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CASE REPORT

Pulmonary Lymphomatoid Granulomatosis: Report of A Case and Review of Literature

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ABSTRACT.

Lymphomatoid granulomatosis (LYG) is a rare angiocentric lymphoproliferative process predominantly affecting the lung. The diagnosis of this condition is often difficult as the physical signs, history, chest x-ray, and routine laboratory investigations are usually non-specific. Nevertheless, it is important to establish a tissue diagnosis, as this lymphoproliferative disorder can be refractory to treatment and even progress to overt lymphoma. We report a case of pulmonary LYG in a 52-year old Nigerian man of Ibo extraction treated in our centre in 2001 and followed up for a year. The difficulty in making diagnosis is highlighted and treatment modality discussed.

INTRODUCTION

Lymphomatoid granulomatosis (LYG) is a multisystem disorder of unknown aetiology; although recent data indicate that LYG is an Epstein-Barr virus (EBV) positive B-cell proliferation associated with an exuberant T-cell reaction[1-5]. It is an angiocentric malignant lymphoma characterized by a polymorphic lymphoid infiltrate, an angiitis, and granulomatosis. Although it may affect virtually any organ, it is most frequently characterized by pulmonary, skin and central nervous system involvement[6].

PLG was first described as a clinicopathologic entity by Averill Liebow and colleagues in 1972[7]. Since that time, the clinical implications of this lesion have remained controversial, as evidenced by a long list of competing synonyms including angiocentric immunoproliferative lesion and angiocentric lymphoma [8-10]. Some have argued that the histopathologic pattern of lymphomatoid granulomatosis, which can occur in pulmonary and extrapulmonary tissue, is a nonspecific manifestation of diverse pathogenetic conditions, including autoimmunity, infection, and malignancy[11].

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The diagnosis of this condition is often difficult as the physical signs, history, chest x-ray, and routine laboratory investigations are usually non- specific.

As far as we know no case of Pulmonary LYG has been reported in Nigeria. We present one such case managed recently in our centre. The difficulty in making a diagnosis is highlighted and treatment modalities discussed.

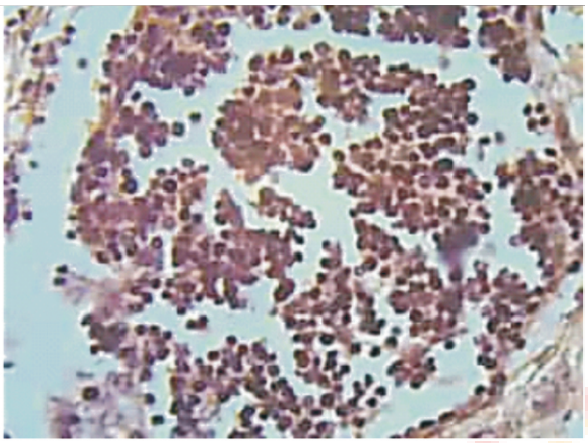
CASE

Patient is a 52-year old Nigerian male of Ibo extraction working with a road construction company, and was admitted into our hospital on 27th March 2001 on account of recurrent right–sided, non-radiating chest pain of 25 years duration, breathlessness of 6 years duration; and recent onset of weight loss of 4 months duration. He claimed the pain started a year after joining the construction company. There was neither cough nor haemoptysis but occasional low-grade fever. He drinks alcohol occasionally but does not smoke. He had earlier been treated by three private hospitals for pneumonia and tuberculosis although the sputum was negative for acid- fast bacilli as was the Mantoux test. He was referred to the unit on account of chest x-ray and CT-chest findings suggestive of right thoracic empyema.

Physical examination revealed a middle age man in no distress. He was afebrile, anicteric, not pale and had no digital clubbing, nor peripheral oedema. The chest examination showed

tracheal deviation to the left, diminished excursion of the right hemithorax with stony dull percussion notes on the right mid- and lower zones. The tactile fremitus and vocal resonance were diminished on the same zones with absent right basal breath sounds. The left lung was clear. The other body systems were normal. The unit's admitting diagnosis was that of right pleural effusion of uncertain aetiology to rule out mesothelioma.

Figure1: Biopsy of lung and pleura (H &E X40).



There is polymorphic cellular infiltrate with plasma cells, immunoblasts and lymphocytes, and complete effacement of normal structure.

A diagnostic thoracentesis using a size 21G hypodermic needle was dry. However, there was the feeling of traversing through thickened parietal pleura. The haemogram and blood chemistry were normal. The retroviral screening test was negative. Bronchoscopy was scheduled but was not done due to faulty venturi system.

On 30th March 2001, he was scheduled for a right minithoracotomy and biopsy. This was later converted into a formal posterolateral thoracotomy, decortication of lung, and biopsy of lung parenchymal nodular masses following intraoperative diagnostic thoracentesis that yielded 200mls of purulent exudate. Other findings intra-operatively included very thick nodular parietal pleura = 2.0cm and thickened visceral pleural = 0.5cm with nodularities of the right lung parenchyma, right hemidiaphragm, and the oblique fissure. There was a firm nodular mass measuring 6.0 x6.0cm on the right retrosternum.

The pleural fluid microbiology yielded coliform organism sensitive to co-trimoxazole, ampicillin, gentamycin, and cefuroxime. He had a 5-day course of co-trimoxazole. The rest of the post-operative period was uneventful.

Histopathologic examination of the pleural specimen showed several pieces of whitish greyish tissue, firm and rubbery in consistency and aggregating 12 x 11 x 4cm. The cut surface was whitish with a well -circumscribed core in some parts.

The specimen of the lung consisted of a piece of brownish tissue soft in consistency and measuring 2x 1x 1.5cm.

The histologic section of both specimens showed complete effacement of normal structures by an infiltrating sea of lymphocytes of varying sizes, plasma cells, and numerous large immunoblast–like cells. These infiltrates were angioinvasive. There were no giant cells and no necrosis seen (figure 1).

The histopathology of the lung and pleura was consistent with Pulmonary LYG.

Based on this histology he was commenced on cytotoxic chemotherapy consisting of tabs cyclophosphamide 400mg/m^2 daily x $5/_7$ and tabs predinosolone 100mg/m^2 daily x $5/_7$. The course would be repeated every 3 weeks until remission or no further improvement. Additionally, he had intrapleural cyclophosphamide instillation prior to removal of the chest drains. He was discharged to the clinic on the 24th post –operative day.

On 14th May 2001 he had his first post-discharge clinic attendance. The repeat chest x-ray at this time showed some improvement with residual patchy nodularities in the right lung, ipsilateral pleural fluid and thickening . A second course of chemotherapy was given. He thereafter defaulted until a year later (15th April 2002) when he re-presented with loss of appetite and weight loss x 3/12; fever and shortness of breath x 2/52. Physical examination revealed pallor, grade 2 pitting leg oedema, and bilateral mobile axillary lymphadenopathy. The chest examination showed increased tactile fremitus and vocal resonance with diminished breath sounds over the right basal hemithorax. There was a mild hepatomegaly of 4cm below the costal margin. He declined re- admission for further evaluation, and had since been lost to follow-up. However, oral communication with a neighbour as of September 2003 would seem to indicate that he had remained in some apparent health.

DISCUSSION

LYG is a rare pulmonary disease of dogs and humans[12]. It is a slowly progressive and characterized histologically by the angiocentric proliferation of large, atypical lymphohistiocytic cells with variable numbers of small lymphocytes, plasma cells, histiocytes, and eosinophils. The disease has characteristics of an inflammatory granulomatous process as well as those of a lymphoproliferative disease hence the term 'lymphomatoid granulomatosis'[13]. Although the disease affects primarily the lung, extrapulmonary manifestation especially in the central nervous system, skin, kidney, spleen, liver, heart and lymph nodes has been described[6,14,15]. Involvement limited to tongue, nasal cavity and nasopharynx may mimic Wegener's granuloma (WG)[16,17].

However unlike WG, poorly controlled LYG often evolves into, and terminates in a malignant lymphomatous process[18]. In addition, LYG does not show as favourable a response to chemotherapy and corticosteroid as does WG, nor does it share the relatively good prognosis of extranodal lymphomas in general and primary pulmonary lymphomas in particular. The key microscopic picture is the presence of a polymorphic infiltrate rich in plasma cells, immunoblasts and atypical large lymphoid cells, with a tendency to involve the walls of pulmonary vessels and to collect in the subendothelial spaces. The multinucleated giant cells and necrotizing changes of WG are lacking in this condition. Although immuno histochemistry was not done, it typically shows that most of the malignant cells react to B- cell markers with few normal T cells.

LYG commonly affects middle age as was the case presented. However, occurrence in childhood has been documented[15,19], as well as in the immunosuppressed[20]. Our case had the diagnosis made after 25 years of symptoms. This may not be unrelated to the indolent nature of the pathology[21]. Additionally, misdiagnosis by peripheral hospitals could have contributed to the delay in definitive diagnosis. The symptoms in our case were mainly respiratory as has been noted by Katzenstein, Carrington, and Liebow [14]. Indeed lung involvement is the sine qua non of LYG[17].

As was the experience of others, the laboratory findings in our case were non-specific and although pleural effusion has been known to occur in LYG[12], commoner causes of pleural effusion in our environment like pneumonia, empyema and tuberculosis needed to be ruled out. This may explain the rationale for anti-tuberculous trial in the peripheral centre. Besides pleural effusion of uncertain aetiology, differential diagnosis of mesothelioma in our patient was considered on account of the long duration of history and the nature of his work even though it was difficult to establish history of direct exposure to asbestos[22,23]. The definitive diagnosis was made by open biopsy as was the experience of others[5,15,18,19]. Serology for EBV was not done in our case although EBV need not be present to incite this illness[15].

Our patient received two courses of cyclophosphamide and prednisolone before defaulting. There was evidence of some remission, even though incomplete, following the first course of chemotherapy. However, his representation a year later with evidence of relapse was a pointer to the on-going process of the lesion. Whether this case had progressed to lymphoma was difficult to say as he declined a re-admission and further investigation. Nonetheless, as noted by Fauci, Haynes, Costa et al [16], cyclophosphamide with corticosteriod can induce long-term remission in LYG and if complete remission occurs, lymphoma does not develop. However in patients in whom this regimen does not induce satisfactory remission, the disease almost invariably evolves into a lymphoma that is generally refractory to therapy.

LYG should be considered in long-standing nodular pulmonary lesion and pleural effusion of uncertain aetiology.

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