Cancer Association of South Africa (CANSA)

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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

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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.

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 (2017) 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.

Sood, A., Parihar, A.S., Malhotra, P., Vaiphei, K., Kumar, R., Singh, H. & Mittal, B.R. 2020.
"Lymphomatoid granulomatosis (LYG) is a rare, extranodal B-cell lymphoproliferative disorder. The disease commonly presents with nonspecific symptoms and imaging features, making the diagnosis and therapeutic response assessment difficult. While histopathology is the mainstay of diagnosis, different imaging modalities such as computed tomography (CT), magnetic resonance imaging, or F18-fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) can help in identifying the different organs involved. We present a case of LYG, post chemotherapy in remission for the past 5 years, presenting with symptoms of disease recurrence."

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.

Melani, C., Jaffe, E.S. & Wilson, W.H. 2020.
"Lymphomatoid granulomatosis (LYG) is a rare Epstein-Barr virus (EBV)-driven B-cell lymphoproliferative disease (LPD). This disease is hypothesized to result from defective immune surveillance of EBV, with most patients showing evidence of immune dysfunction, despite no known primary immunodeficiency. Pathologically, LYG is graded by the number and density of EBV+ atypical B cells, and other characteristic findings include an angioinvasive/angiodestructive reactive T-cell infiltrate and various degrees of necrosis. Clinically, LYG universally involves the lungs with other common extranodal sites, including skin, central nervous system, liver, and kidneys. Nodal and/or bone marrow involvement is extremely rare and, if present, suggests an alternative diagnosis. Treatment selection is based on histologic grade and underlying pathobiology with low-grade disease hypothesized to be immune-dependent and typically polyclonal and high-grade disease to be immune-independent and typically oligoclonal or monoclonal. Methods of augmenting the immune response to EBV in low-grade LYG include treatment with interferon-α2b, whereas high-grade disease requires immunochemotherapy. Given the underlying defective immune surveillance of EBV, patients with high-grade disease may have a recurrence in the form of low-grade disease after immunochemotherapy, and those with low-grade disease may progress to high-grade disease after immune modulation, which can be effectively managed with crossover treatment. In patients with primary refractory disease or in those with multiple relapses, hematopoietic stem cell transplantation may be considered, but its efficacy is not well established. This review discusses the pathogenesis of LYG and highlights distinct histopathologic and clinical features that distinguish this disorder from other EBV+ B-cell LPDs and lymphomas. Treatment options, including immune modulation and combination immunochemotherapy, are discussed."
Conflict of interest statement
Conflict-of-interest disclosure: The authors declare no competing financial interests.

Mooneyham, J., Gentille, C., Barvieri, A. & Shah, S. 2020.
"A 33-year-old woman presented to the emergency room with severe headaches. A CT scan of the head revealed two brain lesions with associated vasogenic oedema. Diagnostic resection of one of

the lesions followed by pathological analysis revealed grade III lymphomatoid granulomatosis (LYG). Staging investigations elsewhere in the body were negative, isolating this case of LYG to the central nervous system, an atypical presentation. After the resection, she was treated with single-agent rituximab 375 mg/m^2 The follow-up MRI demonstrated the resolution of brain lesions and no progression of the disease."

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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