Lymphomatoid Granulomatosis : A Case Report and Review of the Literature

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A case of lymphomatoid granulomatosis involving the subcutaneous tissue, muscles, pleura and lung in a 40 year-old male is reported. The initial presentation consisted of subcutaneous nodular lesion of the right anterior chest wall with involvement of intercostal muscles of the third and fourth ribs. Upon surgical excision of the mass with thoracotomy, pleural and lung involvement were then identified. The lung lesions were of nodular type confined to the lower lobe and hilum, subpleurally. The diagnosis was made on the subcutaneous lesion. Groups of diseases, namely the limited form of Wegener's granulomatosis, malignant lymphoma, allergic granulomatosis and infectious granulomas were to be considered in the differential diagnosis.

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INTRODUCTION

Lymphomatoid granulomatosis has been introduced as a new disease entity by Liebow et al[1] since 1972, that in some aspects, resembles malignant lymphoma especially Hodgkin's disease, and Wegener's granulomatosis. The disease was defined on the basis of study of 40 patients, and a year later 34 more cases were added by the same authors.[2] The disease is characterized pathologically by an angiocentric, angiodestructive lymphoreticular, and proliferative lesion, which predominantly involves the lungs. The infiltrate is polymorphous, consisting principally of lymphocytes, plasma cells and immunoblasts intermingled with large mononuclear cells with some degree of nuclear atypicality. Plasmacytoid cells are frequently observed as well as cells resembling Reed-Sternberg's cells. Ultrastructural examinations show that the cutaneous infiltrates differs from mycosis fungoides and histiocytosis X. The atypical cell is of primitive reticular cell.[3]

Clinically, men predominate in a ratio of two to one and most of the patients are in elderly middle age. Productive cough and fever are mostly the chief complaints. Radiographically, pulmonary lesions predominate in the lower lung fields, peripherally and bilaterally. Cutaneous involvement accounts for 45 per cent of the cases. Nodular renal lesion occurs likewise in 45 per cent. Central nervous system involvement as well as peripheral neuritis could also be seen in twenty per cent of the cases.

The purpose of the present report is to present a case of lymphomatoid granulomatosis of the subcutaneous tissue involving muscles of the anterior chest wall, and the lung. We believe that this is the first case having been detected in Thailand.

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CASE REPORT

A 40 year-old Thai male came for medical attention in January 1980 with the chief complaint of a bulging mass in the anterior chest wall for 2 months duration. The mass gradually increased in size and lately became tender with occasional rest pain. There was however no skin rash or ulceration. Two weeks prior to admission, he had noted daily fever and weight loss. There was no history of chronic cough or dyspnea. No history of chronic headache, drowsiness or peripheral neuritis was detected. On physical examination, he appeared tired, weak and feverish but not pale. No superficial lymphadenopathy was detected. A large subcutaneous mass, 6 x 4 x 4 cm was noted in the anterior chest wall between third and fourth intercostal spaces. The mass was not movable, and adhered firmly to the ribs and underlying tissues but the covering skin was free and movable with smooth surface. Pertinent laboratory findings showed only leukocytosis with a shift to the left. The chest roentgenogram showed a soft tissue mass without involvement of the ribs and sternum and the lung revealed no definite lesion (Figure 1).

Surgical excision with thoracotomy was performed. The mass extended downward to involve the intercostal muscles and parietal pleura, and upward to involve the mediastinum. A few yellowish nodules about 1 cm in diameter were noticed in the lower lobe of the right lung, subpleurally, and also in the hilum. The soft tissue mass was removed en block with an adjacent rib and submitted for histologic examination. A diagnosis of lymphomatoid granulomatosis involving the subcutaneous tissue, intercostal muscles and parietal pleura was made. Postoperatively he was placed on ampicillin. Two weeks after surgery, he developed dialy fever with productive cough. Chest film showed definite evidence of pneumonitis and hazy hilar shadow (Figure 2 A). Prednisolone 20 mg/day was then added. Fever and cough were prompty relieved. Repeated chest film a weak later, revealed no residual pulmonary infiltration and the hilar shadow was decreased in size (Figure 2 B).

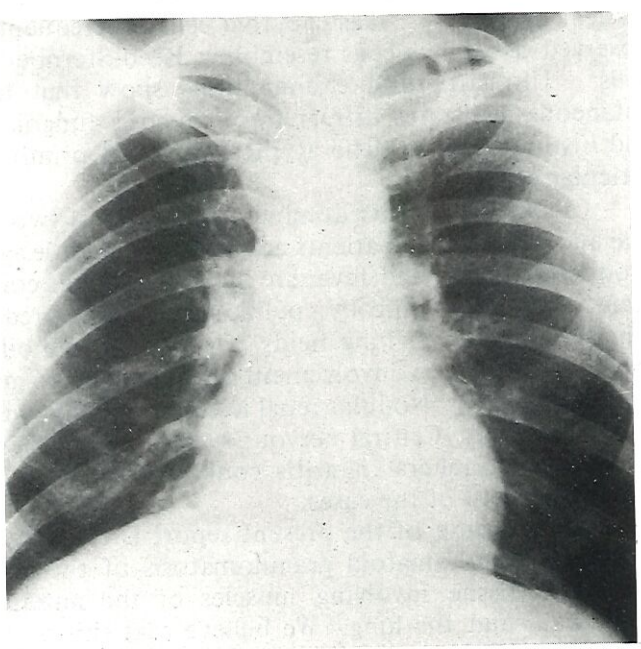

Fig. 1 Initial chest film revealed no abnormal pulmonary lesion. Soft tissue shadow was hardly identified.

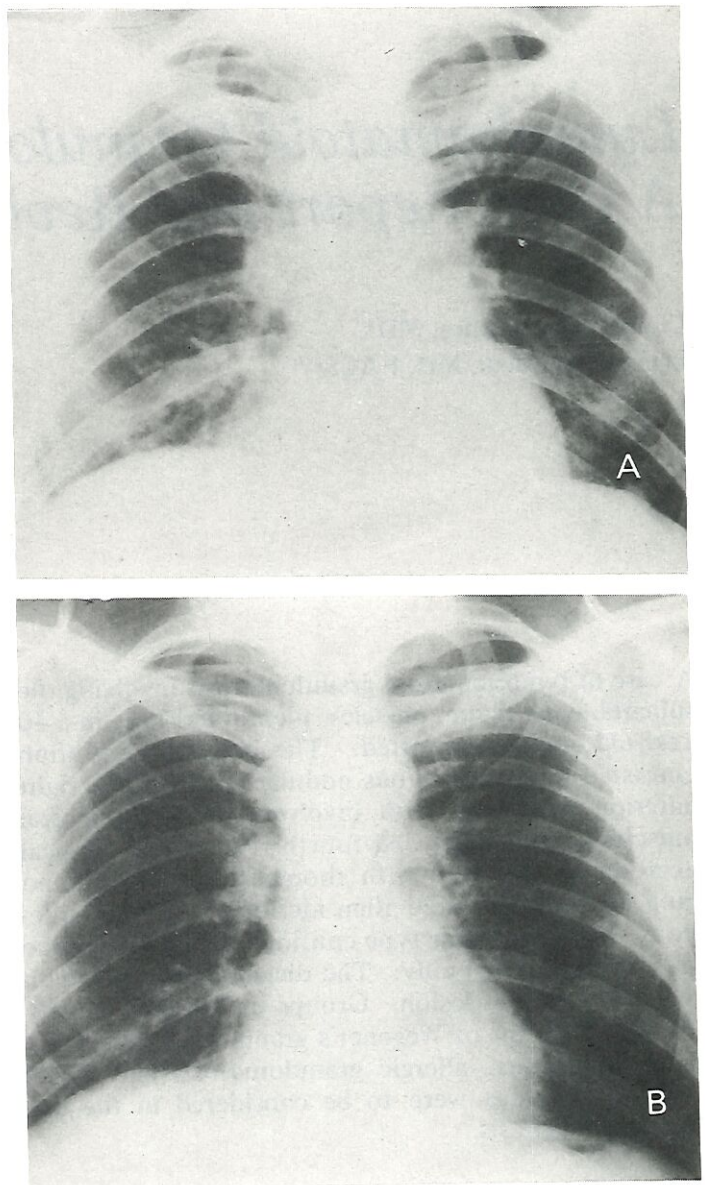

Fig. 2 A Chest film, postero-anterior view taken two weeks post-operatively showed evidence of infiltration of the right lower lobe with hazy hilar shadow.

B Chest film, postero-anterior view taken after steroid treatment revealed disappearance of the right lower lobe infiltration. Ill-defined nodules were observed in the lower lobe, subpleurally.

Four weeks postoperatively, he was seen with low grade fever. Repeated WBC still showed leukocytosis. A bone marrow puncture was performed and revealed only myeloid hyperplasia with no evidence of leukemic infiltration. He was still on prednisolone after the 6th postoperative week and this was continued to the subsequent follow up.

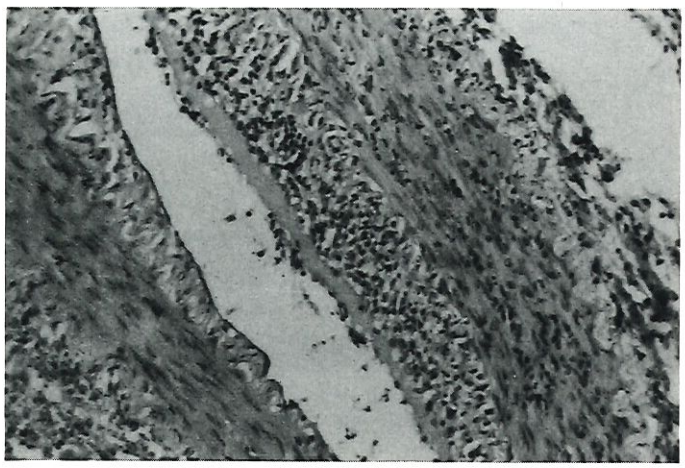

Fig. 3 A medium-sized artery showed an evidence of angiitis with polymorphous infiltration (x 100).

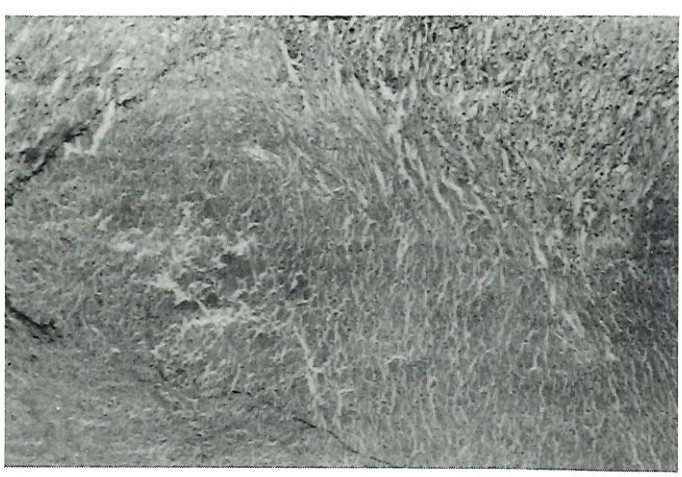

Fig. 4 Lymphomatoid granulomatosis showing angiocentric and angiodestructive areas intermingled with areas of necrosis. The elastic tissue was still discernable by Verhoeff elastic stain (x 40).

PATHOLOGY

The gross specimen consisted of fragmented, irregular, yellowish brown rubbery masses attached to a portion of a rib. The mass measured 8 x 7 x 3 cm, and the rib was 3.5 cm long and 1.5 cm in width. The cut surface of the mass had a yellowish and lobular appearance. The rib showed no gross pathology. Microscopically, there was marked angiitis with arterial walls infiltrated by mononuclear cells in which plasma and plasmacytoid cells were prominent (Figure 3). Occasionally, this infiltrate filled and partially occluded the lumen. This necrotizing angiitis was frequently incorporated into the surrounding necrotizing granuloma of the subcutaneous tissue and striated muscles (Figure 4). In areas of the granulomatous lesion, there were however few mitoses with occasional

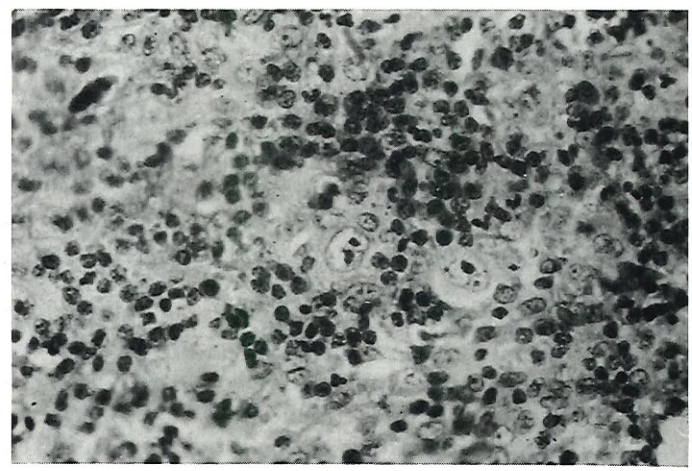

Fig. 5 Mixed infiltrate of lymphocytes, plasma cells, reticuloendothelial cells and two immunoblasts [center] (x 400).

atypical reticular cells but no Reed-Sternberg's cell (Figure 5). This polymorphous infiltrate was also noted in the attached pleural tissue.

DISCUSSION

Since Liebow et al[1] has introduced the unique disease entity designated as lymphomatoid granulomatosis in 1972, many more cases of the disease have been added.[4-6] In the majority of the reported cases, including cases in the original articles, the initial complaint was clearly suggestive of disease in the lower respiratory tract and led to immediate roentgenographic examination and the discovery of puzzling and often massive lesions, occasionally resembling metastatic tumors. There was skin involvement in approximately 45 per cent and in most instances was confined to the dermis. In only a few cases, subcutaneous tissue was involved as was recognized in our present reported case. In one patient described by Liebow et al[1], infiltration of the subcutaneous tissue was discovered nine years before the lung lesion was detected, and 14 years after the initial skin biopsy, fascia and muscle as well were noted to be involved. Our case herein would also be the other example of the rare type of primary skin and subcutaneous tissue involvement. The pulmonary lesions seen at the time of surgery consisted only of a few small yellowish nodules seated subpleurally in the lower lobe of right lung. We would believe that these lung nodules might have been developed later in the course of the disease and because the size of the lesions were so small abnormal roentgenographic shadow did not come up in the initial examination.

Because of the close relationship and similarity of lymphomatoid granulomatosis to localized Wegener's granulomatosis, malignant lymphoma and infec-

tious granulomas, it is worthwhile to give a brief review, and to compare the clinical features, pathological and roentgenographic appearances of these diseases, particularly Wegener's granulomatosis to the present entity. In 1897, McBride was the first to report a case of the disease, designated later as Wegener's granulomatosis by Wegener F. who, in 1936 and 1939, characterized and classified this distinct clinical-pathologic syndrome. Godman and Churg[7], in 1964, reported nine new cases and have introduced a triad of necrotizing granulomatous lesions in the upper and lower respiratory tracts, generalized focal vasculitis and focal glomerulonephritis. Two years later, Carrington and Liebow[8] described sixteen cases, ten women and six men, in whom a lung biopsy had shown a localized pulmonary lesion with features similar to those seen in Wegener's granulomatosis, but without involvement of the upper respiratory tract or glomerulonephritis. Various names have been appied. Liebow designated it as the localized (limited) Wegener's granulomatosis which, in a later review (1973) 85 cases were presented.[2]

At pesent, the limited form of the disease is more commonly recognized than that of the classic generalized forms. The disease predominantly affects women, while the sex ratio is almost reverse in lymphomatoid granulomatosis. Clinical manifestation of limited Wegener's granulomatosis and lymphomatoid granulomatosis is sometime indistinguishable unless the central nervous system involvement or peripheral neuritis are encountered in the latter, as well as the abnormal kidney function. Radiographic and distribution of the pulmonary lesions of both disease entities are almost similar except the cavitation evident roentgenographically occurs more commonly in the limited form. At any rate, the important differential diagnostic features, histomorphologically, are the more extensive proliferative activity and more conspicuous cellular atypicality, particularly the reticular cells in lymphomatoid granulomatosis.[1,2] In other words, lymphomatoid granulomatosis is regarded as a pre-lymphomatous condition occuring in the lung analogous to other conditions in other organs, such as Sjögren's syndrome, angio-immunoblastic lymphadenopathy[9] and immunoproliferative small intestinal disease[10]; but such a course was not found in the limited forms of Wegener's granulomatosis.[8,11]

To differentiate lymphomatoid granulomatosis and pulmonary lymphoma can be difficult because both conditions show atypicality and active proliferation of the reticular cells. However the polymorphous nature of the infiltrates, Hodgkin's disease of the lung is the only type of lymphoma to be considered. Primary pulmonary Hodgkin's disease is so rare and when it occurs, angiocentric and angiodestructive type lesions are even more rarely encountered.

Infectious granulomas, including tuberculosis and pulmonary systemic fungal diseases, can sometime bear a clinical and histologic resemblance to lymphomatoid granulomatosis, but roentgenographically the multiplicity of the lesion with cavitation are more favorable for the possibility of infectious granulomatous disease. Certainly, histomorphologic examination of the surgical specimen would give more precised differential diagnosis. Langhan's giant cells, epithelioid cells and caseation are not seen in lymphomatoid granulomatosis. Special stains for fungus and acid fast bacilli can be readily and easily done in order to demonstrate the organism.

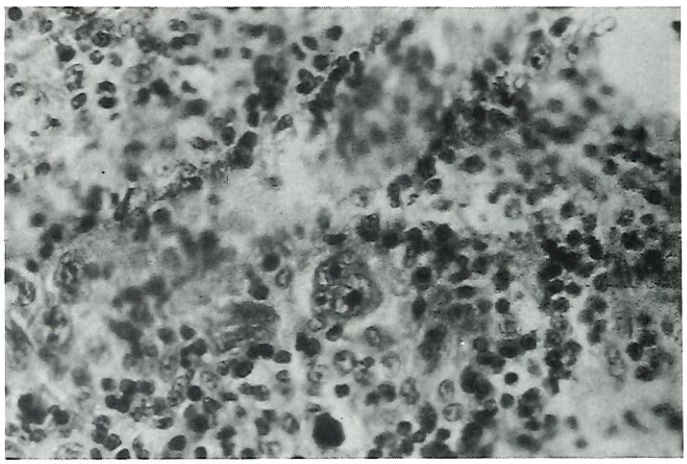

Fig. 6 Demonstrates an atypical reticular cells resembling Reed-Sternberg's cells [center] (x 400).

At the present time, the etiology and pathogenesis of lymphomatoid granulomatosis remain uncertain. The close clinical and histomorphologic resemblance of lymphomatoid granulomatosis and the limited form of Wegener's granulomatosis suggests that these two disease entities might be variants of the same disease process, but at opposite end of the spectrum.[1] The more favorable prognosis of the latter may be a reflection of its non-neoplastic process, where as the less favorable prognosis of the former may be associated with its neoplastic nature. Progress to atypical lymphoma with involvement of the lymph nodes and other reticuloendothelial tissue occurs in approximately 12 per cent of patients with lymphomatoid granulomatosis.[1,4]

Although there is clinical and radiographic evidence that steriods and possibly immunosuppressive agents can control or reverse the disease process at least temporarily, and at least one reported case had a spontaneous remission for years, two-thirds of the patients with the disease have died with the median survival rate of 14 months.[4] The major causes of death are the lung lesions and/or the central nervous system involvement.

We would believe that our case herein is another

example of the rare case of lymphomatoid granulomatosis with an unusual clinical presentation. Even though definitive tissue diagnosis was obtained only from the subcutaneous lesion we would be ascertained that the lung lesion seen at the time of surgery, undoubtedly will display the similar histopathologic features. Evidences of angiocentric and angiodestructive patterns of the large and medium-size arteries and veins were clearly demonstrated in the tissue sections, particularly under the elastic stain. Evidence of lymphomatous alteration was not detected in our case but atypical reticular cells resembling Reed-Sternberg's cells were occasionally observed (Fig. 6). This would raise the possibility of Hodgkin's disease and would be easily missinterpreted unless evidence of vascular damage was demonstrated by the elastic stain.

As mentioned earlier, the lung lesion might have been developed later in the course of the disease, and may persist or progress even with steroid therapy. However, at present, our patient is still alive, without evidence of central nervous system involvement, and with the less extensive pulmonary lesions. We believe that the patient is likely to have a favorable prognostic course.

At any rate, further study to elucidate the pathogenesis and etiology of the disease in order to have promising treatment and a longer period of survival remains a challenge to all investigators in this field.

Acknowledgement

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