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Full-lung Tomograms and Bone Scanning in the Initial Work-up of Patients with Osteogenic Sarcoma. A Review of 126 Cases*

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Abstract—*The value of full-lung tomograms and of bone scanning in the initial work-up of patients with osteogenic sarcoma is evaluated in* 126 *consecutive cases observed at the Bone Tumor Center of the Istituto Ortopedico Rizzoli from July* 1976 *to December* 1980. *Full-lung tomograms and bone scanning showed unsuspected metastases in* 3 *patients and* 2 *patients respectively. False abnormal results were observed in* 4 *cases by tomography and in* 3 *cases by bone scan. The authors conclude that in osteosarcoma, the yields of full-lung tomography and of bone scanning are small in detecting unsuspected lung and bone metastases at the time of presentation. It therefore appears improbable that the improvements recently observed in this tumor with adjuvant chemotherapy are the result of unintentional case selection bias due to these examinations not having been performed in the historical group.*

INTRODUCTION

SINCE 1970 considerable improvements have been observed in the mean disease-free interval after primary treatment and in the survival rates of patients with osteogenic sarcoma. These improvements have commonly been related to the use of adjuvant chemotherapy [1–4].

Unfortunately, the results of these researches have not emanated from randomized studies but from historic case series comparison.

Because almost all centers have improved their initial work-up in the last decade, with the use of full-lung tomography (F.L.T.), bone scan (B.S.) and more recently with computed tomography, the possibility exists that the reported improvements may not be the result of adjuvant chemotherapy but the consequence of unintentional case selection bias due to earlier detection of lung or bone metastases.

The value of these new techniques, in particular B.S. and F.L.T., in detecting unsuspected metastases at the time of diagnosis is controversial (Tables 1a and 1b).

Because of the rarity of osteosarcoma, reported data has been derived from a relatively modest number of patients. It is obvious that in considering a small number of cases, the major value of these techniques in comparison to traditional radiography may result in over or underestimation purely by statistical accident.

The present report is a retrospective analysis of the role of lung tomography and bone scan in discovering metastases not detectable clinically or with conventional radiology in 126 consecutive patients with 'classic' osteosarcoma of the extremities observed between July 1976 and December 1980 at the Bone Tumor Center of our institute.

MATERIALS AND METHODS

From July 1976 to December 1980, 161 histologically confirmed cases of osteosarcoma have been seen at our Bone Tumor Center (Table 2). In this study we consider only 126 cases with the typical features of central and high-grade osteosarcoma. This diagnosis was determined on the basis of specimens obtained

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Table 1a. Osteosarcoma. Metastases at the time of presentation detected only by lung tomography

Authors	Metastases detected	Percentage
Rosenberg *et al.* [5]	4/43	9.3
Frei *et al.* [6]	1/53	1.9
Muhm *et al.* [7]	5/121	4.1

Table 1b. Osteosarcoma. Metastases at the time of presentation detected only by bone scanning

McNeil *et al.* [8]	0/14	—
Goldman *et al.* [9]	1/13	7.7
Goldstein *et al.* [10]	1/46	2.2
McKillop *et al.* [11]	1/55	1.8

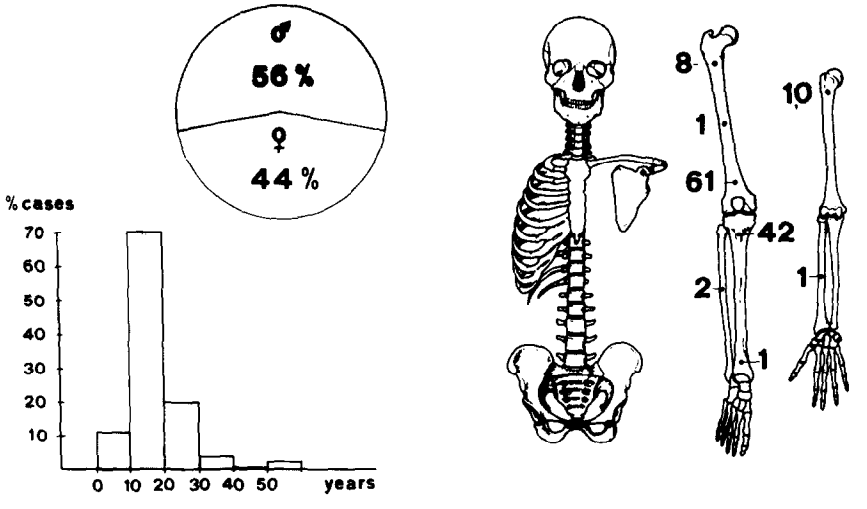

Fig. 1. Osteosarcoma (July 1976–December 1980), 126 cases.

from both open biopsy and/or large surgical samples obtained from amputation or resection. Primary tumor sites, and the age and sex of patients are listed in Fig. 1. The patients were treated by surgery plus adjuvant chemotherapy. This was conducted according to 3 different protocols undertaken successively as already reported [12]. In those cases with definite metastatic osteosarcoma surgery was not performed. These patients were moved to other institutions where the initial lesion was treated by radiotherapy associated with chemotherapy and, in some cases, with surgical resection of lung metastases.

In all cases, before the open biopsy (or frozen biopsy) there was performed: (a) standard postero-anterior and lateral projection chest radiograms; (b) a full-lung tomography in antero-posterior projection with films at 1 cm levels through the thorax. Usually 12–16 tomographic cuts were obtained for each patient; and (c) whole-body scan obtained 2–4 hr after injection of [^{99}Tc]-MDP (methylene 1-diphosphonate); bone scans were recorded using a wide-angle gamma camera or whole-body rectilinear scanner.

All chest radiograms, tomograms and scans were reviewed for each patient, together with the clinical charts. The presence of lung metastases was considered to be confirmed by histological examination (biopsy or resection) or by historical evolution (progressive roentgenographic enlargement of lesions and appearance of new lesions within three months).

Table 2. Patients with osteosarcoma observed at the Istituto Ortopedico Rizzoli from July 1976 to December 1980

Total cases = 161	
Cases included = 126	Cases excluded = 35
Non-metastatic 108	Osteosarcoma's varieties 30*
Metastatic 18	Inoperable osteosarcoma 5

*Parosteal OS, periosteal OS, low-grade OS, telangiectatic OS, OS in Paget's disease, radiation-induced OS, OS in jaws.

False abnormal results were considered to be the initial interpretation of pulmonary metastases, with the lesions subsequently shown to be benign by biopsy specimen or by lack of radiological progression during successive follow-up. The presence of bony metastases was considered to be confirmed by biopsy, by the simultaneous combination of scintigraphic findings with radiological findings or by the historical evolution of the lesion. Scintigraphic abnormalities suggestive of metastatic disease which were never associated with radiologic evidence of bone metastases and which remained stable or regressed on scintigraphic examination during a 1 yr period were considered as 'false positive', even though the patients were receiving chemotherapy.

RESULTS

Lung tomography

At diagnosis 16 patients showed pulmonary metastases (Table 3). Thirteen of these were detected by conventional chest roentgenograms (6 single, 5 multiple monolateral and 2 bilateral) and 3 by lung tomograms. In these 3 cases 2 patients showed single pulmonary metastases and 1 patient had multiple monolateral nodes. Of the 6 patients with solitary metastasis on chest roentgenogram 2 had multiple metastases on tomography.

Erroneous interpretations of chest tomograms, the so called 'false-abnormal', occurred in 4 patients. The initial interpretation of metastasis was notified because the lesions were subsequently revealed to be benign by biopsy specimen (1 case), or because they regressed (1 case) or remained stable (2 cases) on successive tomograms. All of the 4 patients were treated by surgery (delayed in 2 cases) plus adjuvant chemotherapy.

The yield of pulmonary metastases identification in the initial osteosarcoma work-up increased therefore from 10.3% (13/126) by chest roentgenography to 12.7% (16/126) by tomography.

Bone scan

Of the 126 patients scanned at the time of presentation 5 showed distant bone metastases. Three of these patients presented a clinical history (bone pain) suggestive of metastasis. In these 3 cases the bone metastases, localized in the spine (2 cases) and in the skull (1 case), were always associated with pulmonary metastases. In these same 3 patients bone metastases were clearly demonstrated by radiography. Bone scan showed unsuspected distant bone metastases in 2 asymptomatic patients. Both of these metastases were localized in the spine (5L, 7D). In 1 patient radiographic examination of the diseased area confirmed the lesion. In the other patient bone scanning demonstrated abnormalities in bone 3 months before these would have been evident by means of conventional radiography. In both cases metastatic lesion was confirmed by histological examination performed on the surgical specimen obtained intra-operatively to relieve the symptoms related to spinal cord compression (decompressive laminectomy). Three other patients had bone scan evidence strongly suggestive of bone metastases (sternum, ileus and femur) which were not confirmed by radiography. In none of these patients was the lesion

Table 3. Usefulness of lung tomography and bone scan in detecting unsuspected metastases

	Total metastases detected	Unsuspected metastases detected	'False abnormal' results
Lung tomography	16 (12.7%)	3 (2.4%)	4 (3.2%)
Bone scan	5 (4.0%)	2 (1.6%)	3 (2.4%)
Total	21*(16.7%)	5 (4.0%)	7 (5.6%)

Results obtained in 126 cases of osteosarcoma observed at the Istituto Ortopedico Rizzoli from July 1976 to December 1980.
*Three patients presented both pulmonary and bone metastases.

biopsied, but the successive evolution led us to consider these findings as false positives. In fact, 2 patients have remained clinically and radiologically disease-free for 24 and 36 months after surgery. The last patient died from pulmonary metastases 18 months after amputation. At that time there was no clinical or radiological evidence of disease in the suspected area. The cause of these false positive bone scans is not known.

Therefore bone scan showed 1.6% (2/126) metastases that were not detected by clinical or conventional examinations.

There was fundamental agreement between the scan and radiographic finding as to the extent of the primary lesion. In 2 cases pathological findings showed 'skip metastases', both not detected by radiography and bone scan. One of these was, however, evident with computed tomography.

DISCUSSION

Several reports in recent literature suggest that adjuvant chemotherapy improves both the disease-free interval and the survival for patients with osteogenic sarcoma [1–4, 12]. These reports compare disease-free intervals in recently treated patients (approx. 1972–1978) with control historical series (approx. 1950–1970). Certain authors [5, 13, 14], however, suggest that improved radiological techniques have led to early detection of lung and bone metastases that would have been undetectable by conventional roentgenographic techniques, and therefore to the exclusion of cases which would have been previously included. Because of this type of favorable case selection comparison with historical controls would no longer be a valid basis for evaluating the efficacy of new treatment regimens; randomized prospective studies using concomitant controls are essential [5, 13]. Our study, which has examined the value of lung tomography and of bone scanning at presentation in patients with osteogenic sarcoma destined to be treated by surgery plus adjuvant chemotherapy, indicates that in only a very small number of cases can these examinations show unsuspected metastases. Improvement in the results achieved by us [12] and other authors [1–4] with adjuvant chemotherapy can be only marginally attributed to lung tomography and bone scanning. The absence of these two examinations in the historical group would have caused patients to be incorrectly classified as non-metastatic osteosarcoma is less than 5% of the cases. On the other hand, improvements cited in adjuvant chemotherapy studies are of the order of 30%. It is possible that computed tomography of the lungs, recently adopted as part of the initial work-up of osteosarcoma, could modify that trend [7]. This examination, however, was not employed in any of the adjuvant chemotherapeutic series mentioned above. Despite the rare capacity of F.L.T. and B.S. for detecting unsuspected metastases, these procedures, that are non-invasive, of minimal radiation exposure risk and relatively inexpensive, should be part of the routine initial evaluation in patients with osteogenic sarcoma. In fact, the presence of metastases at the time of presentation may considerably alter the management of the patient, as in the cases observed in our institute. Due to the illustrated possibility of false positives, it remains essential to confirm bone and lung metastases detected by F.L.T. and B.S. with other methods of investigation, including biopsy and careful control of patients.

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