Lethal midline granuloma: a case report

Salman Ahmed Mangrio[a], Rahim Dhanani[a], Mubasher Ikram[a], Muhammad Usman Tariq[b]

[a]Section of ENT/Head and Neck Surgery, Department of Surgery, [b]Section of Histopathology, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Correspondence to Dhanani Rahim, MBBS, Block 3-E/II, Flat number 604 Alkausar homes, Nazimabad near gole market, Karachi, 74800, Pakistan; Tel: +92 300 394 5260; fax: 92 21 3493 4294; e-mail: dr.rahimdhanani@gmail.com

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The rarity of lethal midline granuloma and lack of knowledge by the majority of clinicians about this disease makes this disease a difficult entity to diagnose. Nonspecific symptoms of this disease present obstacles in correct diagnosis and lead to a delay in proper treatment. Surgeons play a limited role in this condition. We present a case report of a 38-year-old man with this rare condition.

Keywords:
lethal midline granuloma, lymphoma, T-cell lymphoproliferative disorder

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Introduction

Lethal midline granuloma syndrome (LMG) is a very rare condition with a difficult diagnosis because of the nonspecificity of the symptoms with which it presents and the widespread array of diseases related to it. It was first described in 1897, and later it was given multiple names. A common factor that was found in all such lesions is the destruction of nasal architecture, leading to cosmetic and functional deformity, due to the development of an ulcerative lesion [1]. Here, we present a case of LMG in a 38-year-old man who came with a clinical history.

Case report

A 38-year-old man with no known comorbidity was referred to the outpatient clinic of Otolaryngology, Head and Neck Surgery, Department of Surgery, at Aga Khan University Hospital with a complaint of an ulcer on the face for the past 1 year. It was a painful ulcer that initially developed over the tip of nose and gradually increased in size over 1 year. There was no history of trauma, nasal obstruction, or epistaxis. The patient did not take medical advice and opted for other options; during this period the patient developed maggots in the wound. He underwent multiple debridement of the wound and an unsuccessful attempt at facial reconstruction was also made at another surgical center.

On examination, the patient was found to be well oriented to time, place, and person and was vitally stable. There was an ulcerative lesion with absence of nasal structures, upper lip, and hard palate. Black necrotic areas were seen around the lesion and it emanated a foul smel. There was no neck lymphadenopathy. A pedicel flap was also seen around the right-side of the face, which represented a previous unsuccessful attempt at reconstructive surgery (Fig. 1).

The patient was admitted to the ward and subjected to laboratory investigations, which revealed low hemoglobin and hematocrit levels and normal total leukocyte count. A chest radiograph was acquired, which was normal. Computed tomography scan of the head and neck with contrast was taken, which showed extensive facial deformity with nonvisualization of hard palate, anterior walls of bilaterally maxillary sinuses, nasal turbinate and nose, and enhancing soft tissue lesion in the right buccogingival sulcus seen with no lymphadenopathy and pan sinusitis (Fig. 2). The patient was planned for surgical intervention and underwent debridement of facial wound and biopsy of the lesion. Intraoperative findings included necrotic wound and black tissue involving the face, nose, maxillary sinuses, right-side oral cavity, and alveolar bone. Debridement of necrotic tissue was carried out and cultures from the wound and tissue were sent for multiple biopsies (Fig. 3).

Cultures that were sent intraoperatively were negative for acid-fast bacillus and fungus. Nasal tissue showed growth of *Staphylococcus aureus* and *S. proteus*. Biochemical markers like c-ANCA and p-ANCA were negative. Final histopathology showed an upper lip lesion and nasal septal lesion, and maxillary tissue showed T-cell

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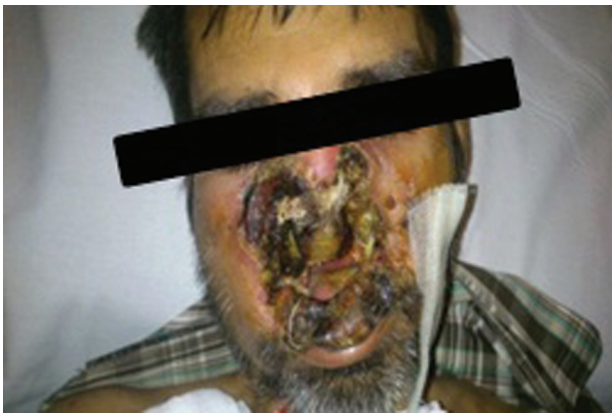
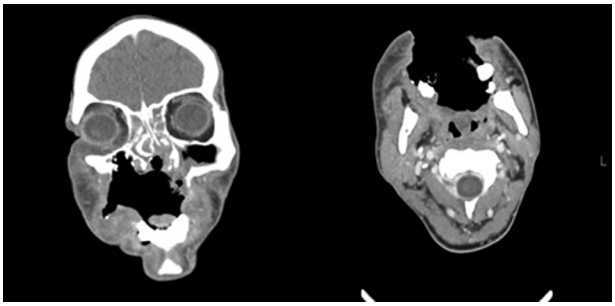
Figure 1



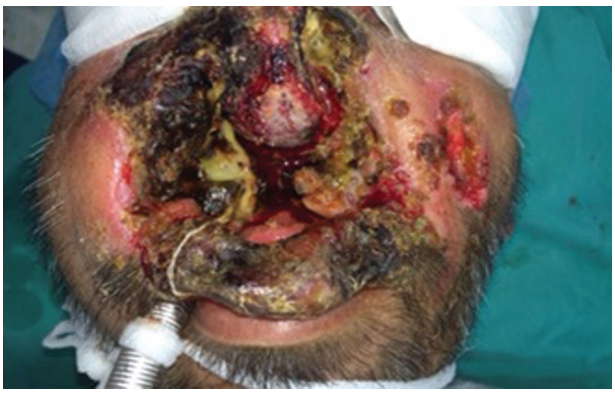
Patient having a midfacial wound.

Figure 2



Coronal and axial CT images showing defects. CT, computed tomography.

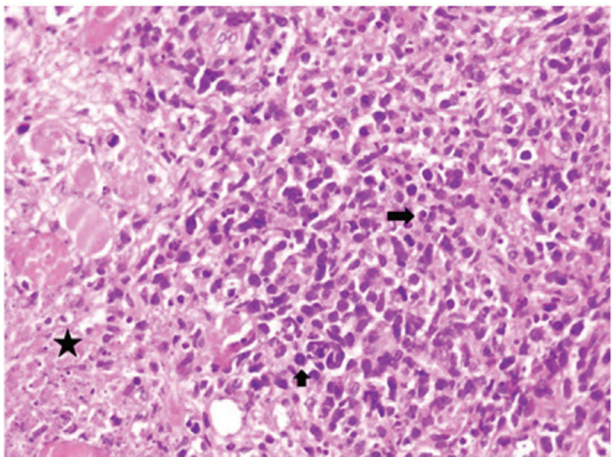
Figure 3



Intraoperative image showing the necrotic wound.

lymphoproliferative disorder. Differentials included peripheral T-cell lymphoma and natural killer (NK)/T-cell lymphoma. Immunohistochemical staining showed a positive reactivity pattern in neoplastic cells for LCA, Pan T (CD3), Ki-67 (Mib-1) 70–80%, CD56, CD30 (patchy positive), and Mic-2 (patchy positive) (Figs 4 and 5). The patient was referred to the oncology department and was later lost to follow-up.

Figure 4



High power magnification of large-sized tumor cells exhibiting marked nuclear pleomorphism, hyperchromasia, frequent mitosis (short arrow), and apoptosis (long arrow). Areas of necrosis are also seen on the left side of the figure (star) (H&E stain; ×400 magnification).

Discussion

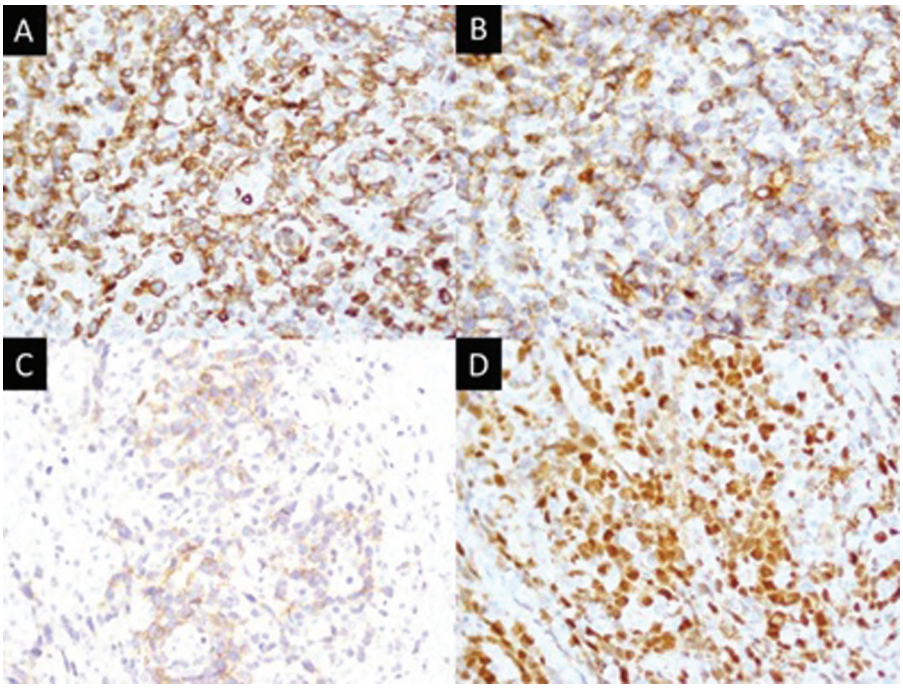
Malignant lymphomas of the sinonasal region and nasopharynx are mostly non-Hodgkin's lymphoma type and fall either into NK/T-cell type, B-cell type, or peripheral T-cell type. The most common of the nasal type in which the nasal cavity is the site of involvement are the extranodal NK/T-cell lymphomas [2]. This disease has been referred to by different terms such as LMG, polymorphic reticulosis, and malignant midline reticulosis [3]. The term 'Lethal midline granuloma' was first described by McBride in 1897 [4].

Grossly, the lesion looks like a necrotic granuloma, which is characterized by ulceration and destruction of the nose and paranasal sinuses with soft tissue, bone, and cartilage erosion of the region. The course of the disease is so aggressive and lethal that it has been termed LMG [5].

It most commonly occurs in Asians and Mexicans at around the fourth decade of life. The male to female ratio ranges from 8 : 1 to 2 : 1 and shows association with Epstein–Barr virus [5]. The major symptom is nasal stuffiness with or without nasal discharge. Oral or nasal ulcer with conjunctivitis may also occur, and perforation of the nasal septum with mutilation of the surrounding tissues eventually occurs [6].

The treatment plan should be a multispecialty team approach and should include consultations with hematologists, oncologists, and radiation oncologists. As the disease is very rare and uncommon, a standard for treatment is still evolving and definitive treatment has

Figure 5



Immunohistochemical stains with positive expression: (a) CD3 (diffuse expression), (b) CD56 (diffuse expression), (c) CD30 (focal expression), and (d) Ki-67 (Mib-1) index (~70%).

not yet been delineated. Multiple protocols like CHOP and smile are being used along with radiation [7].

The results of the combined treatment are not encouraging and have yielded 5-year survival rates ranging from 20 to 80%; unfortunately, disease progression occurs rapidly despite the treatment [8]. The role of the surgeon is limited to biopsy, stabilization of the airway if necessary, and debridement of the disease; in later stages, if the patient survives, the surgeon has a role in reconstruction. As the rate of relapse is high and response to treatment is low, regular follow-ups are required.

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Conflicts of interest
Presentation at a meeting in Aga Khan University Hospital, Karachi, Pakistan; 17th October 2015. There are no conflicts of interest.

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