



Lethal Midline Granuloma Presenting as Facial Cellulitis

M Ashraf Teli, Baba KM*, Meenu Gupta, Syed Arshd, SS Katoch, Imran Nazir

Abstract

Lethal midline granuloma (Midline granuloma, Midline reticulosis, Polymorphic reticulosis, and Angiocentric immunoproliferative lesion) is relatively a rare entity of unknown etiology characterized by a massive destruction, erosion and mutilation of the tissues of nose and upper respiratory passages. Unlike Wagner's granulomatosis which is known for its multi organ involvement, lethal midline granuloma remains usually localized. Without therapeutic intervention it has a very high mortality. Radiotherapy is the treatment of choice which considerably improves both quality and quantity of life. Addition of chemotherapy gives additional benefit. Sporadic cases have appeared in literature from time to time under various synonyms.

Key Words

Lethal midline granuloma, Reticulosis, Wagner's granulomatosis, Immunoproliferative lesion

Introduction

Lethal midline granuloma 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 an 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. Lethal midline granuloma (LMG) was first described by McBride in 1897 (1). Since then, this disease entity has attracted attention of otolaryngologists, general physician and oncologists and sporadic cases have appeared in literature from time to time under various nomenclature (2). A review of literature suggests that the sporadic cases reported under various names may actually represent a large evolutionary spectrum from almost benign to a fulminant malignant lymphoma (3). Ultra-structural analysis has shown T-cell involvement in LMG (4).

Case Report

RT 377/96, a 40 year rural male developed nasal swelling after an attack of acute coryza. This had been associated with occasional bouts of epistaxis. He was managed conservatively without any relief. He was admitted in a local hospital with diagnosis of nasal cellulitis and managed with broad spectrum antibiotics and steroids which led to slight regression and decrease in angry look of the lesion. Subsequently, a biopsy was performed and diagnosis of LMG was made on microscopy. Patient was put on cyclophosphamide which he received irregularly. Patient was referred to our Department and was admitted for evaluation. There was no history of cough, haemoptysis, breathlessness, urinary dysfunction, swelling/ulceration anywhere else in body. No history of seizures or paralysis. No history suggestive of tuberculosis, leprosy or syphilis. He was a smoker without history of cocaine addiction. His examination revealed normal higher functions, Normal B.P and pulse. He was febrile (Temp-39⁰ C). Rest of systemic examination was normal. Local examination revealed right sided peri-orbital

From the Department of Radiotherapy & * Pathology, SKIMS Soura, Srinagar- Kashmir (J&K)-India

Correspondence to : Dr. Mohmad Ashraf Teli, Add. Professor, Radiation Oncology, SKIMS, Srinagar, Kashmir (J&K)-India



swelling and ulcer; 7-8 cms with surrounding erythema. There was lot of slough and crusting. The erosive lesion had eaten away the nasal ala on right side and was extending up to lip commissure and eroding deep into the nasal cavity (Fig-1 & 2) with erosion of nasal septum up to hard palate which was involved too. Lab investigations revealed a moderate leukocytosis, a raised ESR. Blood urea was increased but, serum creatinine was normal-ray of his chest was normal-ray of PNS revealed soft tissue haziness in the maxillary region but, maxilla was normal. Urine examination was normal. CT scan facility was not available. Review of slide material revealed extensive necrosis with mixed inflammatory cell infiltrate and vessel necrosis. These features favoured the diagnosis of LMG (Fig- 3). Patient was planned to receive external beam radiotherapy of 50 Gy/5 weeks by 2 wedged portals. He showed a good response but was later lost to follow-up.

Discussion

LMG was first described by McBride in 1897. This disease commonly occurs around 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 averaging 29 months and has been reported in all races. Many patients have recurrent sinusitis and allergic rhinitis. The major symptoms are related to nose with nasal stuffiness with/without nasal discharge being the most common. Some patients have associated conjunctivitis and in many ulceration of oral/buccal mucosa occur. Nasal symptoms progress steadily till an irregular ulcer is formed. Thereafter, the disease takes a relentless course especially if surgical intervention is attempted. Perforation of nasal septum with collapse follow and the pathological process erodes into the surrounding tissue leading to mutilation of nose and facial tissue with/without extension into the hard palate (Fig-1 & 2), The disease however, does not cross the neck which if present should arouse doubt about the diagnosis of LMG. Untreated, the disease has a very high mortality touching almost 100% due to refractory septicemia, erosion into major blood vessels or penetration into CNS (5,6).

Etiology of this disease is not known fully. In view of the intense granulomatous inflammation the disease was thought to be a localized hypersensitivity phenomenon with local tissue destruction. However, the responsible agent(s) is unknown and there is no support to this hypothesis (1, 3, 5). Bacterial etiology has been suspected but bacterial cultures have not documented bacterial cause. Association of this entity with infection with type -2 Epstein Barr virus has been reported relating this disease to a covert immune defect (3). Current emphasis supports the view that MLG and idiopathic midline destructive disease (IMDD) is a localized form of recently termed angiocentric immunoproliferative lesions characterized by angiodestructive atypical post thymic lymphoreticular infiltrate of vessels leading to massive necrosis which is a pathological hallmark of LMG (6- 8).

There is no absolute distinctive histopathological criteria for diagnosis of LMG. A non specific granulation response with wide spread necrosis is the hallmark of this disease. Giant cells are not seen unlike Wegner's granulomatosis. There may be a lymphocytic infiltration in the adventitia of veins and small arteries. There is often a sub-mucosal lymphoid infiltration with necrosis through mucosa, bone and cartilage. Aozasa in a series of 19



Fig 1 & 2: Showing erosive lesion of nasal ala on right side extending up to lip commissure & eroding deep into the nasal cavity with erosion of nasal septum up to hard palate

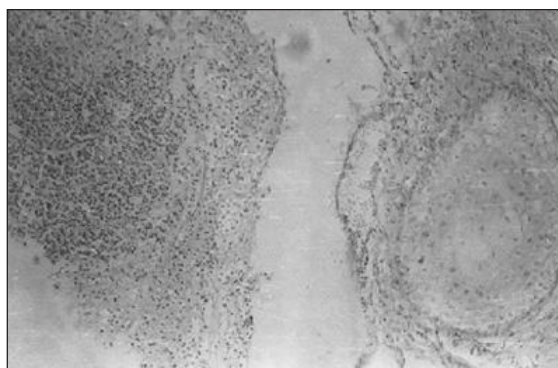


Figure 3: Photomicrograph (black and white) showing extensive necrosis with mixed cell infiltrate and vessel necrosis H&E x40



cases of nasal lesions presenting clinically as LMG and few others authors have reported necrosis and infiltration of atypical histiocytic cells with a diffuse positive reaction for non specific esterase (7,8,9). Some authors support the view that these are angiocentric immunoproliferative lesions involving the mid face, nasal cavity, paranasal sinuses and upper aerodigestive tract and diagnosis is by exclusion of neoplastic, infective and vasculitic causes. Repeated biopsies are usually needed to establish a diagnosis. Biopsy should be obtained from deeper portions of the lesion especially to rule out underlying malignancy, lymphoma, Mycosis fungoides, Tuberculosis, Syphilis, Leprosy, Tularemia, actinomycosis and other protozoal infections (5,6,8)

For bonafide LMG radiotherapy is the treatment of choice, Steroids and cytotoxic drugs are of limited help (3,5,6,9,10,11,12). However, some authors recommend use of combination chemotherapy on the lines of lymphoma (5). Apart from biopsy, attempt for radical surgery is not indicated in this disease because this only accelerates the progression of LMG. Because of the rarity of this disease experience is limited regarding the dose of radiation. Radiotherapy was first used in this disease in 1925. In 1960, low doses of external beam radiotherapy with encouraging results (1). Several authors have described complete responses with doses of 35-40 Gy/3-4 weeks. Doses of 10-50 Gy have been used in treatment of this disease. Fauci *et al* (10) have reported results of EBRT in 10 patients of LMG. Three, 3 of their patients received dose of 10 Gy and all of these failed within 2 years of follow-up but were salvaged by additional 40-46 Gy with complete response. Doses of 10-50 Gy have been used in treatment of this disease. The remaining 7 patients received doses of 40--50 Gy. Of these 2 patients had recurrent disease with one patient failing outside radiation portals. In this study local control rate of 77% was observed with mean survival of 7.4. Reports from Mayo clinic and from several authors suggest use of high dose of radiation in this disease. Doses of 40-50 Gy seem to be adequate for curing LMG using portal arrangement as used for the planning of para-nasal sinus tumors giving adequate margins to prevent marginal failure (10,11,12). Because, survival of patients with recurrent disease is poor with mortality of 73% within 8 months. Untreated, LMG takes a relentless course and once disseminated; it is fatal regardless of therapy (3).

Hence, an aggressive treatment approach with radical radiotherapy; chemotherapy and supportive recommended to ensure a survival of 60 %, 56 % and 41 % at 5,10 and 20 years respectively (13).

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