MALIGNANT LYMPHOBLASTOMA

A REPORT OF TWO CASES

JAMES SHEALER McCARTNEY, JR.

(From the Department of Pathology, The Medical School, University of Minnesota, Minneapolis, Minn.)

The following cases of malignant lymphoblastoma are reported in detail chiefly because of the recent interest among pathologists in the interrelations of Hodgkin’s disease, lymphosarcoma, leukemia and endothelioma of lymph nodes.

CASE 1

A woman, 52 years of age, was well until the latter part of 1926 at which time she began to lose weight. Loss of weight and strength were progressive during the next year, the weight loss amounting to 60 lbs. When first seen in the fall of 1927 by a local physician she had marked dyspnea on the slightest exertion and was pale and appeared sick. Shortly before this she had noticed hard lumps at the back of her neck which rapidly increased in size and new nodules which appeared in the anterior portion of the neck. A lymph node was removed in Brooklyn, New York, and diagnosed small round cell sarcoma. Shortly thereafter hard discrete nodes appeared in both axillary and inguinal regions.

In October 1927 laboratory studies gave the following results: Blood, hemoglobin 47 per cent; red cells 2,480,000; white cells 4,500; differential count, polymorphonuclears 56 per cent; small lymphocytes 24 per cent; large lymphocytes 19 per cent; basophils 1 per cent. A subsequent blood smear showed 3 per
cent neutrophilic myelocytes. Wassermann negative. Urine showed a faint trace of albumin.

On November 22, 1927, nodes were removed from the posterior cervical region and from the left axilla. A diagnosis of lymphatic aleukemia was made. Because of increasing dyspnea and asthmatic attacks, deep X-ray therapy over the mediastinum was instituted. Three exposures at short intervals were given. A marked relief from cough, dyspnea and wheezing took place almost immediately. The cervical and axillary nodes definitely decreased in size. The patient was fairly comfortable until the latter part of January 1928 when the dyspnea returned and nodes were again noted in the inguinal regions. In January 1928 nodes were removed from the right axilla and right inguinal regions but no report was made on them.

The patient’s course from this time was progressively downward. Dyspnea and cachexia increased. Fluid appeared in the abdomen and a few days later in both pleural cavities. Until death March 1 she suffered extremely from dyspnea. Clinically death appeared to be due to actual strangulation.

Postmortem examination. The body showed marked emaciation. The upper abdomen showed a large bulging protrusion which was roughly spheroidal in outline and about 15 cm. in diameter. Cords of hard nodules, about 1 cm. in diameter, were palpable in the anterior and posterior cervical and in both axillary and inguinal regions. Fluid wave was demonstrable in the abdomen. Nodules 1 cm. or more in diameter were felt in the skin over the insertion of the right deltoid and over the left triceps.

The peritoneal cavity contained at least 2 liters of thin grayish white, whey-like fluid which contained no clots or fibrin. The small intestine, pylorus and pancreas were pushed very definitely forward by a large tumor mass which was situated retroperitoneally. The peritoneum showed no evidences of inflammation. The liver edge protruded about 3 cm. below the costal margin. The spleen was not visible. The diaphragm on the right was at the level of the second interspace, on the left at the third rib.
Each pleural cavity contained about 1 liter of fluid, similar to that in the peritoneal cavity. The lungs were compressed to masses hardly larger than the clenched fist. Hard irregular masses were palpable in the region of the hili of the lungs.

The pericardial fluid was clear, yellow in color and normal in amount. The heart was normal.

The right lung weighed 400 grams, the left 375 grams. Crepitation was present only at the apices. The lungs showed marked congestion. Whitish nodules resembling in appearance the lymph nodes and measuring up to one centimeter in diameter were present.

The spleen weighed 650 grams. It was of a grayish blue color. The cut surface appeared as a soft pulpy mass with eversion of the capsule.

The liver weighed 2,150 grams. Beneath its capsule were about a dozen irregular white patches about 1 cm. in diameter. These nodules were all located beneath the capsule and none in the deeper parts of the organ.

Fig. 1.
The mucous membrane of the gastrointestinal tract was normal. The pancreas was closely incorporated with the retroperitoneal mass but was apparently otherwise normal. The left kidney weighed 325 grams, the right 200 grams. In the central part of the left kidney was a large yellowish white, rather sharply circumscribed tumor mass, about 6 cm. in diameter. A similar but smaller mass was found in the right kidney. The tissue at the poles of the organs was apparently normal. The appearance of the kidney is shown in Fig. 1.

Overlying the lumbar vertebrae was a large mass of rounded nodes which were in part conglomerate, in part discrete. These nodes completely enveloped the abdominal aorta. They varied in size from a few millimeters to 5 cm. On section they were fleshy and grayish or yellowish white in color. The cut surfaces bulged prominently. No gross areas of necrosis were visible. No gross connection was found between the retroperitoneal masses and the nodules in the kidneys. Similar enlarged lymph nodes were found in the superior mediastinum. The peribronchial and hilic lymph nodes were markedly enlarged and
measured up to 3 cm. in diameter, differing from the nodes elsewhere only in color, which was due to anthracosis. Marrow from the center of the shaft of the right femur was red. The receptaculum chyli and thoracic duct were not found.

Microscopic Examination

Lymph Nodes.—The microscopic structure varies markedly from node to node and even in different parts of the same node. Some nodes are very cellular with relatively little reticulum (Fig. 2). The cells are small, round, free and somewhat variable in size. The cytoplasm is for the most part inconspicuous. It stains faintly with eosin and shows no granules. Most of the cells are small, but occasional ones are about twice the average size. Mitotic figures are occasionally found. Occasional large mononuclear cells with abundant cytoplasm are encountered.

The normal structure of the node is obliterated, the sinuses being indistinct. No germinal centers are seen. As shown in Figure 3, occasional structures are present which at first glance appear to be large coalescing follicles. Closer examination shows that these do not have the structure of true follicles, as there are no germinal centers. These pseudofollicles have a loose reticular structure and contain cells similar to those described above. At the edges are found narrow bands of lymphocytes, separating the “follicles.”

In one lymph node four distinct histologic types are present.
In some areas (Fig. 4) one sees the typical picture of Hodgkin's disease with the Dorothy Reed type of cell. In other areas (Fig. 2) the appearance is that of lymphatic leukemia. In many places (Fig. 5) there are numerous spaces lined by an endothelial type of cell, giving an appearance simulating closely but not quite duplicating that of primary endothelioma of lymph nodes. Finally certain areas (Fig. 6) show a large type of cell with marked evidence of active growth, with numerous mitotic figures and a small amount of reticulum, an appearance commonly called lymphosarcoma. Scattered through this node are microscopic areas of necrosis and marked fibrosis.

Lung.—The lung nodules, microscopically, resemble the cellular areas in the lymph node shown in Figure 2. In the involved
area the lung structure is completely replaced by the infiltrate, no normal structure remaining. Numerous small blood vessels and capillaries are present and there are areas of rather marked fibrosis (Fig. 7).

Liver.—The subcapsular nodules show a structure similar to that seen in the lymph node pictured in Figure 3. In certain areas the typical structure of Hodgkin's disease is present, as is shown in Figure 8. Outside of the nodules, the portal spaces are filled with lymphocytes, giving the appearance characteristic of lymphatic leukemia. This is shown in Figures 9 and 10, the latter being a high power view of one of the portal spaces in Figure 9. This portal infiltration is widespread in the liver. Transitions between the leukemic infiltrations and the typical structure of Hodgkin's disease are quite distinct in certain areas.

Kidney.—The structure of the large kidney tumor is shown in Figure 11. Numerous pyknotic nuclei and nuclear fragments are present. Connective tissue fibers are prominent. Mitotic figures are rather numerous. Occasional renal tubules and glomeruli are found scattered through the tumor.

Sections from grossly normal kidney tissue show focal accumulations of lymphocytes, as is shown in Figure 12.

Spleen.—This organ has almost entirely lost its normal microscopic structure, only occasional corpuscles and trabeculae being recognizable. The pulp is occupied by large, pale staining cells and lymphocytes and the sinuses are not visible. Megakaryocytes are occasionally seen.
Bone Marrow.—This is very cellular and hyperplastic. Its structure is shown in Figure 13. An interesting feature is that in some areas more than half of the cells are eosinophiles.

Clinically the patient showed the picture of lymphatic leukemia. Anatomically in the lymph nodes there are the typical lesions of Hodgkin’s disease, endothelioma, lymphosarcoma and lymphatic leukemia. In addition the spleen shows a myeloid metaplasia, and the bone marrow, although hyperplastic, shows many eosinophiles, which are not supposed to be present in lymphatic leukemia. No evidence of Hodgkins' disease or lymphosarcoma is present in the spleen or the bone marrow. The liver shows nodules of Hodgkin’s disease and the infiltrations typical of lymphatic leukemia. The kidney shows
leukemic infiltrations and a large tumor, having the structure of sarcoma.

CASE 2

A white boy, 15 years of age, who had been well until a short time before, was first seen at the University Dispensary in October 1926, complaining of pain in the "shin bones." On February 24, 1927, he was admitted to the University Hospital, still complaining of pains which radiated up the legs and, in addition, of severe pain behind one ear and through the head, of loss of appetite, sleeplessness, weakness and loss of weight. Weakness of the legs began about four weeks before admission and during the past week had been so marked that he was unable to walk. For one week he had complained of difficulty in breathing.

The family and past history were negative, except that his mother is syphilitic and blind (diagnosed primary optic atrophy) and has a positive Wassermann reaction.

Physical examination was negative except for a bilateral cervical adenopathy which was most marked on the right. The nodes seemed to be matted together and were not tender.

Blood examination on February 25, 1927 showed hemoglobin 76 per cent; red blood cells 3,830,000; white blood cells 12,050; differential count: polymorphonuclears 89 per cent; lymphocytes 11 per cent. Spinal fluid under increased pressure; Wassermann reaction negative; colloidal gold curve 011000000. Blood Wassermann March 11, 1927, positive.

On March 21, a note reads as follows: "Pain in the neck and shoulder for a week or more, with slight swelling in the region of the right sternocleidomastoid muscle. Today the swelling is the size of a hen egg, very tender and inflamed." Three days later the area had decreased to one half its former size, was red and fluctuated.

Several injections of neoaarsphenamin were given, followed by a chill, faintness, thirst and severe headache. Because of these reactions neoaarsphenamin was discontinued and three injections of 0.4 cc. bismuth salicylate were given intramuscularly.

The urine on March 3 was normal; on April 11 it contained a trace of albumin.
Blood examination April 1: hemoglobin 82 per cent; red cells 4,000,000; white cells 15,400. April 20: white cells 22,000. Differential count: polymorphonuclears 87 per cent; lymphocytes 9 per cent; mononuclears 3 per cent; eosinophiles 1 per cent.

The tonsils and adenoids were removed on May 5. During the stay in the hospital the temperature showed a daily rise above 99° F. Patient discharged May 8 with diagnosis of congenital syphilis and bilateral cervical adenopathy.

He was readmitted on August 19 with the same complaints as on previous admission. Physical examination showed a fairly well marked, hard nodular swelling in the left cervical region, suggesting a matted group of lymph nodes. The neck was stiff and there was some difficulty in turning the head to the left. There was tenderness over the left sacroiliac joint.

Laboratory findings: Urine normal. August 20: hemoglobin 80 per cent; red blood cells 4,660,000; white cells 17,150. Differential count: polymorphonuclears 95 per cent; lymphocytes 5 per cent. August 23, white blood cells 30,600.

On August 25, the following note was made: "Generalized lymphadenopathy, most marked in cervical region. The large mass on the right probably represents more than simple lymphoid hyperplasia, that is, the process is not limited to lymph nodes, but is involving muscle and fascia." During the summer of 1927 he lost about 8.5 pounds in weight. X-ray examinations of the chest, ankles, hands, wrists, knees and skull were negative.

He was seen at the University Dispensary at different times and received antisyphilitic treatment. In the dispensary a cervical lymph node was removed on November 2, 1927 and diagnosed endothelioma. From November 1927 he was absolutely helpless.

On January 1, 1928 he was admitted to the Minneapolis General Hospital. Here the physical examination showed extreme emaciation. The face and neck were greatly swollen, particularly on the right. He appeared to be in great pain and unable to open his mouth. The right cheek was puffy. There was marked bilateral cervical adenopathy, particularly on the
right. The swelling was firm and brawny; on the right it extended from the clavicle up behind the ear. The inguinal nodes were slightly enlarged. The chest was markedly emaciated. The heart and lungs were negative. Blood pressure 95 systolic. The abdomen showed a marked brownish "freckle-like" pigmentation. The liver margin was barely palpable. The spleen was palpable (?)..

Diagnostic impressions: congenital syphilis; Hodgkin's disease; chronic leukemia. The patient died about 24 hours after admission.

Postmortem examination was limited to exploration through a small abdominal incision.

The body (embalmed) was that of a poorly developed, poorly nourished white boy, 156 cm. in length and weighing about 80 lbs. The cervical lymph nodes were palpable, the inguinal nodes barely palpable. As the body was dressed for the coffin, a complete survey of the surface of the body was not made. There was no edema or jaundice. The peritoneal cavity was normal.

The left chest was examined through the diaphragm. A few adhesions were present at the apex. No nodules could be felt in the left lung. The heart on palpation was of normal size. Search of the mediastinum through the hole in the diaphragm revealed two small anthracotic lymph nodes, which were but slightly enlarged. They were not indurated. The liver was apparently of normal size and consistence. The spleen was of normal size. There were no adhesions about it. On section the pulp appeared to be normal. The corpuscles were distinct. The gastrointestinal tract, pancreas, adrenals and kidneys showed no gross lesions.

The retroperitoneal lymph nodes along the aorta and beside the bodies of the lumbar vertebrae were very hard, several times the normal size and tightly adherent to the underlying muscle. On cutting them loose, the nodes were found to be inseparably incorporated with the muscles. No lymph nodes were palpable along the iliac vessels. In the mesentery soft, normal sized lymph nodes were present.
Microscopic Examination

**Lymph Nodes.**—The tissue of the retroperitoneal and tracheobronchial nodes is almost entirely replaced by narrow anastomosing cords and broad sheets of pale staining cells. The nuclei of these cells vary very considerably in shape. No definite cell boundaries can be made out. The broader sheets of cells at first glance suggest metastatic squamous cell carcinoma, but no intercellular bridges, spines or evidences of cornification can be made out. Separating the cords and sheets of cells is a loose reticulated connective tissue in which there are scattered lymphocytes. The same structure is present in the cervical node removed for diagnosis. The structure is shown in Figure 14. The mesenteric lymph nodes are normal.

The muscles adjacent to the retroperitoneal nodes show extensive invasion by the endothelioma, with marked atrophy of the muscle fibers.

The spleen shows no evidence of overgrowth of endothelium but does show marked vacuolization. Sudan iii shows that these vacuoles are due to lipoids (lipoid histiocytosis).

The liver shows a rather marked fatty change in the peripheral portions of the lobules. The kidneys, pancreas and adrenals are normal.

In none of the sections from this case is there anything found which suggests Hodgkin’s disease, tuberculosis or leukemia. Although the possibility of metastatic carcinoma must be considered and cannot be entirely ruled out, since a complete post-mortem examination could not be made, the microscopic findings seem to show that in this case we are dealing with a primary endothelioma of lymph nodes. The clinical course was very similar to that of an ordinary case of Hodgkin’s disease.

**DISCUSSION**

These two cases, while they show very marked anatomical differences, have clinical features which are very much alike. In the first patient several types of lymph node lesions are present; in the second case the lesions are all of one type. From the findings one must conclude either that there is a close
relation between Hodgkin’s disease, endothelioma of lymph nodes, lymphosarcoma and aleukemia, or that in the first patient each of these diseases was present.

**SUMMARY.**

A case of malignant lymphoblastoma is described in which the organs showed a variable histologic structure corresponding in different areas to Hodgkin’s disease, aleukemia, lymphosarcoma and endothelioma.

A case of pure endothelioma of the lymph nodes is described.