From time to time primary tumors of bone present puzzling clinical and pathologic pictures which confuse the clinician as to treatment and the pathologist as to classification. In discussing the classification and treatment of bone sarcomas at the London Cancer Conference in 1928, Ewing (1) stated that he could find no record of primary liposarcomas of bone-marrow, but that in his material there were two or possibly three interesting cases of this type. These cases were later reported in detail by Stewart (2), who believed they were true primary liposarcomas of bone, but stated that the conclusions drawn rested entirely on circumstantial data. He published these rare cases with the idea of enabling other pathologists to look for similar tumors. The next publication on this subject was Fender's (3) in 1933, in which he described a liposarcoma originating in the right fibula and having intracranial metastases. This author pointed out that these tumors are relatively slow growing, the duration being measured in years rather than months after the first appearance of the growth. Cranial metastases seem a common feature, and the tumors appear to be sensitive to irradiation. Barnard (4), in 1934, reported the sixth case mentioned in the literature. The patient had the primary tumor in the left shoulder. The author considered trauma as an etiologic factor in the production of the tumor. He stated: "It may be well in the future to stain more of the frozen sections of biopsy specimens with some standard fat stain to establish more accurately the frequency of these malignant processes."

Owing to the difficulty in diagnosis and rarity of liposarcoma of bone, the following two cases are reported in detail. Case I is No. 1904 of the Bone Sarcoma Registry of the American College of Surgeons.

**Case I:** J. F., Hungarian female, aged fifty-six, applied to the Cleveland City Hospital Out-patient Department on Aug. 26, 1933, complaining of pain in the right hip and leg of two months' duration. There was no history of an injury. The pain was dull, at times becoming sharp and knife-like.

Examination revealed no limitation of motion in the right hip. Slight tenderness was elicited about the joint. The impression gained of the patient's illness was that of a chronic arthritis of the right hip, possibly associated with numerous infected teeth. The patient was referred to the dental clinic, where several teeth were extracted.

On Sept. 30, 1933, the patient returned, stating that her pain had become worse and was sharp and aching. A ten-pound weight loss was noted.

On Nov. 22, 1933, the patient was admitted to the hospital. The day before admission she stumbled without falling to the floor, following which she was unable to walk because of pain in the right thigh.

Read before the American Association of Pathologists and Bacteriologists, Boston, April 9, 1936.
Examination revealed an obese, elderly white woman with the right lower extremity 4 cm. shorter than the left. A deformity was noted in the right thigh just above the knee. No crepitus could be elicited. The knee jerk on the left was greatly diminished. Pupils were unequal, the left being larger than the right.

Radiographic studies revealed a transverse fracture through the midportion of the shaft of the right femur (Fig. 1). There was slight irregularity in the bony cortex above and below the fracture with a marked periosteal reaction. There was also some motting in the bone at the site of the fracture, which had the appearance of being due to a destructive process.

The blood Wassermann reaction and the Kline diagnostic and exclusion tests were negative, on Oct. 28, Nov. 24, and Nov. 28, 1933.

| Table 1: Liposarcoma of Bone |

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Primary Site</th>
<th>Metastases</th>
<th>Duration of Illness Prior to Admission</th>
<th>Subsequent Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Stewart)</td>
<td>33</td>
<td>M</td>
<td>Right hand, phalanx of third finger</td>
<td>None</td>
<td>4 years</td>
<td>Amputation of arm. Living and well 9 years after admission</td>
</tr>
<tr>
<td>II (Stewart)</td>
<td>28</td>
<td>M</td>
<td>Left fibula</td>
<td>Pulmonary</td>
<td>1 year</td>
<td>Died 5 years after admission of metastases</td>
</tr>
<tr>
<td>III (Stewart)</td>
<td>28</td>
<td>M</td>
<td>Not found</td>
<td>Generalized</td>
<td>Unknown</td>
<td>Died 11 days after admission. Disease far advanced</td>
</tr>
<tr>
<td>IV (Bone Sarcoma Registry No. 1224, Rehbock and Hauser)</td>
<td>60</td>
<td>M</td>
<td>Right ilium</td>
<td>None</td>
<td>1 year</td>
<td>Died soon after admission. Disease far advanced</td>
</tr>
<tr>
<td>V (Fender)</td>
<td>23</td>
<td>F</td>
<td>Right fibula(?)</td>
<td>Intracranial</td>
<td>5 years</td>
<td>Living 22 months after admission</td>
</tr>
<tr>
<td>VI (Barnard)</td>
<td>30</td>
<td>F</td>
<td>Left scapula</td>
<td>Pulmonary</td>
<td>4 months</td>
<td>Died one month after admission</td>
</tr>
<tr>
<td>VII (Bone Sarcoma Registry No. 1904, Rehbock and Hauser)</td>
<td>56</td>
<td>F</td>
<td>Right femur</td>
<td>Generalized</td>
<td>5 months</td>
<td>Died 11 months after admission</td>
</tr>
</tbody>
</table>

_Hospital Course_: Treatment consisted of immobilization and traction of the right femur, followed in two months by a hip spica and antiluetic therapy. Radiographs showed an increase in periostitis and no healing of the fracture. On June 24, 1934, a walking caliper was applied and an attempt made to have the patient walk, but weight could not be borne on the right leg. The left hip was painful, and a radiograph showed another pathologic fracture just below the left greater trochanter. This was thought to be due to a metastatic tumor.

An aspiration biopsy from the right femur on Aug. 3, 1934, showed fibrous connective tissue. Another aspiration biopsy, Aug. 21, showed a malignant tumor, the nature of which was not clear. A large firm mass appeared over the right fronto-parietal region and the nodes in both cervical regions became enlarged. Radiographic examination of the skull showed bone destruction at the site of the tumor (Fig. 2). A biopsy of the cervical node
showed an undifferentiated malignant tumor. Low-voltage roentgen therapy was applied to some of these masses to test the radiosensitivity. The mass over the right fronto-parietal region showed slight but definite regression with a small dose. The metastatic lesions continued to enlarge, and the swelling in the right thigh reached enormous proportions. The patient's condition became progressively worse, and death occurred on Oct. 2, 1934.

*Autopsy:* At autopsy there was a great enlargement of the right lower extremity, the mid-thigh measuring 69 cm. in circumference and the mid-calf 40 cm. The left mid-thigh measured 43 cm. in circumference and the mid-calf 28 cm. The skin of the right leg was tense, and there was a severe pitting edema extending up to the iliac crest. There was free mobility in the right mid-thigh and in the left hip, the latter giving crepitus. On the right temporo-parietal region of the skull was a firm, raised, circular mass 8.5 cm. in diameter which was fixed to the skull, but not to the overlying scalp. A similar mass measuring 2.5 cm. in diameter was present in the midline of the parieto-occipital region.

In the abdomen there were pale, firm nodular masses in the greater and lesser omentum, in the mesentery, and about the head of the pancreas and biliary ducts. The spleen was enlarged and nodular; and there were moderately firm, nodular masses retroperitoneally about both kidneys. The parietal pericardium was firmly adherent to the heart anteriorly near the apex. In the upper mediastinum were several enlarged, moderately firm nodes.
The heart weighed 275 grams. There was a moderate dilatation of all chambers with flattening of the internal musculature. The myocardium was firm and dark red and contained five nodules of moderately firm, pale, yellowish-gray tumor situated in the walls of the right ventricle, left auricle, left ventricle, and inter-auricular septum. One nodule in the left ventricular wall approximated the epicardium at the point where pericardium was adherent to it. The largest tumor nodule measured 1 cm. in diameter.

The lungs weighed 1385 grams. The right lung showed fibrous adhesions over the entire pleural surface and there were areas of severe pleural thickening. Scattered throughout both lungs were small, pale, firm tumor nodules. Some of these lay immediately beneath the pleura and some involved the peribronchial lymph nodes. There were areas of bronchopneumonia in the base of the right upper, right lower, and left lower lobes. The bronchopulmonary and bifurcation lymph nodes were enlarged and involved by tumor, and the

![Image](image-url)

**FIG. 2. CASE I: IRREGULAR BONE DESTRUCTION IN RIGHT FRONTO-PARIETAL REGION, REPRESENTING A METASTATIC MALIGNANT PROCESS**

The area of increased density above and anterior to the destructive process is due to the soft tissue mass in the scalp. This mass responded to a small dose of roentgen therapy.

eparterial bronchus on the right was surrounded and infiltrated by a large tumor narrowing its lumen.

The liver showed no metastases.

The spleen weighed 350 grams and was nodular with tumor masses bulging beneath the capsule. These tumor nodules ranged from 1 to 4.5 cm. in diameter and were rounded, moderately firm, granular and pale yellow streaked with red.

The pancreas was firm and its lobular architecture largely obscured by firm, pale tumor. The head was adherent to large masses surrounding it.

The adrenals were of natural size and shape and were not invaded by tumor, although both were surrounded by tumor nodules.

The right kidney weighed 225 grams and the left 250 grams. The capsular surface of the right kidney was studded with circumscribed tumor nodules of varying size, which did not project through the capsule. They involved both cortex and medulla and extensively invaded the pelvis and perirenal fat. The left kidney resembled the right except that the pelvis was encroached upon to a less extent by tumor.

The bladder wall was dilated and thin. Near the neck were two raised, invasive tumor nodules measuring 2 cm. and 5 mm. in diameter.
The internal and external genitalia showed no changes other than atrophy.

The stomach was moderately dilated and thin-walled. The mucosa was hyperemic and showed three crater-like ulcers with raised, firm, nodular margins and smooth, pale bases. These lesions varied from 1 to 3 cm. in diameter and were situated, two in the midportion and one near the pylorus. There was a tumor nodule 2.5 cm. in diameter in the midportion of the ileum, involving the entire wall. A similar nodule 7 mm. in diameter was present in the wall of the ascending colon.

The thyroid gland weighed 100 grams, was symmetrically enlarged, and showed a normal structure, except for one adenoma 1.5 cm. in diameter.

The musculature of the greater part of the right thigh and pelvis was replaced by firm, dense, grayish-white tumor tissue having a flat, glistening cut surface. The fascial planes and muscle sheaths were preserved. There were numerous irregular, soft, dark gray areas of necrosis. The shaft of the femur was firmly adherent to tumor and areas of bone were softened and invaded. The midportion of the femur was extensively fragmented. Where tumor was applied to the bony cortex, radial striations were readily discernible in the tumor. The tumor was adherent to the wall of the femoral vessels, but did not penetrate them in any situation. The femoral vein was thrombosed.

The upper portion of the left femur was involved by tumor similar to that on the right. The bone was softened, fractured, and fragmented below the neck. The architecture of the joint was completely destroyed.

Tumor invaded the bony calvarium and tissues of the scalp over the right frontal, temporal, and parietal regions and also the bone of the right middle fossa. It invaded the dura and pia-arachnoid without extending into the brain.

The tenth and eleventh thoracic vertebrae were infiltrated by tumor and the spinal canal was encroached upon at this point. The dura of the spinal cord was intact throughout.
but the cord at the level of the tenth and eleventh thoracic vertebrae was compressed and softened.

Microscopic sections of thyroid, heart, lungs, liver, spleen, pancreas, adrenal, kidney, bladder, bowel, brain, spinal cord, dura mater, bones, and tumor were examined. The tumor in the many situations was similar to that in the right thigh. It was highly cellular with only a small amount of fibrous reticulum (Fig. 3). Necrosis of tumor was a prominent feature. There was no architectural arrangement of tumor cells, and they were widely diffused through the tissue in a disorderly manner. Invasion of lymphatics was common. In most areas the nuclei were ovoid, rounded, or spindle-shaped, with great variation in individual size and shape. The nuclei were hyperchromatic and mitotic figures were numerous. There was an occasional cell with a double nucleus. In most areas the cytoplasm was small in amount and poorly defined, but in some areas the cells had abundant cytoplasm and eccentrically placed nuclei. Sections stained with Sudan III showed minute fat droplets within the cytoplasm of numerous tumor cells.

The pathologic diagnosis was liposarcoma of right thigh, probably originating in the femur; generalized tumor metastases; bilateral bronchopneumonia; thrombosis of right femoral vein; suppurative sphenoiditis and ethmoiditis.

**COMMENT:** Only when the autopsy was performed and the diffuseness of the disease recognized did the idea occur that this tumor might be a liposarcoma of bone. The widespread metastases, especially in lymph nodes and bone, and the radiosensitivity of the tumor are not in keeping with the usual findings in osteogenic or periosteal sarcomas. That the tumor was primary in the femur seems most probable. The histologic diagnosis of liposarcoma is supported by the presence of tumor cells resembling embryonic fat cells and by minute fat droplets within the cytoplasm of apparently undegenerated cells. Confirmation of the histologic diagnosis of liposarcoma was given by Dr. Howard T. Karsner, Dr. James Ewing, and Dr. Fred W. Stewart.

The following case, which is filed with the Bone Sarcoma Registry of the American College of Surgeons, No. 1224, is reported in detail through the kind permission of Dr. B. Earle Clarke of the Rhode Island Hospital, Providence, Rhode Island.

**CASE II:** W. H., a white male broom-maker, approximately sixty years of age, entered the Rhode Island Hospital on Oct. 3, 1930, in a state of delirium. A relative stated that the patient had complained of pain in the right lower abdomen for a year and had lost much weight. Examination revealed an emaciated old man with pitting edema of feet and forearms. A mass was felt in the right lower quadrant, just within the pelvic brim. It was hard, not tender, fixed and smooth. A barium enema showed displacement of the cecum by an extrinsic mass. There was a rough systolic murmur over the mitral area transmitted to the axilla, and a loud, rough systolic murmur over the aortic area. Later there was slow fibrillation. The red blood count was 2,000,000 and the hemoglobin 25 per cent (Sahli). The white blood count was 10,000. The urine was negative and the blood chemistry normal. The patient died two weeks after admission. The clinical diagnosis was chronic rheumatic heart disease, malignant abdominal tumor, and organic delirium.

**Autopsy:** At autopsy, pigmentation was noted over the forearms and backs of hands. No nodes were palpable in the neck, axillae, or groins. In the abdomen the cecum was firmly adherent to a retroperitoneal mass measuring 10 cm. in diameter. This mass occupied the central portion of the right ilium, projecting anteriorly and posteriorly and extending medially into the sacrum. On section the tumor was pale, firm, and friable, with many yellow necrotic areas. There was a hydrothorax of 800 c.c. on each side. The heart weighed 600 grams and showed a healed mitral valvulitis. The lungs, liver, and spleen showed a severe chronic passive hyperemia. The remaining viscera and the head and brain showed no pathologic changes of significance.
Fig. 4. Case II: Low-power and High-power Photomicrographs of Tumor Showing Pleomorphism of Cells and Minute Vacuoles in the Cytoplasm. X 275 and X 600
Microscopic sections of heart, lung, liver, spleen, pancreas, adrenals, brain, and tumor were examined. No tumor metastases were found.

The tumor was highly cellular with only a fine supporting reticulum. There was a great variation in size and shape of cells and nuclei, but the predominant type was large, ovoid or polyhedral, with abundant acidophilic cytoplasm and relatively small, eccentric, deeply stained nuclei. Mitotic figures were infrequent, but there were numerous double nuclei and an occasional multinucleated giant cell. In the cytoplasm of many cells were tiny vacuoles, and Scharlach R stains showed minute fat droplets within the cytoplasm. Some of these fat-containing cells showed some nuclear degeneration, but others did not. Many cells resembling embryonic fat cells contained no fat in the cytoplasm. There were variations from this large cell type to compact spindle cells forming a coarse interlacing pattern. Large areas of hemorrhage and necrosis were present (Fig. 4).

The pathologic diagnosis was liposarcoma of right ilium with extension to sacrum; chronic rheumatic heart disease; cardiac hypertrophy and dilatation; chronic passive hyperemia of lungs, liver and spleen; and generalized arteriosclerosis.

Comment: The gross destruction of the iliac bone by the tumor and the extensive anterior and posterior projections of the soft tissue from the bone are factors in favor of the ilium being the primary site. The histologic diagnosis of liposarcoma seems unquestionable. The characteristic feature is the presence of tumor cells having the morphology of embryonic fat cells. Fat droplets in the cytoplasm are frequent, although numerous cells show degenerative nuclear changes and the presence of fat in these cells may be interpreted as a degenerative change. There was unanimous agreement on the diagnosis by the committee on bone sarcoma of the American College of Surgeons.

Summary

Two cases of liposarcoma considered to be primary in bone are reported in detail, and the literature on the subject is briefly reviewed. The tumor in Case I is grossly differentiated from other types of primary bone sarcoma by bony and extensive lymph node metastases. It has the histologic structure of liposarcoma. In Case II metastases were absent, but the histologic structure of liposarcoma is typical.

Note: The authors are indebted to Dr. Howard T. Karsner for the photomicrographs and to Dr. Bernard B. Larsen for his kind permission to use the clinical records in Case I.

References