HODGKIN'S DISEASE OF THE LUNG

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A little more than a century ago—in 1832—Thomas Hodgkin, Curator of the Museum and Lecturer in Anatomy at Guy’s Hospital, London, described before the Medical and Chirurgical Society of that city certain "morbid appearances" of the spleen and the lymph nodes which have since become known as lymphogranuloma (1). Like many epoch-making discoveries, that of Hodgkin remained practically unnoticed during his lifetime. In 1863, however, Sir Samuel Wilks (2) carefully repeated and extended Hodgkin's observations, and designated the clinical syndrome as "Hodgkin's disease." Ten years later Wilks again emphasized Hodgkin's priority and further noted that Morgagni, who died in 1771, had described an autopsy on an adolescent boy, in whom he had found enlarged nodes in the neck and axillae and similar conditions in the lymph nodes of the thorax and abdomen. Superficial enlarged nodes had been visible during life.

It is significant that the earliest recorded observation of what we now term Hodgkin's disease refers to its manifestation in the thorax. Recent opinion on the subject of Hodgkin's disease of the lung is that "the lung parenchyma is one of the less common situations in which the lesions may occur" (3) or, to quote the German writer, Terplan (4), that primary lymphogranulomatous foci within the lung are too rare a phenomenon to permit any conclusions to be drawn regarding the pulmonary relations of this disease. This rarity adds to the difficulties of diagnosis when pulmonary manifestations are a prominent part of the picture and makes further study and collection of data imperative if we would increase our knowledge of this special manifestation of a relatively common ailment.

Estimates of the prevalence of lung involvement in Hodgkin's disease vary considerably. Versé (5), in Henke and Lubarsch's recently published Handbuch der speziellen pathologischen Anatomic, places the incidence above 40 per cent. Moolten (6) of Mount Sinai Hospital, New York, states that of 18 cases of Hodgkin's disease examined post mortem at that hospital, 9, or 50 per cent, showed pulmonary lesions, but this does not give information as to the number of primary foci in the lungs. As far back as 1920, Wessler and Greene (7), discussing the roentgen appearances by means of which intra-thoracic lesions can be recognized, stated that "changes within the chest in cases of Hodgkin's disease are found with great frequency;" yet when summing up different types of tumors in more detail, they remarked that isolated nodules or metastases in the lung are found in few cases, if all those having any connection with the mediastinum are excluded. "In a small number of cases there are seen in the pulmonary fields, circular or oval shadows of moderate density. They are usually small, from one to several centimeters in
diameter." The authors then make the significant comment: "By themselves they are not to be distinguished from metastatic new growth in the lungs." Another roentgenologist, Saupe, stated some ten years later that his experience indicated that the lungs were more often the original site of invasion than reports in literature would lead one to believe (8).

In a general review of the whole subject of Hodgkin's disease, under the sub-head of Involvement of Various Organs, Wallhauser (9) gave his impression, derived from the literature, as follows: "Pulmonary involvement is common, depending to a certain extent on the preponderating distribution of the diseased nodes, i.e., mediastinal or abdominal. Baldridge and Awe (10) reported 14 cases, of which 7 (50 per cent) showed involvement of the lungs. It is probably possible to recognize three types of pulmonary involvement: massive invasion of the hilus by mediastinal enlargements, extensions into the lung proper by radiating bands following the interlobular lymphatics (Simonds [11]), or small isolated nodules scattered throughout. The lung may be entirely replaced by the new tissue, according to Schottelius and Chiari."

In a communication made in 1932 to the Anatomical Society of Paris, P. Foulon expressed the theory that the alveolar tissues of the lungs, contrary to orthodox anatomical opinion, are directly concerned in the formation of the lesions of Hodgkin's disease. He believed that under certain circumstances lymphogranulomatosis is not an affair of the lymphatic system alone; that the condition may arise directly in certain cells which offer peculiarly favorable conditions for its development, such as the cells of Kupffer in the liver and the alveolar cells in the lung (12).

This same idea is put forth by Moolten, who holds that Hodgkin's disease is "a primary inflammatory reaction of granulomatous character, rather than a neoplasm." He enlarges upon this view by making comparisons of the pulmonary form of Hodgkin's disease with tuberculosis and actinomycosis in the same location. He feels that the contrast with carcinoma of the lung most strongly emphasizes this point.

The histological and clinical manifestations of Hodgkin's disease as it appears in the lung would seem to be of special importance in assisting us to learn more particulars concerning this still rather obscure ailment. This particular aspect, however, seems to have had little serious attention by students of the disease. Hartfall (3) remarks that, in England at least, there is "almost complete lack of knowledge of the mode of spread to and within the lung." He distinguishes four types of the pulmonary form of Hodgkin's disease, as follows: (1) root infiltration from a mass in the mediastinal nodes; (2) massive development of the characteristic lesions within the lung tissue; (3) diffuse fibrous infiltration (microscopically demonstrable as Hodgkin's disease); (4) discrete or nodular dissemination. In application, however, it is rather difficult to make any such clear cut distinctions as are set forth in this classification. Combinations of two or even three of the types listed may be found in the same individual. "Thus there may be present around a massive deposit, nodular lymphogranuloma, and similar seedlet deposits, inextricably mixed with dense fibrous tissue."

Distinction of these varied pulmonary types is not more difficult, however, than is the recognition of the presence of Hodgkin's disease in the lung in any
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form. Careful x-ray studies have been done by Wessler and Greene, mentioned above, by Whitaker (13), and by several recent writers. Following a classification similar to Hartfall's, these writers distinguish first the type of lung involvement which obviously has its origin in the mediastinum, extending thence into the lung tissue. Eight of Wessler and Greene's 25 cases and 22 of Whitaker's 40 cases showed this type of lesion. In the second or infiltrative type of lesion in the lung, the borders of the mass appear indistinct and irregular in the x-ray film; while in the third type—diffuse fibrous infiltration—circular or oval shadows of moderate density, probably due to "the development of lymphomatous foci in pre-existing lymphatic tissue," appear in the roentgenograms. The fourth type—discrete nodes at the roots of the lung—is regarded by Wessler and Greene as the most common pulmonary manifestation of Hodgkin's disease. Of the manner in which it may be differentiated from carcinoma or tuberculosis they say: "The shadows often extend for a considerable distance from the roots of the lungs and retain a definite outline, [and] though somewhat faint, differing in this respect from other forms as tuberculosis and malignancy." Of Whitaker's 40 cases, 33 showed this radiographic feature, which tends to confirm the very general observation that this is the clinical type most often encountered.

CASE REPORT

R. T., an automobile mechanic, fifty-two years of age, complained of pain in the chest aggravated by deep inspiration, slight elevation of temperature, increasing at night, with cough and general discomfort.

Except for frequent attacks of bronchitis the past history was unimportant, as was the family history.

For several years the patient had not felt well. He noticed that he was becoming weaker and was unable to do his work. The frequent attacks of bronchitis had recently grown worse. Expectoration was scanty and at no time was there blood-tinged sputum. Recently the patient had required cathartics. He had lost about 50 pounds in the past eight months.

On physical examination the patient appeared gravely ill and emaciated, with livid facies. He had a short, hacking, high-pitched, non-productive cough. The pupils were equal and reacted to light and accommodation. The tonsils were not enlarged. The superficial lymph nodes were carefully examined and no enlargements found. Chest examination revealed absence of breath sounds and flatness on percussion with râles at the base. The heart sounds were very weak, and there was left border dullness 10 cm. from the midsternal line. In the abdomen scattered masses were palpable; there was no ascites. The spleen could not be palpated. The liver edge was two fingers below the costal margin.

The temperature was 101°, the pulse practically imperceptible. A blood count showed: hemoglobin 32 per cent (Dare); red blood cells 1,800,000; white blood cells 4,200, polymorphonuclears 68 per cent, lymphocytes 26 per cent, eosinophils 2 per cent, monocytes 4 per cent.

The patient died three hours after admission and roentgen films were not obtained. The clinical diagnosis was bilateral lobar pneumonia.

Autopsy: The superficial lymph nodes were not enlarged. The tonsils were not enlarged.

Both lungs were enclosed within one large confluent mass occupying the upper mediastinum. The entire mass was adherent to the overlying ribs and sternum. On gross inspection and on cut section the mass was found to be composed of yellowish tissue, mainly fibrous, with no areas of hemorrhage or necrosis. The spleen was not involved. The liver was enlarged and congested. The retroperitoneal, peripancreatic and portal lymph nodes
The pale, ill-defined and darker gray mottling is produced by the diffuse lymphogranuloma largely replacing the lung tissue. These had a yellowish tinge and showed considerable fibrosis. Many of them were adherent to one another.

**Microscopic Examination:** Sections taken from various portions show almost the same histological characteristics. The predominating feature is the complexity of the cellular content, forming a diffuse granulomatous process. There are large and small lymphocytes, endothelial and epithelioid cells, fibroblasts, mononuclear and multinuclear giant cells and eosinophils, polynuclears and plasma cells. Very few alveoli are preserved.

**Diagnosis:** Lymphogranulomatosis (Hodgkin's disease) of lung and mediastinum and peripancreatic, portal and retroperitoneal lymph nodes.

**Discussion**

In the rare instances when Hodgkin's disease has its primary focus in the lung, the chief interest for the pathologist lies in the precise mode of entrance of the causative factor. The theories in regard to its alveolar origin and the
likelihood of Hodgkin's disease being an inflammatory reaction rather than a neoplastic growth have already been touched upon. It was established long ago that lymphoid tissue is very abundant throughout the pulmonary structure. In their work at the South African Institute for Medical Research, Simson and Strachan (14) found that such lymphoid tissue invariably lay in relation to the adventitial coats of the bronchial tubes. Such tissue was particularly abundant at the points of branching, where it was found between the muscle coat of the bronchial wall and the cartilage, and was also in evidence in the peribronchial connective tissues surrounding these same points of anastomosis. Considerable lymphoid tissue was likewise observed in the walls of the alveoli situated beneath the pleura, although it seemed to be absent from the subpleural connective tissue. It is certainly not unreasonable to
suppose that the lymphoid tissue of the lungs would be quite as susceptible to the stimulus which gives rise to the characteristic lesions of Hodgkin’s disease as similar tissue elsewhere in the body. Our ignorance of the precise factors involved in no wise makes this unlikely.

Once the disease is established in the lung, the next point of pathological interest is the manner in which the lesions progress. Perusal of the literature, especially that relating to roentgen examination, indicates that this may be any one or a combination of several ways. There may be direct extension into the lung tissue through the alveoli or through the bronchi, or the spread may be strictly confined to the lymphatics that accompany the bronchi, the blood vessels, or the pleura, or it may ramify interstitially. Entrance may be effected into the bronchial or pulmonary vessels, constituting a general vascular involvement. Direct local infiltration would seem to be the most common occurrence, although doubtless extension through the lymph channels is also fairly frequent. Hartfall emphasizes that the macroscopic appearance in these cases, as well as the histological picture revealed by the microscope, tends to confirm the opinion that Hodgkin’s disease is to be looked upon as potentially, if not actually, neoplastic in nature. This is sharply in opposition to the position taken by Moolten, who regards the disease as of purely inflammatory origin.

In examining the case reports upon which the meager literature on pulmonary Hodgkin’s disease is based, one notes that the diagnosis is seldom established until after death, even when visible evidence of lymphogranuloma has existed for a long time ante mortem. Hartfall reports two cases in which the diagnosis was made from roentgenograms during life, from which he draws conclusions in regard to characteristic manifestations which may aid the clinician in arriving at a correct diagnosis much earlier.

Difficulty may attend the differentiation between Hodgkin’s disease of the lung and carcinoma or the extremely rare pulmonary sarcoma. If the patient be already suffering from a recognized malignancy elsewhere in the body, it should not be difficult to distinguish between a metastasis from such a focus and a primary lesion in the lymphoid structures of the lung. But if, as has occasionally happened, no other focus of Hodgkin’s disease has been recognized, and no primary neoplasm has been discovered outside the chest, the chances of making a correct diagnosis before death are indeed slight.

As X-ray examination of the chest is being steadily perfected, it is to be hoped that some of the diagnostic difficulties attending Hodgkin’s disease of the lung may be overcome. Since tuberculosis is so much more prevalent, and carcinoma has been so acutely impressed upon the lay mind, these two conditions are more likely to suggest themselves to the examining physician. The advice with which Hartfall concludes his article will bear repetition: “When the clinical condition suggests tuberculosis, and the X-ray suggests neoplasm of the lung, the observer should consider lymphogranuloma.”

References