SOHO Supplement 2016

Lymphomatoid Granulomatosis: A Single Institution Experience and Review of the Literature

Julio C. Chavez,[1] Jose Sandoval-Sus,[1] Pedro Horna,[1] Samir Dalia,[1] Celeste Bello,[1] Paul Chevernick,[1] Eduardo M. Sotomayor,[2] Lubomir Sokol,[1] Bijal Shah[1]

Abstract

Lymphomatoid granulomatosis is a rare B-cell lymphoproliferative disorder characterized by involvement of the respiratory system and frequently associated with EBV infection. In this study we present the general characteristics in a single institution. Treatment with rituximab based-chemotherapy was effective with long term responses.

Background: Lymphomatoid granulomatosis (LYG) is a rare B-cell lymphoproliferative disorder with frequent extranodal presentation and involvement of the respiratory system. The purpose of this study is to describe the clinical characteristics, pathologic findings, and treatment outcomes of LYG in a single tertiary institution. **Methods:** This is a retrospective review of series of cases of LYG diagnosed at Moffitt Cancer Center (MCC) between 2000 and 2011. We describe clinical presentation, histopathologic findings, and treatment outcomes. **Results:** We identified 11 cases of biopsy-proven LYG at our institution. All patients presented with lung involvement by LYG. Nine patients were treated with rituximab-based chemotherapy. The overall response rate was 63.6% (complete response rate, 36.44%). Extra-pulmonary involvement was common (central nervous system, kidney, adrenal glands, testicles, and liver). The median overall survival and progression-free survival were 23 and 12.2 months, respectively. **Conclusions:** LYG is a rare B-cell lymphoproliferative disorder with involvement if the respiratory system. The presentation is heterogeneous, and response to therapy is variable. Although it is considered a poor prognosis disease, long-term survivors in remission have been described.

Clinical Lymphoma, Myeloma & Leukemia, Vol. 16, No. S1, S170-4
Keywords: B-cell, EBV, Extranodal, Lymphomatoid granulomatosis, Rituximab

Introduction

Lymphomatoid granulomatosis (LYG) is a rare lymphoproliferative disease predominantly involving the lungs. It was first described, nearly 40 years ago, by Liebow et al.[1] It presents in mostly middle-aged adults, and men are affected twice as often as women. It usually presents as multinodular, most of the time as bilateral lesions in the lungs[2]; however, there are rare cases with extrapulmonary involvement, especially the skin and the central nervous system.[3,4] The histology of the neoplasm consists of a necrotizing angiocentric and angiodestructive large B-cell lymphoma composed of Epstein-Barr virus (EBV)-positive B-cells with a background of reactive CD4+ T-cells.[5] It is suggested that the pathogenesis of LYG is associated with an impaired humoral and cellular response to EBV infection, among other viruses.[6]

The course of the disease is highly variable, depending whether it is a low-grade or high-grade neoplasm. Most patients progress to an advanced stage with a median survival of 14 months, regardless of therapy.[2,7] There has not been a standard proven to be effective for this condition. The largest series available have described different approaches that range from observation to radiation and cytotoxic therapy, but none proved to be superior to the others.[7] Owing to its known EBV association, there have been successful reports on the use of interferon-alpha and rituximab.[8,9] However, these reports were disputed by others; hence, the issue remains controversial.[10]

The purpose of the present study is to analyze the clinical and pathologic characteristics of patients with the diagnosis of LYG who were treated in our institution.

[1]Department of Malignant Hematology, H. Lee Moffitt Cancer Center and Research, Tampa, FL
[2]Department of Hematology/Oncology, George Washington University, Washington, DC

Submitted: Feb 9, 2016; Accepted: Feb 9, 2016

Address for correspondence: Julio C. Chavez, MD, Department of Malignant Hematology, H. Lee Moffitt Cancer Center and Research, 12902 Magnolia Dr, FOB3 HEME, Tampa, FL 33612
E-mail contact: Julio.c.chavez@moffitt.org

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2016.02.024

Material and Methods

Patients

This is a retrospective study based on patient data review of consecutive cases of lymphomatoid granulomatosis (LYG), which were diagnosed and treated at Moffitt Cancer Center from January 2002 to June 2011. This study was approved by the institutional review board of the University of South Florida. This is a Health Insurance Portability and Accountability Act-compliant study, and informed consent was not required.

During the time period noted above, we were able to identify 11 patients who fulfilled the diagnostic criteria as per the World Health Organization (WHO) 2008 classification. Medical records were reviewed to collect the following data: age, gender, initial presentation, diagnosis date, performance status as per the Eastern Cooperative Oncology Group, treatment regimen, response rate, date of disease progression, and date of death. We collected radiologic data using contrast tomography scans and positron emission tomography in order to assess chest abnormalities including: location of the nodules or masses, number and size of the nodules, and maximum standardized uptake value. Histology slides were reviewed for diagnosis confirmation by the Hematopathology Department at the Moffitt Cancer Center.

Patients were staged using the Ann Arbor Staging system for lymphomas. They were divided by risk category using the International Prognostic Index.[11] EBV infection was assessed by in situ hybridization EBV-encoded RNA (EBER) probe. The diagnosis and grading was based using the current 2008 WHO Classification of Haematopoietic Tumours.[12]

Statistical Analysis

Survival curves were generated using the Kaplan-Meier method. We evaluated the patients for complete response (CR), partial response (PR), and overall response rate (ORR) using standardized criteria (reference). Progression-free survival (PFS) was defined from the date of diagnosis to the date of death. The overall survival rate was evaluated by using the rank log method and Kaplan-Meier curves.

Results

Demographics and Clinical Findings

The patient demographics, clinical presentation, staging at diagnosis, and initial treatment are summarized in Table 1. We collected the data of 11 consecutive cases diagnosed and treated at H. Lee Moffitt Cancer Center from January 2001 to January 2011. The median age was 61.6 years; our youngest patient was 30 years old and the oldest 78. The male/female ratio was 1:75. Performance status (Eastern Cooperative Oncology Group; greater than 2) and B symptoms were present in 5 (45.5%) and 4 (36.4%) of cases, respectively. Because all patients presented with lung disease, they were considered as an Ann Arbor stage IV in 100% of cases. However, only 4 (36.4%) of 11 cases presented with respiratory symptoms. These symptoms were variable and included cough with or without sputum production, shortness of breath, and chest pain. One patient did not have symptoms and presented as an incidental solitary lung nodule. Additional extranodal disease was present in the central nervous system (2 cases), adrenal gland/kidneys (2 cases), and testicular infiltration (1 case). Bulky disease was noticed in 4 (36.6%) of 11 cases.

Table 1 Patient Characteristics

Variables	Patients, n (%)
Gender	
Female	4 (36.4)
Male	7 (63.6)
Age (median, range), years	61.6 (30-76)
B symptoms	
Yes	3 (27.3)
No	8 (72.7)
Stage at diagnosis	
IV	11 (100)
IPI score - risk category	
Low	0 (0)
Low intermediate	1 (9.1)
High intermediate	7 (63.6)
High	3 (27.3)
Extranodal disease	
Lung	11 (100)
CNS	2 (18.2)
Adrenal glands/kidney	2 (18.2)
Testes	1 (9.1)
Liver	1 (9.1)
Initial therapy	
R-CHOP	5 (45.5)
R-CVP	1 (9.1)
R-CVE	1 (9.1)
Single agent rituximab	1 (9.1)
R-PEPP	1 (9.1)
No treatment	2 (18.2)
Response rate to initial therapy	
CR	3 (27.3)
PR	2 (18.2)
NR/PD	4 (36.4)
Not assessed	2 (18.2)
Pathologic findings-LYG grade	
Grade 1	4 (36.4)
Grade 2	0 (0)
Grade 3	5 (45.5)
Unknown	2 (18.2)
Immunophenotype and EBV+	
CD20+	9/10 (90)
CD30+	6/8 (75)
EBV+	6/10 (60; 100% grade 3)

Abbreviations: CNS = central nervous system; CR = complete remission; EBV = Epstein-Barr virus; IPI = International Prognostic Index score; LYG = lymphomatoid granulomatosis; NA = not available/not applicable; PD = progressive disease; PR = partial remission; R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-CVE = rituximab plus cyclophosphamide, vincristine, and etoposide; R-CVP = rituximab plus cyclophosphamide, vincristine and prednisone; R-PEPP = rituximab plus cyclophosphamide, etoposide, and procarbazine and prednisone.