Radiotherapy: An Effective Treatment of Cerebral Involvement by Lymphomatoid Granulomatosis*

Hélène Simard, M.D.; and Pierre LeBlanc, M.D.

We report the case of a 40-year-old woman who presented with neurologic complications of lymphomatoid granulomatosis after an initial pulmonary presentation. After treatment failure with immunosuppressive therapy, she responded dramatically to cranial radiation therapy without prior surgery.

(Chest 1993; 103:650-51)

\[LG = \text{lymphomatoid granulomatosis}\]

Lymphomatoid granulomatosis (LG) was first described in 1972 by Liebow et al. The classic description of the lesion is an angiocentric and angiodestructive lymphoreticular proliferative process. LG is a chronic multisystem disease most frequently involving the lung, the skin, the central and peripheral nervous system, and the kidney; any organ, however, can be involved. The etiology of LG is controversial and it has been suggested that it could represent a variant of T-cell lymphoma or a benign condition associated or not with impaired immunity. Laboratory data, including chest roentgenogram, pulmonary function tests, and blood gases are not specific for LG. The optimal treatment is not clear but steroids and cytotoxic drugs, especially cyclophosphamide, are usually beneficial when multiple organs are involved. Radiation therapy has been successful in a few cases of cutaneous, pulmonary, or intracranial lesions. We report an unusual manifestation of LG in which radiation therapy was successful after failure of an immunosuppressive therapy.

**CASE REPORT**

A 40-year-old woman was well until December 1988 when she developed cough and progressive shortness of breath with asthenia and fever. The symptoms were not improved by antibiotics. At the time of hospital admission three weeks later, she was short of breath with moderate respiratory distress. Her temperature was 38.5°C, blood pressure was 96/56 mm Hg, pulse was 120/min, and respiratory rate was 28/min. There were diffuse inspiratory crackles over both lung fields and she had an erythematous maculopapular rash involving the trunk and extremities. Results of neurologic examination were normal.

Arterial blood gas determination at room air showed a PaO, of 48 mm Hg and PaCO, was at 33 mm Hg. All laboratory tests, including CBC, renal function, RA test, antinuclear antibody, protein electrophoresis, and complement fractions, were normal. Blood cultures were negative. A chest roentgenogram showed confluent alveolar infiltrates with some nodules over both lung fields predominantly over the lower two thirds (Fig 1). A moderate obstructive airway syndrome associated with a restrictive pattern was shown on the pulmonary function tests (FVC, 55 percent; FEV,, 45 percent; FEV/FVC ratio, 65 percent; TLC, 70 percent; and Dco, 67 percent of predicted). Results of the bronchoscopic examination were normal; 65×10[6] cells (macrophage 40 percent, lymphocytes 54

*From the Unité de Recherche, Centre de Pneumologie de l'Université Laval, Département de Médecine, Université Laval, Québec, Canada.

Reprint requests: Dr. LeBlanc, 2725 Ch Ste Foy, Ste Foy, Quebec, Canada G1V 2Y1

**Figure 1.** Posteroanterior chest roentgenogram on presentation, January 1989. There is confluent alveolar infiltrates with some nodules over each field with predominance over the lower two thirds.

**Figure 2.** Cerebral magnetic resonance imaging section in November 1989, showing one lesion on the lateral side of the fourth ventricle and another one in the right anterolateral portion of the pons.
percent, eosinophils 5 percent) were recovered by bronchoalveolar lavage. A definitive diagnosis could not be made on transbronchial biopsy specimens. An open lung biopsy was performed and histologic examination of the lung revealed parenchymal infiltrates consisting of histiocytes, lymphocytes, plasmacytoid, and reticuloendothelial cells. There was angitis with infiltration of the wall of both veins and arteries with some thrombosis and necrosis. There also was bronchiolar damage and bronchiolitis obliterans. All these findings were compatible with LC.

Initial treatment consisted of cyclophosphamide 100 mg/day and methylprednisolone 40 mg IV every 6 h for one week. Corticotherapy was then continued with oral prednisone 50 mg/day. Within a few days of this treatment, the patient improved clinically. Cyclophosphamide therapy was continued and prednisone therapy was gradually tapered and then stopped over the next three months.

Six months after the prednisone therapy had been stopped, while still receiving cyclophosphamide, the patient developed neurologic symptoms and was readmitted to the hospital. She presented with headache, dysarthria, right facial hypoesthesia, left central facial paresis, left progressive proportional hemiparesis, and left hyperreflexia. There was no recurrence of pulmonary symptoms. The chest roentgenogram and lung function were normal.

A contrast enhancement cerebral computed tomographic (CT) scan revealed two lesions: one on the right lateral side of the fourth ventricle and the other in the right anterolateral portion of the pons. There was no associated edema. Magnetic resonance imaging showed the same abnormalities and suggested a vascular process (Fig 2). Steroid therapy was reintroduced with prednisone 100 mg/day and cyclophosphamide therapy was continued at 100 mg/day. Within a few days, her condition slightly improved and then stabilized. A control cerebral CT scan done two months later was unchanged. Cerebral radiotherapy, 30 Gy in 15 divided doses, was given over a three-week period. She improved remarkably during treatment and by the end of radiation therapy her left side strength was normal. She had only a slight residual dysarthria. She was continued on a regimen of cyclophosphamide 100 mg/day and prednisone 40 mg/day.

Two months later, the cerebral CT scan showed a complete disappearance of the two previously described lesions. In September 1990, six months after the completion of radiotherapy, chest roentgenogram showed no lesion. All biologic parameters, pulmonary function, and cerebral CT scan were also normal. In September 1991, 18 months after radiotherapy, her neurologic status remains stable with only a persisting mild dysarthria. She is currently treated with prednisone 30 mg every other day and cyclophosphamide 75 mg/day.

**DISCUSSION**

At least three cases of successful radiotherapy in cerebral lesions associated with LC have been reported previously.1,4-5 In all of these cases, the cerebral lesions had been resected prior to the radiotherapy. In this case, radiotherapy alone was successful in treating the cerebral lesions. Although cyclophosphamide successfully controlled the lung involvement, its failure in the treatment of neurologic lesions is probably because this drug does not cross the normal hematencephalic barrier. We believe this case illustrates an important point in the management of intracranial LG. Whether all cases of cerebral LG will respond as favorably as our patient did will have to be confirmed by further studies. Awaiting such data, we believe that cranial radiotherapy should be tried in all cases of cerebral LG, especially those appearing under cyclophosphamide and/or corticosteroid therapy.

**REFERENCES**