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# Midline lethal granuloma: Case report and review of literature

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## Abstract

Lethal midline granuloma syndrome is a clinical term used generally to describe a rare clinical entity, of unknown aetiology, characterized by progressive destruction of face, nose, para-nasal sinuses, and palate, oral and para-oral structures. Diagnosis is often difficult and requires expert clinical and histopathological examination of the lesion. A case of advanced high–grade lymphoma is reported as it was misdiagnosed and not treated properly for several months. After final diagnosis, a combined radio and chemotherapy were offered to the patient, but unfortunately the patient died because there was no response to treatment.

**Keywords:** Lethal midline granuloma, LymphomaWegener's granuloamatosis, Polymorphic reticulosis, Idiopathic midline granuloma.

## Introduction

Lethal midline granuloma (LMG) is a disease entity associated with destruction of the nasal septum, hard palate, lateral nasal walls, paranasal sinuses, skin of the face, orbit and nasopharynx by inflammatory infiltrate with atypical lymphocytic and histiocytic cells; presumably a form of lymphoma in most cases. Considerable controversy exists regarding various disorders characterized by a necrotizing and granulomatous inflammation of tissues of upper respiratory tract, oral cavity and mid face.[1] It is a confusing terminology previously described to include Wegener's granuloamatosis, polymorphic reticulosis, idiopathic midline granuloma, or non-Hodgkin lymphomas, which is now separated into Wegener's granuloamatosis and angiocentric T-cell lymphoma.[2] Lethal midline granuloma also known as 'Stewart's granuloma' or 'polymorphic reticulosis' refers to the presence and sequelae of a destructive lesion in the upper respiratory tract.[3] It is an idiopathic, ulcerative necrotizing lesion with a strong inflammatory component, angiocentric and angiodestructive. The necrosis leads to destruction of structures and frequently to bone sequestration. The initial symptoms are rhinorrhea, nasal obstruction, and epistaxis and in some cases, ophthalmic complications may precede the disease or appear in its course.[4,5] Systemic symptoms, such as fever and weight loss, are only present in advanced stages of the disease.[6] These lymphomas are difficult to diagnosis because the morphology reveals polymorphus and necrotic background containing inflammatory cell intermingled with large typical lymphoid cells.[7] Additionally, diagnostic confusion may result from the variety of pathologic terms that have been applied to this lesion over years including polymorphic reticulosis.[8] Angiocentric lymphomas also have been reported in other extranodalsites such as the skin, soft tissue, testis, upper respiratory tract and gastrointestinal tract.[9] Thereis a controversy whether idiopathic midline destructive disease remains a valid entity because some authors consider such cases as unrecognized malignant lymphoma or Wegener's disease.[10] Histologically, it is characterized by polymorphic inflammatory cell infiltrate

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containing eosinophils, neutrophils, histiocytes and atypical lymphocytes.[11] Due to the extensive necrosis and the inflammatory component, more than one biopsy may be necessary for the tumoral tissue to be identified. Immunohistochemistry can confirm the diagnosis by the T cell markers CD2, CD3 and CD7, as well as the NK cell marker CD56.[5]

**Case Report**

A 28 years-old male was referred to the department of Maxillofacial Surgery, complaining of painless lesion in the hard palate and soft. He reported a burning sensation in the same region for two months duration. Clinical examination revealed an extensively ulcerated partially necrotic lesion with foul-smelling discharge in the median region of the palate (Figure 1). The palatal ulcer showed an obvious perforation in the midline. The associated symptoms included difficulty in eating and breathing. Past medical history was not relevant. A biopsy was performed and showed acute inflammation. A month later, the lesion had a significant progress with larger perforation and another biopsy was carried out with the same histological picture as before and no conclusive diagnosis although the pathologist was asked to look for any feature of vacuities. The condition was discussed with a pathologist and oncologist. The provisional clinical diagnosis was Midline Lethal Granuloma. Before initiating the treatment, the more aggressive and a third biopsy was performed. The lesion showed atypical lymphocytes infiltration and suggesting malignancy. A complete blood picture, differential WBC count blood urea, creatinine, bilirubin, and transaminase levels were within normal limits. Para-nasal sinus and chest radiography were normal. Unfortunately immunohistochemical investigations were not available because this case was seen during war period. The patient was referred to oncology department in Mosul since where he was living, and treatment was started by chemotherapy and radiotherapy without information about the regime of oncology treatment since it was in another hospital and city. He was seen post treatment with no improvement of his condition. The patient died in his city with no further information about real cause of death.

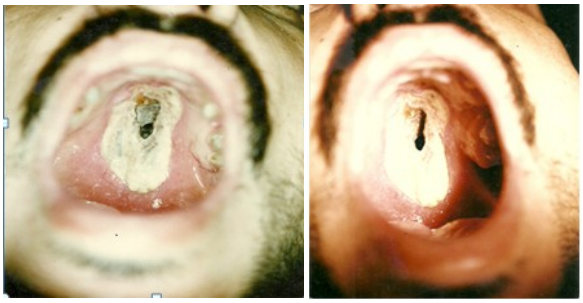

**Figure 1**: Midline lethal granuloma ulceration, necrosis and perforation in the palate.

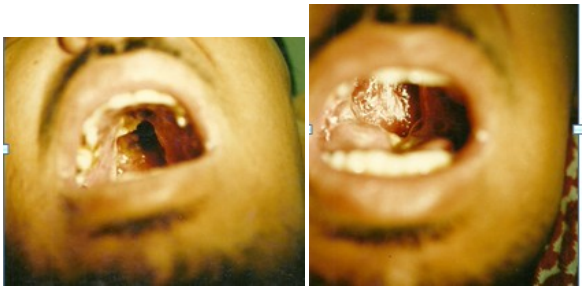

**Figure 2:** Before treatment.

## Discussion

LMG was first described by McBride in 1897.[1] This disease commonly occurs around the 4th decade (range 20-70 years) with a male to female ratio of 2:1 to 8:1. Natural history of this disease is very long with an average of 29 months and has been reported in all races. Many patients have recurrent sinusitis and allergic rhinitis.[12,13] It usually presents a poor quantity of atypical lymphocytes, and the extensive areas of necrosis make it difficult to choose the best site for biopsy. Despite the malignant clinical course, histological diagnosis can be difficult because of extensive tissue necrosis, and often multiple biopsies may be required. The common result of the histopathological diagnosis is acute and chronic inflammation. Necrosis favours the entrance of

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infectious processes that can lead to sepsis. Differential diagnosis can also be confusing since symptoms such as secretion, nasal obstruction and ulceration may characterize other pathologies as well such as Wegener's granulomatosis (WG), blastomycosis, tuberculosis, adenocarcinoma, squamous cell carcinoma and nasal destruction for cocaine abuse.[5] The treatment remains confusing, and some authors believe that the best choice is to associate radiotherapy and chemotherapy,[14] whereas other professionals have good results with chemotherapy alone. Surgery is not an appropriate treatment without adjuvant therapy. Most reported cases in literature seem to follow a similar course; including rhinorrhea, ulceration and necrosis of soft tissue, bone and cartilage of the face (such as the hard palate or nasal septum), leading to perforation. Secondary infections and cachexia commonly lead to death.[11] These characteristics may help the early diagnosis when biopsies are inconclusive.

## Conclusion

Midline Lethal Granuloma carries a poor prognosis, and although the lesion of the reported case remained localized with midline destruction of soft and hard palate for long period but it showed a very aggressive pattern and led to death.

## Conflicts of interest

The author reports no conflicts of interest.

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