cell receptor.

[a]C: calcium elevation > 1 mg/dL above the reference upper limit, renal dysfunction (creatinine > 2 mg/dL), anemia (hemoglobin 2g/dL below the reference lower limit, bone lesions (lytic lesions or osteoporosis with compression fracture).

[b]Follow-up in months as of March 2014.