Cancer Association of South Africa (CANSA)

Fact Sheet
on
Lymphomatoid Granulomatosis

Introduction

Lymphomatoid granulomatosis (LG or LYG) is a very rare lymphoproliferative disorder.

[Picture Credit: LG]

While most commonly found in middle age patients, with males found to be affected twice as often as females.

Lymphomatoid Granulomatosis (LG)

Lymphomatoid granulomatosis (LG) is a rare type of non-Hodgkin's lymphoma.

Synonyms of Lymphomatoid Granulomatosis include:

- benign lymph angiitis and granulomatosis
- malignant lymph angiitis and granulomatosis
- pulmonary angiitis
- pulmonary Wegener's granulomatosis

Lymphomatoid granulomatosis is a rare Epstein-Barr virus–associated systemic angiodestructive lymphoproliferative disorder characterised by overproduction of abnormal white blood cells (lymphocytes). The abnormal cells infiltrate and accumulate (form lesions or nodules) within tissues. The lesions or nodules damage or destroy the blood vessels within these tissues. The lungs are most commonly affected in lymphomatoid granulomatosis.

Symptoms often include cough, shortness of breath (dyspnoea) and chest tightness. Other areas of the body such as the skin, kidneys or central nervous system are also frequently affected.

The abnormal cells in lymphomatoid granulomatosis are B-cells (B lymphocytes) containing the Epstein-Barr virus. There are two main types of lymphocytes: B-lymphocytes, which may produce specific antibodies to 'neutralise' certain invading microorganisms, and T-lymphocytes, which may

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directly destroy microorganisms or assist in the activities of other lymphocytes. Because lymphomatoid granulomatosis is caused by the overproduction of abnormal B-cells, affected individuals may eventually develop B-cell lymphoma, a form of non-Hodgkin's lymphoma. Lymphoma is a general term for cancer of the lymphatic system.

Roschewski, M. & Wilson, W.H. 2012.
"Lymphomatoid granulomatosis (LYG) is a very rare Epstein-Barr virus (EBV)-driven lymphoproliferative disease. The atypical lymphoid cells directly accumulate within affected tissues and clinically present in the form of infiltrative lesions. It is usually a progressive disorder that virtually always involves the lung and characteristically presents as bilateral pulmonary nodules. Other commonly affected organ systems include the skin, central nervous system, and kidneys. The rareness of LYG in conjunction with its nonspecific presentation contributes to delays in diagnosis in many situations. Pathologically, it is characterized by the presence of an angiocentric and angiodestructive accumulation of varying numbers of T cells with varying numbers of atypical clonal EBV-positive B cells in a polymorphous inflammatory background. It can be subclassified using a grading system based on the number of EBV-positive large B-cell malignant cells, which is critical in selecting appropriate management strategies. Lower-grade LYG occasionally undergoes spontaneous remission and is best managed with strategies designed to enhance the host's underlying immune system, whereas high-grade LYG is best managed by combination chemoimmunotherapy but has inferior outcomes. Lymphomatoid granulomatosis can lead to progressive pulmonary failure, central nervous system disease, or progression to overt EBV-positive lymphoma without appropriate recognition and management. Improvements in the modern understanding of the biology of LYG, particularly the precise role of EBV in its pathogenesis, offer promise in the development of improved management strategies."

Pereira, A.A.C., Ferreira, C.B., Hanemann, J.A.C., Paranaiba, L.M.R., Pereira, P.P.I., Rodrigues-Fernandes, C.I., Sánchez-Romero, C., de Almeida, O.P. & Fonseca, F.P. 2018.
"Lymphomatoid granulomatosis (LYG) is a rare B-cell lymphoproliferative disorder driven by Espstein-Barr virus (EBV) that most commonly affects the lungs, although extra pulmonary sites like the central nervous system, skin, liver and kidney can also be involved. It is microscopically characterized by an angiocentric and angiodestructive growth pattern, predominantly composed by small T-cells, although a smaller population of atypical large B-cells is considered the true neoplastic component. Oral cavity involvement of LYG has rarely been described and the diagnosis of this neoplasm is very difficult. The aim of this report is to present a rare case of LYG affecting an 86-year-old female patient that was diagnosed due to an extensive, ulcerated and painful oral lesion affecting the hard palate. Detailed microscopic evaluation together with a large immunohistochemical study are necessary to achieve the correct diagnosis of LYG."

Incidence of Lymphomatoid Granulomatosis (LG) in South Africa
The National Cancer Registry (2014) does not provide information on Lymphomatoid Granulomatosis (LG). It is a form of non-Hodgkin's Lymphoma.

Signs and Symptoms of Lymphomatoid Granulomatosis (LG)
Premature death 70% die within 5 years of onset. The list of signs and symptoms mentioned in various sources for LG includes:

- Persistent rhinitis
- Malaise
- Fever
- Cough
- Severe weight loss
- Coughing up blood
- Seizures
- Hypertension (high blood pressure)
- Breathing difficulty
- Chest pain
- Diarrhoea
- Joint Pains Muscle pain (myalgia)
- Respiratory distress
- Ulcerative lesion
- Nasal obstruction (blocked nose)
- Nose bleeds (epistaxis)

Diagnosis of Lymphomatoid Granulomatosis (LG)
The diagnosis of the clinical and radiological manifestations of lymphomatoid granulomatosis (LG) is extensive and beyond the scope of this Fact Sheet.

Treatment of Lymphomatoid Granulomatosis (LG)
The most effective therapy for individuals with lymphomatoid granulomatosis is unknown. For individuals with minimal disease, observation may be recommended since long-term survival without treatment has occurred as well as spontaneous remission. In most cases, however, treatment is recommended. Treatment recommendations are mostly based on the grade of disease.

Chavez, J.C., Sandoval-Sus, J., Horna, P., Dalia, S., Bello, C., Chevernick, P., Sotomayor, E.M., Sokol, L. & Shah, B. 2016.
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.

Prognosis (Outlook)
The median survival from diagnosis is 14 months. More than 60% of patients die within 5 years. The cause of death is usually extensive destruction of the pulmonary parenchyma, resulting in respiratory failure, sepsis, and, occasionally, massive haemoptysis (coughing up of blood).

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Sources and References Consulted or Utilised

Chavez, J.C., Sandoval-Sus, J., Horna, P., Dalia, S., Bello, C., Chevernick, P., Sotomayor, E.M., Sokol, L. & Shah, B. 2016. Lymphomatoid granulomatosis: a single institution experience and review of the literature. *Clin Lymphoma Myeloma Leuk*. 2016 Aug;16 Suppl:S170-4. doi: 10.1016/j.clml.2016.02.024.

LG
http://article.wn.com/view/2007/04/20/for_the_Treatment_of_Lymphomatous_Meningitis/

Medscape
http://emedicine.medscape.com/article/299751-differential
http://emedicine.medscape.com/article/299751-treatment

National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/lymphomatoid-granulomatosis/

Pereira, A.A.C., Ferreira, C.B., Hanemann, J.A.C., Paranaiba, L.M.R., Pereira, P.P.I., Rodrigues-Fernandes, C.I., Sánchez-Romero, C., de Almeida, O.P. & Fonseca, F.P. 2018. Oral manifestation of lymphomatoid granulomatosis. *Head Neck Pathol*. 2018 Mar 14. doi: 10.1007/s12105-018-0910-x. [Epub ahead of print]

Radiopedia
http://radiopaedia.org/articles/lymphomatoid-granulomatosis

Right Diagnosis
http://www.rightdiagnosis.com/l/lymphomatoid_granulomatosis/symptoms.htm#symptom_list

Roschewski, M. & Wilson, W.H. 2012. Lymphomatoid granulomatosis. *Cancer J*. 2012 Sep-Oct;18(5):469-74.

Wikipedia
https://en.wikipedia.org/wiki/Lymphomatoid_granulomatosis