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BONE INVOLVEMENT IN HODGKIN'S DISEASE*

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HODGKIN'S disease is a neoplastic disease of unknown etiology, primarily involving lymphatic and hemopoietic tissue, but occasionally involving other tissues. Its effects on bone are by:[3]

1. Direct extension
   (a) Pressure irritation leading to periosteal reaction, sclerosis of the "ivory" vertebra type, or anterior marginal erosion of vertebral bodies.
   (b) Direct invasion of bone from without, entering through the periosteum from contiguous diseased lymph nodes.
2. Blood borne emboli or transference of an agent capable of inciting foci (multifocal origin) in the medullary portion of bone, in the same way as by metastases.

Opinion in the literature concerning the prognostic significance of bone involvement in Hodgkin's disease is divided,[2,3,5,6] and some investigators feel that survival time is prolonged in patients with bone lesions.[5,6] From 1949 through 1966, we reviewed 61 cases in our Tumor Board Registry with the primary diagnosis of Hodgkin's disease involving the soft tissue, to determine the incidence and prognosis of patients with bone involvement. These were not all the cases of Hodgkin's disease seen at our institution during this time, in that from 1959 to 1965 the Tumor Board Registry was most incomplete and the majority of cancer cases seen in the hospital were not registered. This report presents our findings together with a brief review of the literature on the subject. Ten cases were excluded because of inadequate pathologic data, and 2 because they were seen merely for diagnostic procedures and were not treated or followed. We have, therefore, 49 cases of soft tissue Hodgkin's disease for analysis, 10 of which also had bone involvement.

Detection of bone involvement roentgenographically depends on changes related to cortical bone involvement. The reported over-all incidence of 15 per cent is probably low because of asymptomatic cortical bone lesions which are not discovered. Four of 10 patients were asymptomatic, and 2 of 4 asymptomatic patients had bone lesions when the diagnosis of Hodgkin's disease was made initially. W.B. and J.C. were discovered because the initial work-up of the majority of patients includes a chest roentgenogram and an intravenous pyelogram, which show the bones most likely to be involved (Table I).

In the literature, Hodgkin's disease is reported to occur twice as frequently in men as in women, and usually between the ages of 35 to 55 years.[3] In our series, the mean age of occurrence of Hodgkin's disease is approximately 40 years, and is also the same mean age in our patients with bone involvement. Our sex ratio is equal. Differing from other reports, we found no significant difference in prognosis between males and females (Table II).

Roentgenographic appearance of Hodgkin's disease of bone simulates that of any metastatic malignancy and may be sclerotic, lytic, or a mixture. Approximately two-thirds of the reported cases showed mixed lytic and blastic lesions. Osteolytic lesions, with areas of sclerosis confined to margins

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TABLE I

DATA ON PATIENTS IN PRESENT SERIES WITH BONE INVOLVEMENT

Name	Sex	Age	Lymph Node Pathology	Site of Lesion	Survival (yr.)		
					Local Treatment	After Diagnosis	After Bone Involvement
R.W.	F	35	Granuloma	L4–L5 spine	3,000 r	7.0	5.0
H.M.*	M	46	Paragranuloma	C7–T1 Spine (Biopsy confirmed)	3,500 r	9.0	4.0
			Granuloma	Lumbar spine	None		
T.S.	F	43	Granuloma	T9–T10 spine	None	1.7	0.8
M.S.	F	22	Granuloma	Left os pubis	None	5.7	5.0
S.H.	F	46	Granuloma	Skull (Biopsy confirmed)	None	7.0	2.5
				Left femur	3.600 r		
P.G.	F	16	Granuloma	Left S-I joint	6,000 r†	3.5 (live)	3.5
J.C.	M	84	Granuloma	Thoracic skeleton	None	1.5	1.5
M.K.	M	33	Granuloma	Right ilium	Yes—?amount	6.8	6.8
W.B.	M	51	Sarcoma	Right S-I joint	600 r	0.3	0.3
J.D.*	M	25	Paragranuloma Sarcoma	L-S spine	Yes—?amount	2.0	2.0
Average		40.1				4.5	3.1

* H.M. and J.D. were histologically classified as paragranuloma on initial biopsy, but subsequently, biopsy showed granuloma and sarcoma, respectively.

† Total dose given in more than 1 course of radiation therapy.

of lesions, or with prominent trabeculation, are most common. Pure osteoblastic lesions are seen almost exclusively in the spine (ivory vertebra).[2] Periosteal new bone formation, as a result of cortical irritation from adjacent gland masses or intramedullary disease, occurs along the lumbar spine, ribs, and long bones.[3]

TABLE II

SURVIVAL BY VARIOUS CATEGORIES OF DISEASE

Category	No. of Patients	Average Survival After Diagnosis (yr.)
Paragranuloma	8	4.0
Granuloma	33	4.1
Sarcoma	8	0.86
Stage I*	6	5.1
Stage II*	12	2.0
Stage III*	31	3.8
Patients with bone involvement	10	4.5
Survival after development of bone lesion(s)		3.1
Patients without bone involvement	39	3.3
Males†	27	3.7
Females†	22	3.4

* Classification according to M. V. Peters.[4]

† Representing comparable stages of disease and pathologic classification.

Our patients showed mostly osteolytic (Fig. 1) and mixed type lesions (Fig. 2) and the majority were located in the lumbodorsal spine. Only 2 of 10 patients with bone involvement, however, had multiple lesions. Two of the 10 patients had histologic confirmation of the bone lesions, whereas in the remainder, the diagnosis was made roentgenographically. A comparison of the bone histology with the lymph node pathology was not made in either instance. Table 1 shows the pertinent data of those with bone involvement.

Radiation therapy of bone lesions in Hodgkin's disease is generally considered palliative. Radiation therapy was delivered with either a 300 kv. Maxitron orthovoltage unit or a 2 mev. G. E. Maxitron. Doses to bone lesions ranged from 600–6,000 r, calculated at the depth of the lesion. All patients had a single course of irradiation

delivered to the bone lesions except for H.M. and P.G., who had 2 courses of radiation therapy. In neither of these cases did the bone lesions heal completely, although the progress of the bone destruction, and pain, were arrested. Several of the patients who had spine and pelvis involvement also received an unknown additional amount of irradiation to the bone lesions during courses of mediastinal and abdominal lymph node irradiation. Most of our patients were also receiving chemotherapy and we can, therefore, not correlate our local therapy for bone lesions with survival, nor state an optimum dose required for bone lesions, based on our study alone.

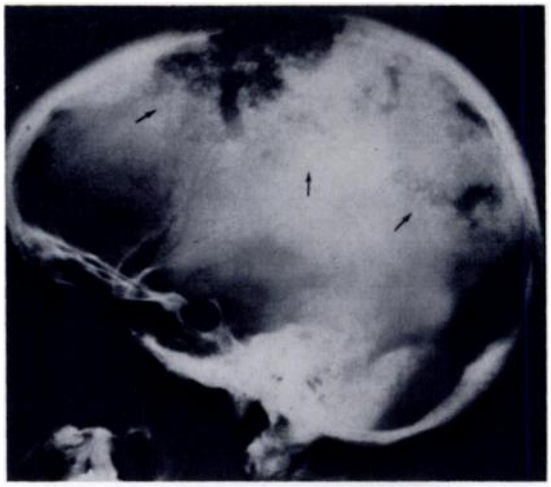

FIG. 2. Same patient as in Figure 1, showing mixed osteolytic and osteoblastic lesions of the skull.

SURVIVAL

In several reports, survival with Hodgkin's disease and bone involvement is better than without demonstrable bone lesions. Vieta *et al.*,[6] in a study of 38 cases with a brief review of the literature up to 1942, concluded that in the 5 year follow-up period, survival was significantly better in the group with bone involvement, but the survival curves approximate each other at 5 years and beyond (Fig. 3). Stuhlbarg and Ellis[5] surveyed the literature more recently and added 30 cases of Hodgkin's disease with bone involvement. They noted increased survival in the group with bone involvement at the end of 5 years compared to the non-involved group (Fig. 4). The foregoing authors were of the opinion that one could not infer that if patients with Hodgkin's disease lived long enough, bone lesions necessarily would become manifest.

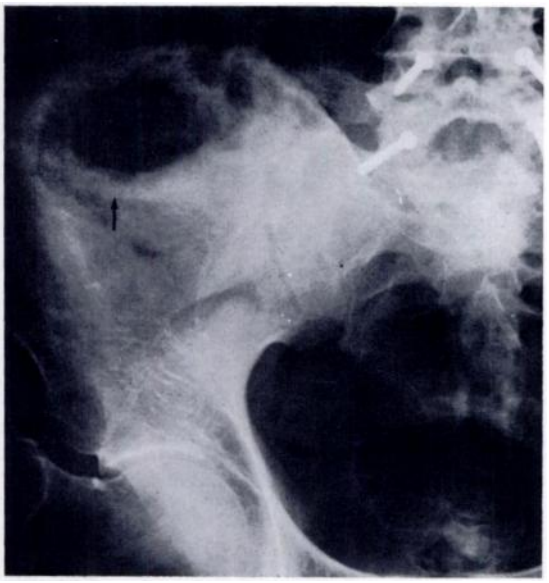

FIG. 1. Purely osteolytic lesion of the right ilium in a 33 year old male (M. K.) with Hodgkin's granuloma.

In our analysis we have considered all patients lost to follow-up, even though clinically free of disease at the last examination, as deceased. Table II shows the average survival by pathologic class, clinical stage, and with and without bone involvement.

The most important determinant of prognosis is the stage of the disease on presentation. Although Hodgkin's sarcoma has a notoriously poor prognosis, there was no difference in survival between patients with paragranuloma and granuloma. In Stage I disease, however, there was a 5.1 year average survival compared with 2.0 years for Stage II and 3.8 years for Stage III.

Those patients with bone involvement had an average survival after diagnosis of 4.5 years, and survival after development of the bone lesion(s) of 3.1 years. Over-all survival of all patients without bone involvement is 3.3 years. The difference in

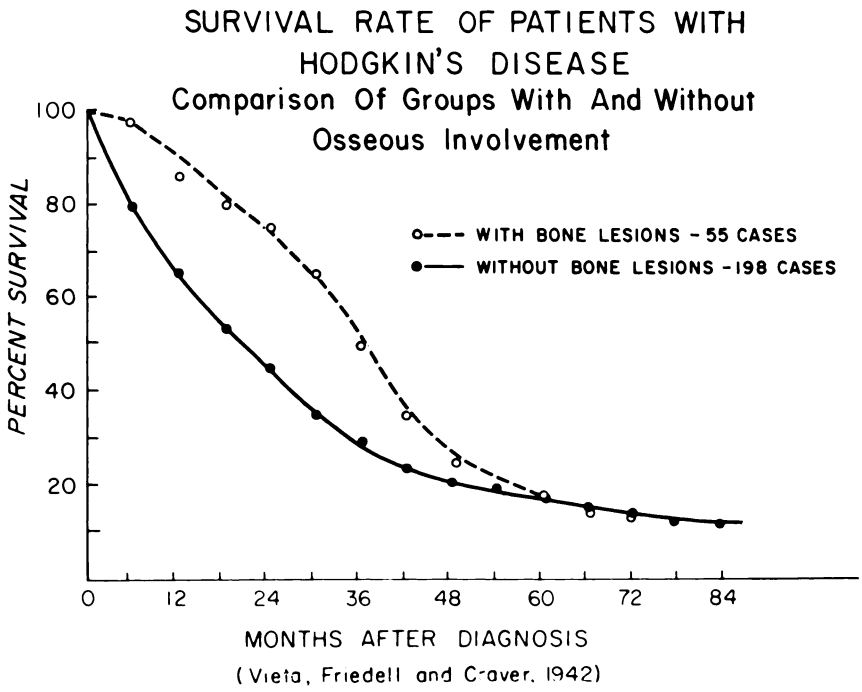

FIG. 3. Survival of patients with Hodgkin's disease. In a 5 year follow-up period, it is noted that survival is better in the group with bone involvement, but that the survival curves approximate each other at 5 years and beyond. (Reprinted through the courtesy of *Radiology*.[6])

survival is not satistically significant, but at least it shows that the survival rates are comparable. Figure 5 illustrates the survival curves for patients with and without bone involvement.

It may be thought that any patient with Hodgkin's disease, if he lives long enough, will develop bone involvement and, therefore, his average survival after diagnosis will appear to be longer. However, in our series, most of the patients (7/10) had the appearance of a bone lesion during the first half of the disease.

SUMMARY

Approximately 15 per cent of all patients with Hodgkin's disease will have roentgenographic evidence of cortical bone involvement. Our series shows a 20 per cent incidence, with no predilection regarding sex, age, or pathologic classification.

Representative roentgenograms are demonstrated. The most frequent areas involved are the spine and pelvis, and the lesions are usually mixed lytic and blastic. Lesions simulate metastatic malignancies of any kind.

Survival curves of 2 previous reports demonstrate an increased survival rate in patients with bone involvement. In our

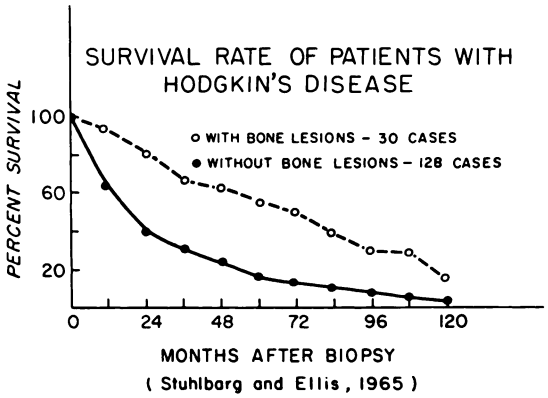

FIG. 4. Survival rates for patients with Hodgkin's disease.[5]

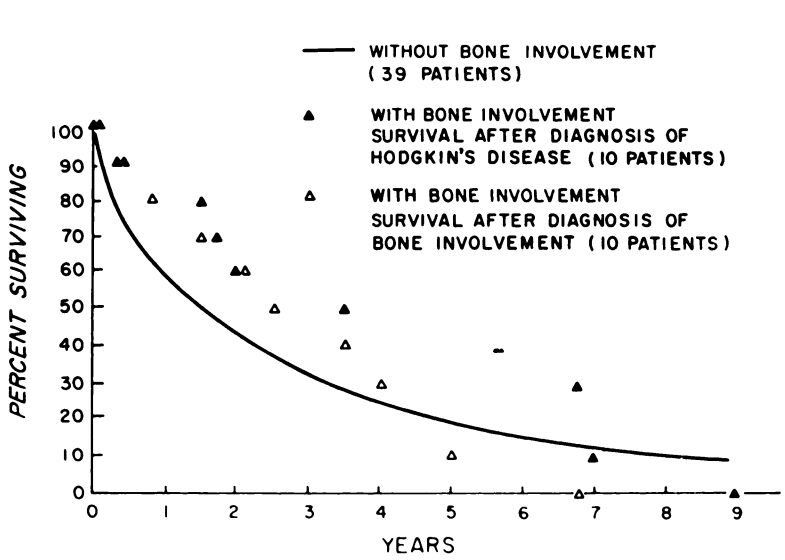

FIG. 5. Survival rates for 49 patients with and without bone involvement seen at the Tumor Board Registry of the Medical College of Virginia from 1949 to 1966.

series, the average survival after diagnosis of patients with bone involvement was 4.5 years, and 3.1 years after the onset of bone involvement. The average survival after diagnosis without bone involvement was 3.3 years. We cannot statistically prove with the number of cases in this study that survival is improved in patients with bone involvement, but we can show that at least there is no significant difference in the survival of the 2 groups.

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