UNUSUAL EVIDENCE OF EARLY HODGKIN'S DISEASE

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Hodgkin's disease is not common; yet it is not so uncommon that we may let down our guard. The number of cases seen by medical officers is disproportionately large, for it is a disease of youth, and armies are composed largely of young men. We should never allow the diagnosis to fall into the rare-and-unusual category of conditions which are "never" encountered in the M.I. Room, nor, in considering the diagnosis, should we hold to the narrow concept of a disease which involves primarily lymph nodes. Hodgkin's disease may affect any sort of tissue, its onset may be insidious or catastrophic and it may mimic other less formidable diseases in a most disarming manner.

The diagnosis of Hodgkin's disease is usually made without difficulty, and the course of the disease thereafter is stereotyped. Death occurs soon or late, the time depending upon the velocity of the disease and, in some cases, upon the treatment. The following case represents the usual course of events.

Case 1.—A 26-year-old Army officer, healthy and fit, noted a lump in his neck beneath the left ear while shaving. During the next two weeks the lump spontaneously grew smaller. Then it again grew large, and the officer reported to his medical officer. The mass proved to be a lymph node which was removed. Microscopy demonstrated changes diagnostic of Hodgkin's disease. The patient was treated by X-ray therapy over the cervical area and by nitrogen mustard. He continued in good health. Five months later he reported that a lump was present in his left axilla.

The enlargement of a cervical lymph node in this patient was an early manifestation of his disease. In such a patient the diagnosis is not a clinical problem. It depends entirely upon examination of the pathological tissue, and the physician has only to ask for a biopsy. It might better be said that the physician must ask for a biopsy. An enlarged lymph node in the absence of a clearly infectious cause demands biopsy. Occasionally the disease does not offer the gambit of a palpable lymph node. It begins in the deeper structures of the reticulo-endothelial system and may progress for months before the symptoms of generalized illness bring the patient to medical attention. In such a case the skill of the clinician is called upon. Illness without lymphadenopathy is not the common concept of Hodgkin's disease. The patient described as Case 2 was intently studied for three weeks and was seen by several consultant physicians. Yet the presence of Hodgkin's disease was not suspected.
Case 2.—A 23-year-old negro soldier was taken ill with fever, nausea and malaise. He was admitted to the infectious diseases service of a military hospital. Physical examination was negative except for fever which was high and unremittent. He had a moderate normochromatic anaemia (R.B.C. 3,700,000). White cell count was 5,000 with 40 per cent of monocytes. No specific evidence of infectious disease was found. Blood cultures were negative, and all agglutination tests were insignificant. During the investigation the patient's condition deteriorated rapidly. The marked monocytosis persisted. He died. Post-mortem examination revealed Hodgkin's disease which involved only the retroperitoneal lymph nodes.

Ultimately the diagnosis of Hodgkin's disease must be established by microscopy. However, the clinical picture is not without its distinctive characteristics, and, since the disease is a profound alteration of the reticuloendothelial system, it is not remarkable that the blood cells derived from that system should commonly show aberrations. Although a normal white-cell differential count is the rule, a high proportion of monocytes is not an uncommon finding, and eosinophilia sometimes as high as 30 per cent may occur. The total white cell count is unusually normal or moderately elevated, but where the mesenteric and retroperitoneal lymph nodes alone are affected, leukopenia is found. A triad consisting of leukopenia, anaemia and fever commonly occurs in "abdominal" Hodgkin's disease. In Case 2 above the triad is present. Only the excessive number of monocytes brings the total white cell count to normal. This characteristic triad is well illustrated by the following case.

Case 3.—A 19-year-old soldier was taken ill with fever and malaise. He was hospitalized for two weeks. The fever by that time subsided, and he returned to his unit feeling almost fit. The fever recurred in three weeks. This time he became severely ill with malaise and nausea. Spleen and liver were enlarged. There was no palpable lymphadenopathy. He was found to be anaemic (R.B.C. 3,500,000). His white cell count was low, 1,900, and later fell to 1,000. Ratio was substantially normal. During the next three weeks the patient was studied and treated as an infectious disease. His fever finally fell, and the white cell count rose to 3,000. The spleen remained enlarged. The patient was given a course of nitrogen mustard as a therapeutic trial. The spleen shrank and there was subjective improvement in the patient's condition.

This case of abdominal Hodgkin's disease is typical of the difficulty encountered where there are no lymph nodes available for biopsy. However, the triad of leukopenia, anaemia and fever was unmistakable. After other diseases had been excluded a therapeutic trial with nitrogen mustard was performed. Response to nitrogen mustard therapy is almost as diagnostic of Hodgkin's disease as the demonstration of Reed-Sternberg giant cells. The diagnosis in this particular case was later confirmed by biopsy when several slightly enlarged lymph nodes appeared in the neck.

The repetition of febrile episodes which occurred in Case 3 is also characteristic of Hodgkin's disease. A week or two of rather high temperature alternating with periods free of fever gives a temperature chart with a "battlement" silhouette. This pattern is sometimes called Pel-Ebstein fever. The reason for the bouts of fever is unknown.

The very illness of these patients may suggest the diagnosis of Hodgkin's disease. There are few conditions which can cause a young man to grow so
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rapidly and profoundly ill. But this is not always the case, and one should not expect the first evidence of this “subterranean” variety of Hodgkin’s disease always to be the devastating sort of illness that occurred in Case 2. The onset may be insidious where the first episode of fever is an elevation to 99° in the evening. Where there is no fever, night sweats may be the first evidence of systemic disease.

Although lymphadenoma is not an infection, the coincidence of infection and Hodgkin’s disease is not uncommon. This, again, is not surprising for the reticulo-endothelial system is involved in the immunity mechanism of the body. Herpes zoster is unusually frequent in Hodgkin’s disease as well as in the other malignant lymphomata. When one encounters herpes zoster in a young adult it should at least cross the mind to look for lymphatic leukæmia, giant follicular lymphoblastoma, lymphosarcoma or Hodgkin’s disease.

Case 4.—An 18-year-old boy developed herpes zoster and recovered from it in several weeks. Six months later he joined the Army and during his second week of service found a lump on the left side of his neck. This proved to be an enlarged lymph node, and on biopsy a diagnosis of Hodgkin’s disease was made. A chest X-ray showed that mediastinal lymph nodes were also involved.

Here one may only speculate whether or not Hodgkin’s disease was present when the herpes occurred. Since the involvement of lymph nodes was somewhat widespread when discovered, it is probable that the disease had existed six months before. One may also speculate whether or not a dormant disease was “lighted up” when the reticulo-endothelial system was stimulated by the vaccinations given when the boy entered the Army.

The immunity mechanisms of the body may show other evidence of dysfunction in Hodgkin’s disease. Haemolytic anæmia is one of the most interesting, for in this complication the reticulo-endothelial system elaborates an antibody against the patient’s own red blood cells. It is probably through this abnormal antibody system that the enormous destruction of the patient’s blood is brought about.

Case 5.—A 26-year-old soldier was admitted to a military hospital with jaundice, anaemia and splenomegaly. He was ill and febrile. There was no lymphadenopathy. There was no bile in the urine. The plasma bilirubin was of the “indirect” variety. His anæmia was normochromic and rather severe (R.B.C. 2,000,000). The red cells showed increased osmotic fragility. A diagnosis of haemolytic anæmia was made, and splenectomy was performed. In the spleen and in nodes at the splenic pedicle were found changes characteristic of Hodgkin’s disease.

The anæmia of Hodgkin’s disease is not always haemolytic in nature. The bone-marrow in “abdominal Hodgkin’s” is rather fibrotic, and the aspirate is hypocellular. This suggests an “aplastic” process. The anæmia in such a case is due to inadequate production of red cells rather than increased destruction. In the terminal stages of the disease there is anæmia without blood loss which is often intractable to transfusion. This is probably due to rapid blood destruction, although the classical signs of haemolytic disease—jaundice, reticulocytosis, urobilinuria—are lacking.
Other tissues than the lymph nodes are commonly found to be involved in Hodgkin’s disease. Sometimes the changes in these organs produce the first symptoms of the disease. The collapse of a vertebral body may cause pain and neurological signs. Involvement of the gastro-intestinal tract may produce abdominal symptoms, even symptoms of peptic ulcer. Swelling of peribronchial lymph nodes may cause respiratory symptoms. These symptoms, of course, are not characteristic of the disease. They are non-specific results of destruction, infiltration and pressure.

The intense itching which sometimes accompanies Hodgkin’s disease is not due to infiltration of the skin. Examination of the affected skin shows no change. This symptom may be the presenting evidence of the disease. A search for lymph nodes in cases of severe, intractable itching may lead to a diagnosis. Of the many symptoms of this disease, pruritis is often most intractable and troublesome.

In summary, the diagnosis of Hodgkin’s disease is made early and easily when the first manifestation is an enlarged peripheral lymph node. But the process frequently begins in deeper tissues. The “subterranean” disease progresses to a symptomatic state before it comes to the attention of the patient. The symptoms, at first glance, may seem non-specific. But some are characteristic of Hodgkin’s disease and so may suggest the diagnosis. Of particular significance is the triad of leukopenia, anaemia and Pel-Ebstein fever in “abdominal Hodgkin’s.” A high proportion of monocytes or eosinophils in the peripheral blood is less indicative, but coupled with an obscure fever it may suggest a lymphadenomatous process. So may intractable itching. The itching and eosinophilia are sometimes to be noted in the same patient. Herpes zoster occurs with disproportionate frequency in patients with lymphoma. Acquired hæmolytic anaemia associated with an abnormal antibody is no rare complication of Hodgkin’s disease. As in the case of these other signs, it may be the first evidence of such a malignant process.