Diagnosis of Hodgkin’s Disease by Bronchial Brush Biopsy*

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Three cases of Hodgkin’s disease of the lung with involvement of the bronchial mucosa are reported. In one of them the initial diagnosis of Hodgkin’s disease was established by bronchial brush biopsy; in the two others the disease was known to exist elsewhere, but this procedure made it possible to establish pulmonary involvement unequivocally. In contrast to epithelial tumors, cytologic examination was negative in all three cases even though the diagnosis could be made without difficulty from examination of histologic sections. Involvement of the bronchial mucosa in pulmonary Hodgkin’s disease occurs by direct extension of the disease from bronchial lymph nodes.

Various methods and techniques have been employed in sampling pulmonary lesions for diagnostic purposes. Bronchial brush biopsy under fluoroscopic control has proved to be a useful and safe procedure for securing cytologic smears and often a sufficient amount of tissue for accurate histopathologic diagnosis. At the University of Chicago Hospitals, the bronchial brushing technique has been modified and applied by Fennessey,1,2 and a preliminary account of histopathologic results has been published.3

This report deals with three cases of Hodgkin’s disease involving the lungs in which the diagnosis was established by the bronchial brushings. The cytologic smears were inconclusive in all three cases, and only tissue sections were diagnostic of Hodgkin’s disease. In one of the three cases the disease was initially diagnosed by this method. This case also illustrates pathogenesis of Hodgkin’s disease involving the bronchial mucosa. In the other two cases pulmonary involvement was confirmed by the brush biopsy, the disease having been previously diagnosed on lymph node biopsies.

CASE REPORTS

CASE 1

This 15-year-old girl had onset of pruritus approximately seven months prior to admission. This was followed by a 20 pound weight loss. Chest x-ray film revealed a density involving the upper half of the right lobe (Fig 1). The patient was referred to the University of Chicago Hospitals for further diagnosis and treatment.

FIGURE 1. The frontal chest radiograph demonstrates a large mass infiltrating the anterior segment of the right upper lobe and blending with the mediastinal shadows. The mass is homogenously dense but has irregularly infiltrating margins.
On admission, generalized erythematous macular lesions of the skin were noted. Liver and spleen were not palpable. Bronchial brush biopsies were then obtained from the upper lobe bronchus (Fig 2) and the diagnosis of Hodgkin's disease was established. For the purpose of staging the disease, the patient underwent an exploratory laparotomy which included splenectomy, liver biopsy, retroperitoneal lymph node dissection and appendectomy. There was no evidence of Hodgkin's disease in any of these tissues. Subsequently, right upper and middle lobes were resected with incomplete removal of a large partially necrotic mediastinal mass. A course of radiation therapy totaling 4,000 rads was administered to the mediastinum, neck, supraclavicular and axillary regions. Another 4,000 rads were given to the upper abdomen and the splenic pedicle. Six months after radiation therapy, the patient was found to have pruritus, right pleural mass and focal destruction of the right second rib.

Pathologic Observations

The specimen from the bronchial brush biopsy consisted of three tissue fragments not exceeding 0.5 by 0.2 by 0.2 cm each. Sections of one of the fragments showed neoplastic histiocytes with admixture of inflammatory cells (Fig 3) and occasional characteristic Sternberg-Reed cells (Fig 4). Hodgkin's disease was diagnosed, but because of the small size of the fragment, classification was not attempted. The cytologic smears from the brushings did not show any cells suggestive of a neoplastic disease. The thoracotomy specimen showed a partially necrotic mediastinal tumor extending into and infiltrating the lung parenchyma (Fig 5). Scattered foci of tumor tissue were present in the middle lobe. These were not contiguous with the main mass. Microscopic sections of the larger mediastinal tumor were diagnostic of Hodgkin's disease of the nodular sclerosing type with involvement of the thymus. Sections of the larger bronchi clearly showed mucosal infiltration by Hodgkin's disease (Fig 6). These bronchi were partly lined with intact epithelium and partly ulcerated. Hodgkin's disease had penetrated the bronchial wall from an adjacent bronchopulmonary lymph node and had extended to the bronchial epithelium. Invasion of veins by Hodgkin's tissue was demonstrated in the mediastinal mass.
CASE 2
This 9¾-year-old boy had a history of frequent upper respiratory infections with fever and swelling of the neck for several years. Cervical lymph nodes had been diagnosed as Hodgkin's disease of the nodular sclerosing type. He had been treated with nitrogen mustard but had responded poorly to it. On admission, the spleen extended 6 cm below the costal margin and a large lymph node was present in the left axilla.

During the next ten years until the time of death the patient received radiation totalling 10,000 rads to cervical lymph nodes, mediastinum, and liver, and chemotherapy. Nine years after the original diagnosis, diffuse infiltrates were noted in the lungs (Fig 7). Culture of gastric washings yielded Mycobacterium kansasii; the patient was placed on triple therapy (INH, PAS and streptomycin). Since the pulmonary infiltrates did not diminish, a brush biopsy was performed. The last and final hospitalization was necessitated by progressive respiratory distress.

Figure 6. Sections of a larger bronchus with extensive mucosal infiltrate of Hodgkin's disease (H & E, X 40).

Figure 7. Widespread diffuse infiltrates are present in both lungs and are especially prominent in the bases medially. The infiltrates are largely interstitial in character, with some scattered areas of alveolar confluence. The biopsy in this case was taken from the area of densest infiltration in the right lower lobe.

Figure 8. Pulmonary parenchyma in brush biopsy showing Hodgkin's disease (H & E, X 100).

Figure 9. The frontal chest radiograph reveals an ill-defined infiltrate in the left lower lobe just above the cardiac apex (arrows). The biopsy was taken from this area. This is an alveolar infiltrate of nonspecific type. A somewhat similar but smaller infiltrate is seen adjacent to the cardiophrenic angle on the right side. Also noted is medial retraction of the upper lobe vessels bilaterally, haziness in the lung adjacent to the superior mediastinum and bilateral apical pleural thickening. These latter changes are a result of previous radiation therapy.
Pathologic Observations

Although the bronchial brush biopsy specimen showed Hodgkin's disease (Fig 8), the cytologic smears from the brush specimen were reported as containing no tumor cells. At autopsy, Hodgkin's disease was found to involve the lungs, liver, bone marrow, and spleen. Bilateral Pneumocystis carinii pneumonia was the immediate cause of death.

Case 3

This 22-year-old woman had initial symptoms of generalized pruritus, bilateral cervical lymphadenopathy and night sweats. Diagnosis of Hodgkin's disease of the nodular sclerosing type was made on cervical lymph node biopsy. This was treated by radiation therapy to the neck and supraclavicular areas. During the following eight years the patient experienced several episodes of enlarged cervical lymphadenopathy and a nasopharyngeal tumor for which she received additional radiation therapy. At the end of this period, she was admitted to the University of Chicago Hospitals because of recurrent lymphadenopathy. A routine chest x-ray film demonstrated a mass in the left lower lobe of the lung (Fig 9) and an abnormal bronchogram (Fig 10). Because of progressive enlargement of pulmonary mass, the patient was readmitted for a bronchial brush biopsy. The cytologic smears were not diagnostic. Subsequently both lung fields were irradiated with 4,000 rads. Presently the patient continues to do well.

Pathologic Observations

Initial sections of the brush biopsy specimen (Fig 11) contained a variety of inflammatory cells and scattered neoplastic histiocytes. After several deeper sections typical Sternberg-Reed cells were found and Hodgkin's disease was diagnosed. As in the previous two cases, the small size of the specimen did not permit classification.

Discussion

To our knowledge these are the first cases of Hodgkin's disease in which pulmonary involvement was established by bronchial brush biopsies. This was possible only because of the availability of tissue section rather than cytologic smears. Ever since the introduction of the brush technique by Hattori and co-workers only cytologic smears have been prepared by him and others.

Techniques that are limited to the examination of cytologic preparations often yield only presumptive results and must be corroborated by histologic examination of tissues. The brush biopsy technique is particularly useful because it very often provides both material for cytologic studies and tissue fragments for histologic examination. When Hodgkin's disease is suspected it is even more important to employ this technique than in cases of epithelial tumors, since in our series the cytologic smears were negative in all three instances, and the diagnosis depended entirely upon the histologic examination of tissues. This can be readily explained by the fact that in most epithelial cancers the neoplastic cells
form the bulk of the tumor tissue while in Hodgkin's disease inflammatory cells predominate and the diagnostic Sternberg-Reed cells or other neoplastic histiocytes may be scarce. Thus, brush biopsy with histologic examination of the tissue fragments has proved to be a useful diagnostic tool in establishing bronchopulmonary involvement by Hodgkin's disease.

The availability of the surgical specimens of the involved lungs of the first patient enabled us to study the pathogenesis of bronchial Hodgkin's disease. It appears to be the result of direct extension of Hodgkin's disease from bronchopulmonary lymph nodes into the bronchial mucosa. This makes the disease accessible to histologic study by use of the bronchial brush technique.

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REFERENCES

Altering Human Beings Through Biotechnology

The intensity of efforts devoted to problems of human development makes it likely that techniques will soon become available to affect the human brain by prenatal or early postnatal intervention. Even at present, mental states can be influenced by many different techniques, from yoga to hypnosis and drugs. In man as well as in animals, electric stimulation of a particular area of the brain can produce a sense of well being. Similar effects can be produced by drugs, such as mescalin, lysergic acid and psilocybin. This kind of knowledge is immensely exciting because it enlarges the understanding of the human mind, but by the same token, it is also frightening because, almost inevitably, knowledge is used for control. It takes little imagination to realize how the power to manipulate human behavior could become an instrument of tyranny. The moral aspect of biomedical techniques that alter man's nature must be emphasized because it will often be difficult to recognize the real motivation of those who use them.