BONE SARCOMA IN POLYOSTOTIC FIBROUS DYSPLASIA*

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WITHIN THE PAST DECADE the syndrome now commonly designated as fibrous dysplasia of bone has become increasingly recognized. In 1934, Goldhamer[1] recognized a disease which he characterized as osteodystrophia fibrosa unilateralis with pubertas praecox, and, in the same year, Borak and Doll[2] described what they called unilateral Recklinghausen's disease of bone with pubertas praecox. Almost simultaneously in this country appeared papers by Lichtenstein,[3] who employed the term "polyostotic fibrous dysplasia," and by Albright, Butler, Hampton and Smith[4] and Albright, Scoville and Sulkowitch,[5] who defined the process as a syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation, and endocrine dysfunction, with precocious puberty in females. In 1942, Lichtenstein and Jaffe,[6] published an account of a large number of cases, with descriptions of their accessory features in addition to the skeletal lesions.

The present authors have no intention of again describing the syndrome. Their sole purpose is to place on record two instances of malignant bone tumor arising on the basis of fibrous dysplasia. Heretofore, so far as they know, this event has not been described, although cases doubtless exist.

In our first case, initially seen in 1929, the syndrome was, quite naturally, not recognized, although the characteristic pigmentation is described. Not until about ten years later did this case reach the proper clinicopathologic category.

CASE REPORTS

Case 1.—The patient, J. W., No. 40833, was a female, age 42, of Lithuanian ancestry. Her past history was uneventful. Five months prior to admission, she noted slight stiffness in her left shoulder. This increased during the following month and pain developed, especially on motion. Apparently, she first noted swelling in the shoulder region about two months after her first symptom. The swelling became progressively worse and two weeks prior to admission to the Memorial Hospital, the patient entered another hospital where a presumptive diagnosis of malignant bone tumor was made, whereupon she was referred to Memorial. During the two months prior to admission, the patient had lost about eight pounds in weight, suffered from occasional headaches and complained of a burning sensation over the left anterior chest wall.

The pertinent part of the initial examination concerns the local condition and the radiographic findings. The left scapula was the site of a large tumor mass, firm, rounded, nontender, possibly somewhat fluctuant. The entire shoulder region, anterior and posterior chest walls were the site of a brownish pigmentation which extended upward both anteriorly and posteriorly in the neck region. This pigmentation was essentially unilateral but reached slightly beyond the midline (Figs. 1 and 2).† There was marked limitation of motion of the left arm; abduction was essentially absent and anteropostero motions were but moderate.

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† 1941 photos; roentgen changes present in pigmented areas.

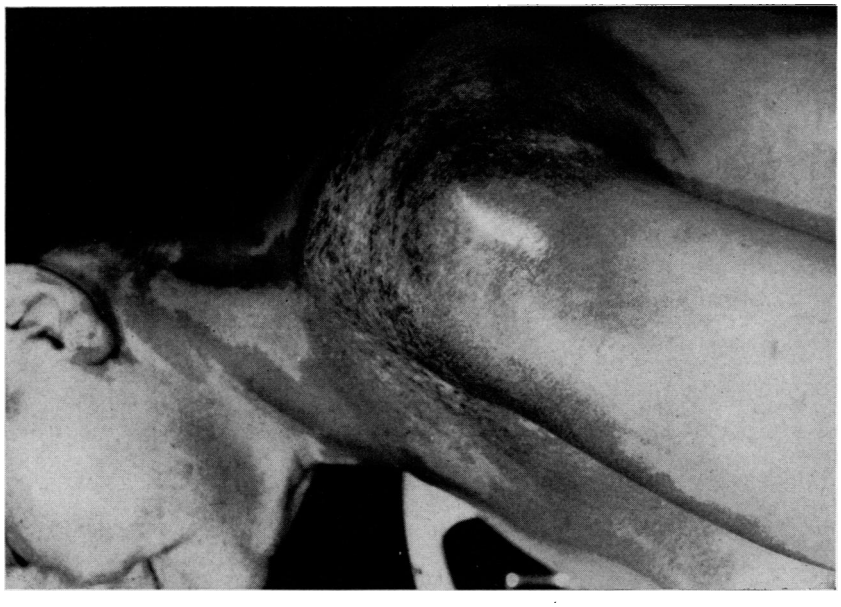

FIG. 2.—Pigmentation and enlargement of scapular area due to tumor. A late photograph.

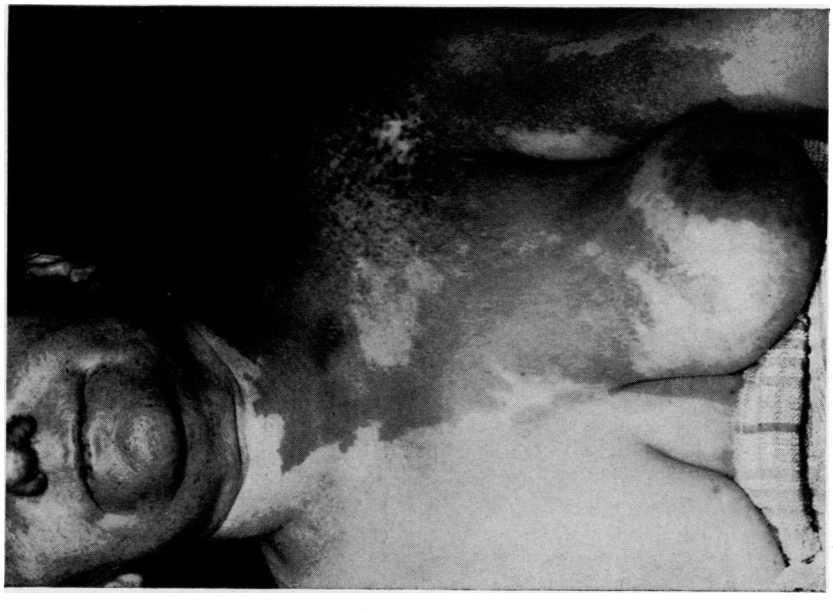

FIG. 1.—Typical pigmentation essentially unilateral in character. Late photograph after treatment by irradiation. In the shoulder area the pigmentary changes are partly the result of irradiation.

Films of the left shoulder taken November 21, 1929, (Fig. 3) showed almost complete loss of outline of the left scapula which was replaced by a very large tumor mass, completely osteolytic, with only a few bony remnants remaining. The entire shaft of the left humerus showed altered architecture, with thinned cortex and multiloculated appearance of the medullary cavity.

Films of the chest of the same date (Fig. 4) showed marked deformity of most of the ribs, particularly on the left, with irregular expanded multiloculated areas. The lung fields appeared clear.

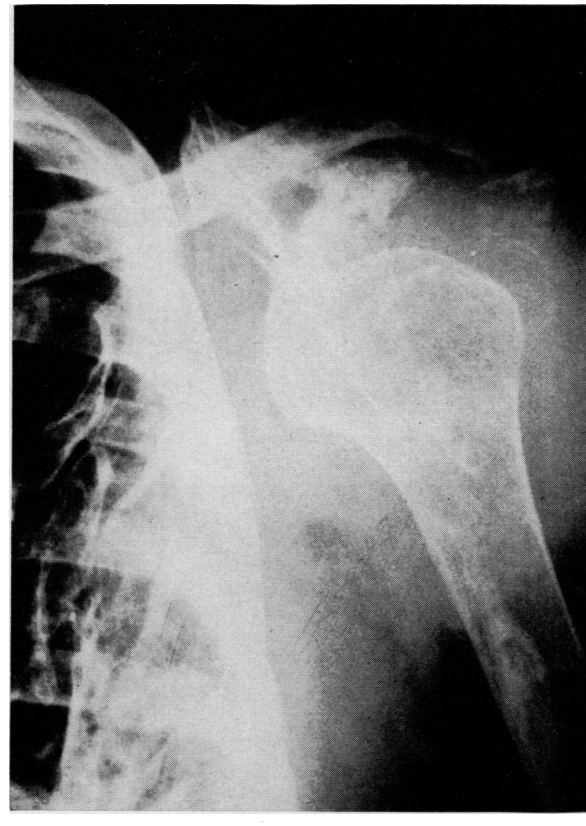

FIG. 3.—Osteolytic lesion of left scapula. Humeral architecture with thinned cortex and multiloculated medullary cavity.

Films of the spine, pelvis and femora (Fig. 5) taken in December, 1929, showed no changes in the spine but the left ilium and the right pubis showed slight expansion and areas of decreased density similar to those seen elsewhere. Both femora showed widespread changes with decrease in density of the medullary cavities which latter were irregularly expanded.

Lateral films of the skull (Fig. 6) showed a pagetoid appearance of the entire skull and facial bones, with thickening of the tables and irregular areas of decreased density.

The scanty laboratory studies during this patient's first admission revealed nothing of significance unless a basal metabolic rate of plus 20 is indicative of some hyperthyroidism, since the latter has been emphasized in this disease. An aspiration biopsy was performed and yielded rare large atypical spindle cells, diagnostic of some type of sarcoma. Hence, a tentative diagnosis of medullary spindle cell sarcoma of bone was made.

The tumor was not considered suitable for radical surgery, since at that time it was not realized that the process in other areas was probably not sarcomatous, and the patient received a rather small amount of treatment with a radium emanation pack. This totaled but 28,000 mg. hrs. at 6 cm., and was administered on five successive days, between November 19, 1929, and November 23, 1929, through anterior and posterior portals. At the same time the patient received three roentgen-ray treatments to the left shoulder region, two over the rib areas and two to the skull, and between November 27, 1929, and January 7, 1930, she received Coley's toxin both intramuscularly and intravenously, with, on the whole, rather little reaction. Despite the seeming total inadequacy of the radiation, the patient's condition considerably improved. The tumor diminished in size, pain became much less severe and eventually vanished except for what the patient described as "slight pain with weather changes."

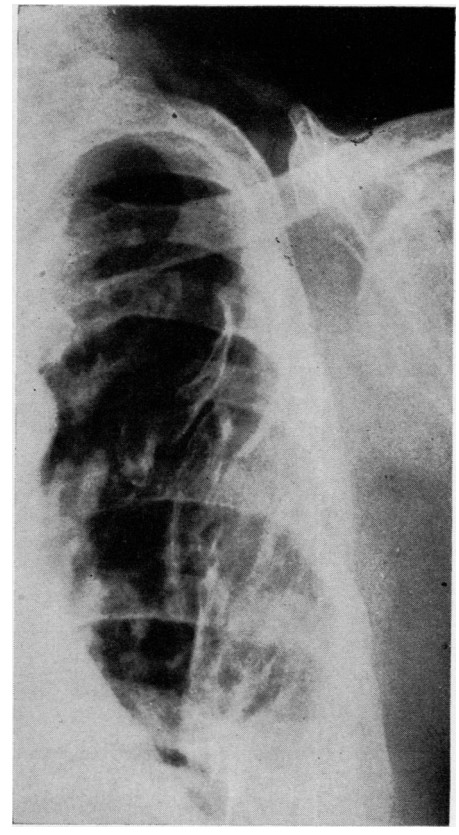

FIG. 4.—Rib deformity with numerous expanded multiloculated areas.

Radiographic reëxamination of the left shoulder on December 24, 1929, showed a marked improvement in the appearance of the scapula, with marked decrease in size of the tumor and beginning calcification suggesting regeneration.

The patient was again able to conduct her housework in a normal fashion and persistently refused to return to the clinic for observation. In fact, despite numerous appeals, she remained away for 11 years.

She reëntered the Hospital on July 9, 1941, and so far as the local findings were concerned the situation in the left shoulder was somewhat improved over that observed in 1929. Radiographs were reported as follows:

"Reëxamination of the left shoulder on July 10, 1941, shows some residual soft-part tumor, but there has been marked regeneration of the scapula, with reformation of the glenoid and vertebral border. The humerus shows no significant change from previous status."

Films of the chest on July 10, 1941, showed no apparent new changes in the ribs but there was increased density over the left chest, probably due to radiation. There was a large rounded shadow in the periphery of the right upper lung field which had the appearance of metastasis. The right humerus appeared normal. The pelvis showed no significant change. The skull again showed extensive changes which were better demonstrated and seen to be largely on the left.

The pigmentation was unchanged except for the addition of a large area of roentgen pigmentation, with scaling and telangiectasia. The patient's general condition had considerably declined. On this admission the laboratory studies were considerably more extensive. Red blood cells ranged from 2.5 to 2.9 million, except for a transient peak following transfusion. Calcium varied from 10.0 to 13 mg.; phosphorus from 2.82 to 4.11 mg.; alkaline phosphatase from 17.8 to 28.0 mg.; acid phosphatase was 0.56

units. Serum protein level on two determinations showed 7.8 and 8.1 per cent. Prothrombin level was 51 per cent. Chlorides ranged from 582 to 591 mg. Chloride tolerance was abnormal and appeared suggestive of adrenal cortical insufficiency. Blood cholesterol studies showed total cholesterol 164.3 mg., free 55.7 mg.; esters 108.6 mg. Bence-Jones studies were negative on several occasions. Two basal metabolic rate determinations were reported as plus 25 and plus 20.

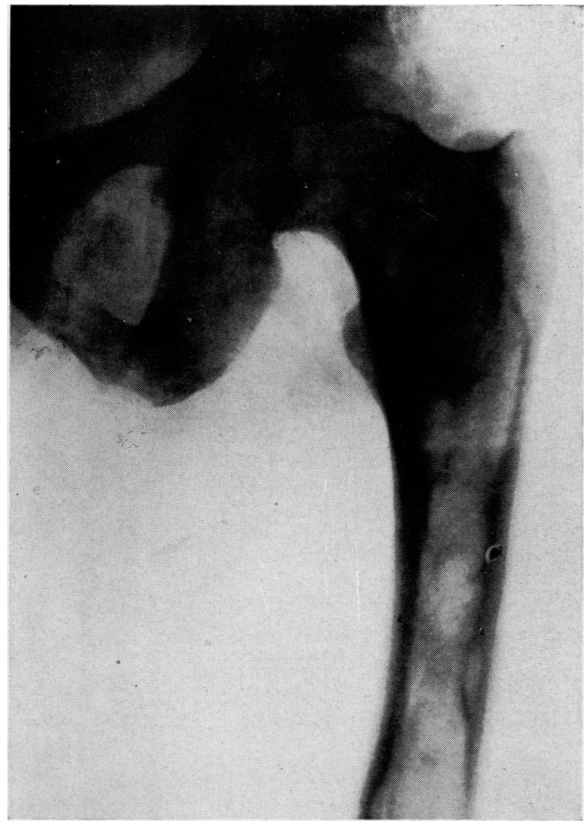

FIG. 5.—Expanding areas of decreased density in femur.

Shortly after admission, but after a second aspiration biopsy, the patient developed a septic temperature ranging up to 103° F., and since no cause could be otherwise elicited, it was assumed that the source was infected tumor tissue. On July 30, 1941, an open biopsy was made of the scapular tumor.

The tumor tissue was soft, friable, yellowish to grayish, in places very hemorrhagic. It was about the consistency of chicken fat clot. On section (Fig. 7), it proved to be a highly pleomorphic, nonbone-forming, spindle and giant cell sarcoma. Giant cells reached enormous proportions and numerous atypical mitoses could be found. It was quite obvious that the tumor cells were identical with those obtained in the first material aspirated in 1929, and in the subsequent aspiration. This should be sufficient to dispel any doubt as to the existence of a malignant process in 1929, even in the mind of sceptics of aspiration as a diagnostic method, but poses a difficult question as to why a large osteolytic malignant tumor had remained for so many years prior to dissemination. This naturally is a question which the authors are unable to answer.

Since it became desirable to prove, by something other than radiographs, that this lesion had arisen on a basis of polyostotic fibrous dysplasia, it was determined to biopsy a supposedly nonneoplastic area for confirmation of this diagnosis. Hence, on August 14, 1941, an 8.5-cm. portion of left 8th rib was removed. On section, this tissue showed no evidence of tumor, and fulfilled all criteria for a microscopic diagnosis of fibrous dysplasia.

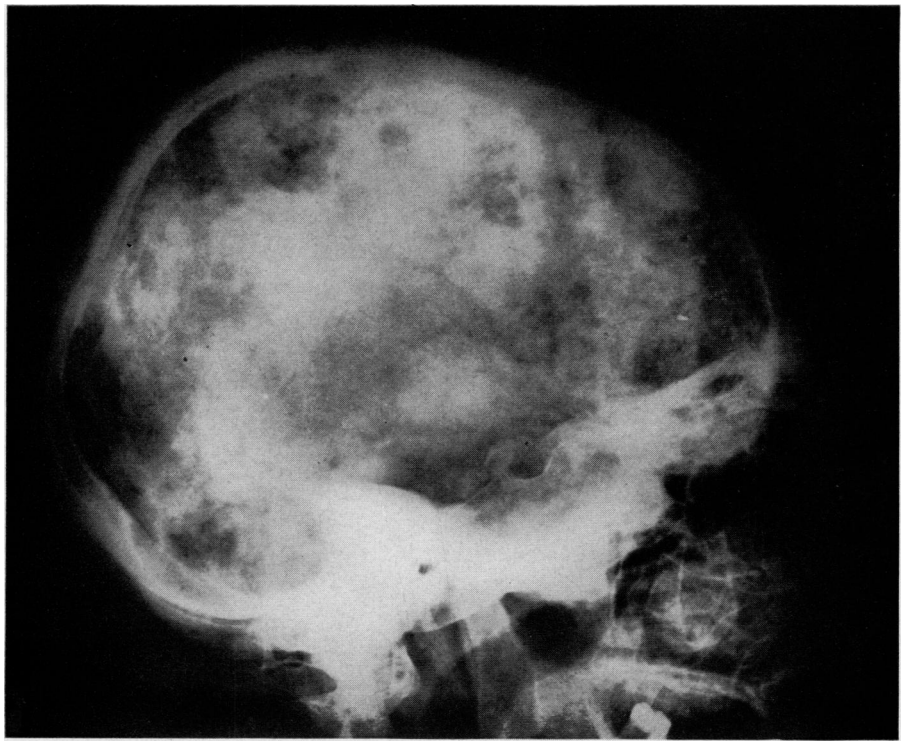

FIG. 6.—Pagetoid areas in skull and facial bones. An anteroposterior view revealed these to be mainly unilateral.

The patient was discharged, August 28, 1941, clinically improved. Again, she failed appointments, but this time evidently because of progress of tumor. Repeated attempts to persuade her to return to the hospital failed and she died at home on December 2, 1941. During the terminal phase of the illness she complained of abdominal discomfort, diarrhea and, evidently, the tumor of the left scapula had ulcerated and begun to fungate. A letter from her family physician stated that she had developed "intestinal" metastasis. Naturally, the authors are unable to confirm this finding in the absence of autopsy but in view of the radiographic finding in the right chest, see no reason to doubt the presence of abdominal disease.

Obviously, this tumor ran a most unusual clinical course. It was diagnosed as malignant bone tumor in 1929 on pathologic evidence, which we believe entirely reliable. With treatment, which should not have sufficed to control it, the patient experienced prolonged relief of symptoms, with regression and apparent quiescence of the tumor, and remained in relatively good condition for over 11 years.

Case 2.—The second patient, G. deP., No. 55274, was a male Italian, age 34. His past history was uneventful except for a primary luetic lesion many years prior to admission for which limited treatment had been given. His present illness began nine months prior to admission, when he noted pain in the left lower thigh and leg. This became worse and, about three months prior to admission, swelling of the left hip was first noted. The swelling increased rapidly in size and was accompanied by severe pain.

On admission, there was a bulky tumor mass involving the left hip laterally and posteriorly, and measuring 24 x 20 cm. in greatest dimensions. There was marked tenderness laterally over the greater trochanter. The bulk of the tumor was situated

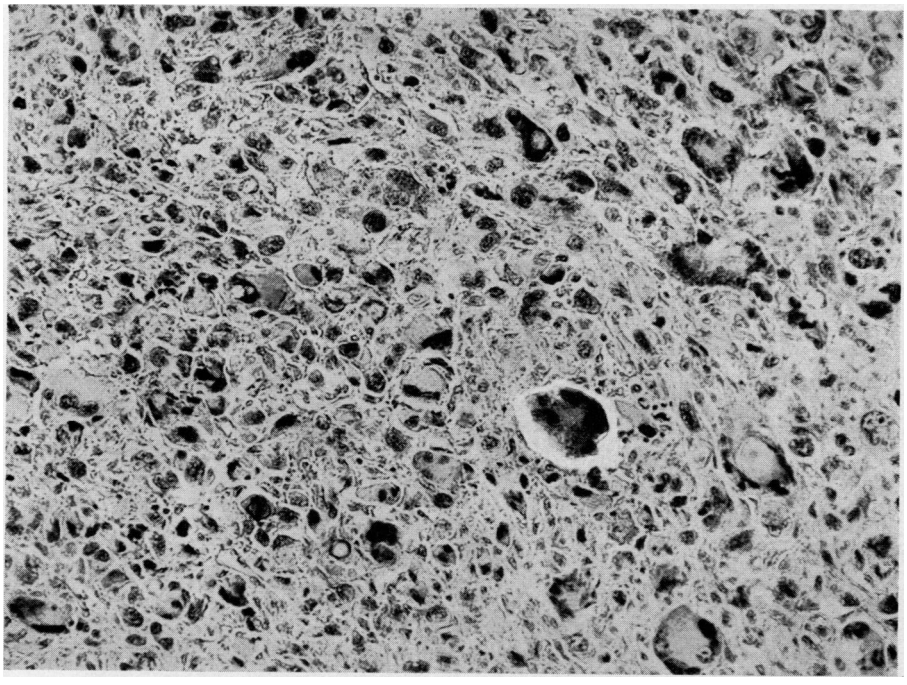

FIG. 7.—Pleomorphic large spindle and giant cell sarcoma.

posteriorly and was of firm, rubbery consistency. There was limitation of motion of the left hip in all directions mainly because of pain. There was no increase of local heat.

Films taken at the time of admission revealed a pattern considered classical for fibrous dysplasia. There were multiple somewhat expanding areas of bone rarefaction, together with zones of increased density involving the left pubic bone, left femur, particularly the neck region, and left tibia (Figs. 8 and 9).

On May 25, 1938, an aspiration biopsy was performed and a few cells were recovered which suggested malignant tumor. On May 31, 1938, the aspiration was repeated and a giant and spindle cell sarcoma, consistent with primary spindle cell sarcoma of bone, was diagnosed, both on smear and sectioned fragments of clot (Fig. 10). The resemblance to the previous case was striking.

Blood calcium ranged from 10 to 10.8 mg.; blood phosphorus from 2.6 to 3.8 mg. Phosphatase which ranged from 10 mg. on admission to 24.9 mg. on June 17, 1938, fell with treatment to 5.7 mg. on August 17, 1938. His basal metabolic rate was reported as plus 35, but for certain reasons this was considered inaccurate.

The patient was treated by roentgen ray, receiving a total of 18 treatments between

June 1, 1938, and June 21, 1938. Portals were anterior, lateral and posterior, approximately 15 x 18 cm. each. Daily doses were 300 r. for a total of 1800 r. per port. The patient experienced remarkable relief from pain, this relief being much more than would be expected for the ordinary malignant bone tumor. Flexion and extension returned to a considerable extent. On January 4, 1939, radiograms of the femur revealed considerable evidence of bone regeneration.

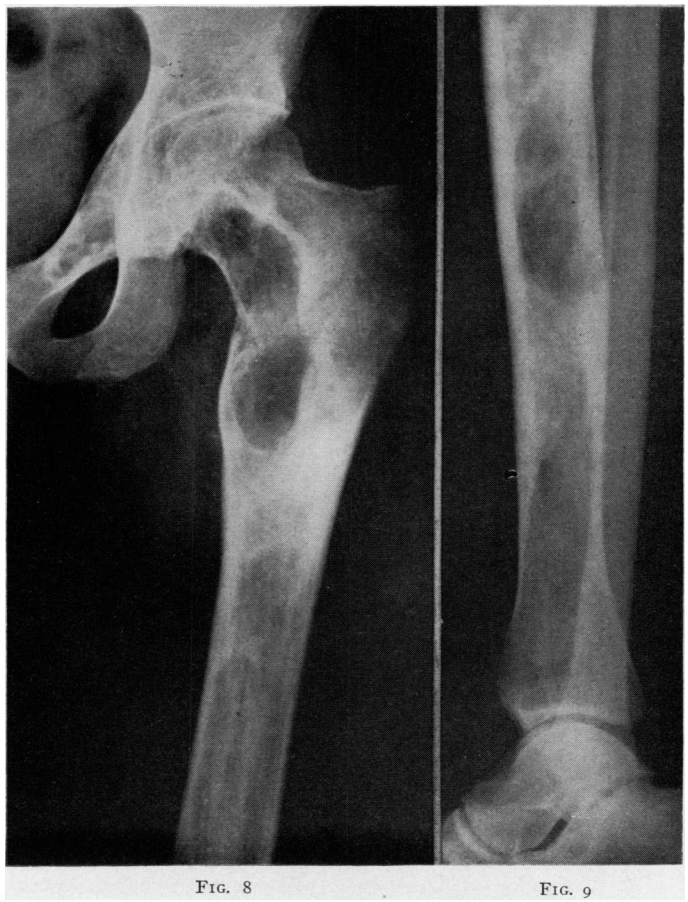

FIG. 8 FIG. 9

FIG. 8.—Multiple expanding areas of decreased density together with zones of increased density, left pubis and femur.
FIG. 9.—Similar areas of decreased and increased bone density, left tibia.

On March 8, 1939, the clinical improvement was regarded as so paradoxical that the question was raised as to the correctness of the diagnosis of osteogenic sarcoma. On November 8, 1939, the patient reported that he was essentially free from symptoms and no tumor was palpable, although diffuse thickening and firmness of muscles and subcutaneous tissues were noted. When referred for a check-up radiographic examination of the pelvis and left femur, however, he was found to have a pathologic fracture in the region of the intertrochanteric line with considerable shortening of the femoral shaft and coxa vara deformity. Approximately two months later further examinations showed no significant change. It appeared that a diagnosis of spindle cell sarcoma in an area of fibrous dysplasia was warranted, but to make more certain it was decided to obtain

tissue from the involved area of tibia and an open biopsy was performed on February 8, 1940. This tissue was reported as fibrous dysplasia.

The patient returned to the Follow-up Clinic until July 15, 1942. He had remained essentially symptom-free. In August, 1942, he entered another hospital complaining of epigastric pain and vomiting. His condition grew progressively worse and death occurred eight days after admission. No autopsy was obtained. Radiographs, however, are described as revealing an enlarged hilar shadow, with pulmonic infiltration, retraction

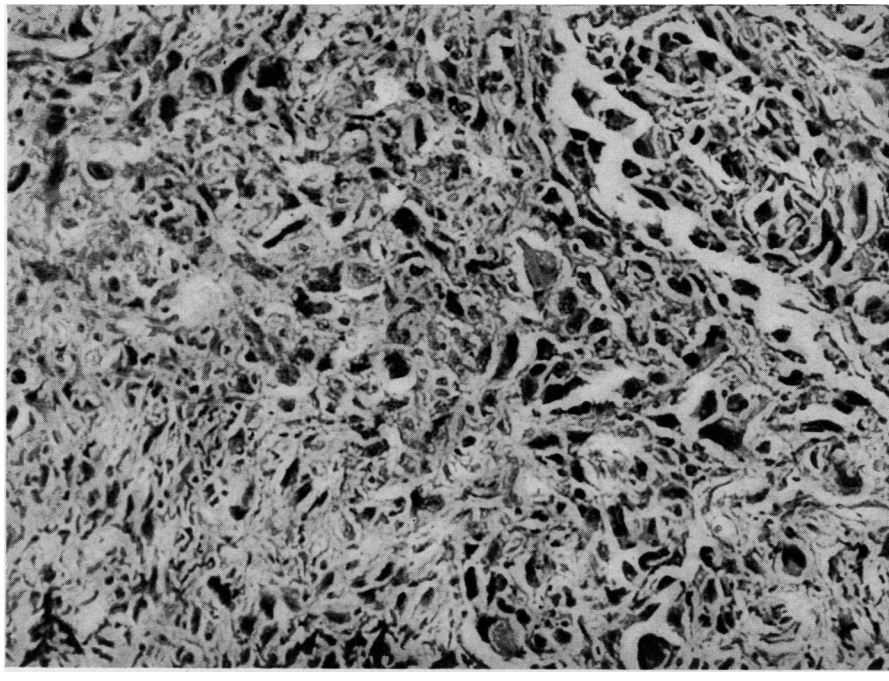

FIG. 10.—Pleomorphic spindle and giant cell sarcoma of left femur.

of heart and trachea to the right, thickened pleura, partial atelectasis of right lung. The radiologist's conclusion was tumor of the left hilar region with metastasis to bone. Naturally, the evidence points entirely toward the left femur as a primary source of tumor. Again, in the absence of autopsy, one cannot be absolutely certain that metastasis had occurred, but given the radiographic evidence pointing to metastasis, with full knowledge that a malignant bone tumor existed, a doubt seems scarcely justified.

SUMMARY

In conclusion, it may be stated that (1) polyostotic fibrous dysplasia may be added to the group of diseases of bone which may, in certain instances, develop malignant bone tumors. (2) In the two examples so far studied by us, the tumors have been essentially identical histologic pattern, namely, non-bone-forming pleomorphic spindle and giant cell sarcomas. (3) Both tumors appear to have produced metastases. (4) In both instances the response to radiotherapy has been unusual when compared to expected behavior of similar histologic types in different clinical settings. Whether this behavior will eventually prove part of a general clinical entity or not must await further cases.

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FINNEY-HOWELL FOUNDATION FELLOWSHIPS

At the meeting of the Board of the Finney-Howell Research Foundation, Inc., on March 2, 1945, fellowships were renewed for the third year for Dr. Nelicia Maier; for the second year for Drs. Muriel Virginia Bradley and Margaret Aston Kelsall; and a new fellowship was awarded Dr. Elizabeth Cavert Miller, to work in the University of Wisconsin.

Applications for fellowships for 1946 must be made to this office before December, 1945, to be eligible for consideration.