Radiographic and Scintigraphic Skeletal Imaging in Patients with Neuroblastoma: Concise Communication

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Bone scans, bone-marrow scans, and radiographic skeletal surveys have been reviewed in 40 children with neuroblastoma. Bone scans are the most sensitive method for detecting metastases and should be used first. The additional yield from a skeletal survey is very small, so it should be done only if the bone scan is negative and major therapeutic decisions are to be made. Bone-marrow scans provide a sensitive method of identifying metastases, and may help in staging a patient as stage IV when the bone scan is negative.

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Accurate identification of bone and marrow metastases from a neuroblastoma is very important, since therapy and prognosis relate directly to their presence. The main objective of radiographic and nuclear medicine evaluation is to obtain the required information for the lowest cost with minimal radiation dose. The results obtained from bone-marrow scans, bone scans, and bone radiographs (skeletal surveys) in 40 patients are analyzed and appropriate recommendations made for the utilization of these imaging modalities.

MATERIALS AND METHODS

Forty patients with pathologically proven neuroblastoma were seen between 1975 and 1980 at our hospital. The case records and radiographic and nuclear medicine studies done on these patients were reviewed. Skeletal surveys included radiographs of all extremities, pelvis, lateral spine, chest, and lateral skull. On radiographs a diagnosis of metastasis was made by observing the well-recognized patchy destructive lesions, with or without areas of sclerosis or periosteal new-bone formation.

Tc-99m-labeled diphosphonate compounds were used for the bone scans. Multiple spot views of the skeleton were obtained on x-ray film using a stationary gamma camera (27 photomultiplier tubes) and low-energy all-purpose collimator. Metastases usually appeared as areas of increased uptake, but very destructive lesions were decreased. Special attention was paid to the metaphyseal region (*1*). The bone-marrow scans were performed with i.v. Tc-99m sulfur colloid. Spot gamma images of the upper and lower extremities and thoracic and lumbar spine were obtained. Metastases were seen as areas of decreased uptake.

If bone scans and skeletal surveys were performed within 14 days of each other, they were included in the study to compare the accuracy of these two modalities for identifying metastases.

Bone scans and skeletal surveys were compared to see which was the more sensitive for diagnosing metastases. Each study was read as either positive or negative for metastatic disease; the actual number of metastases present at any particular time was not counted. In the clinical situation the first metastasis is by far the most important. For this reason the results were analyzed in three groups. The skeletal survey and bone scintigrams were compared, first for their ability to diagnose metastases at the time of initial presentation; secondly for their ability at follow-up to diagnose new metastases in a child with no previous metastasis or previously healed metastases; and finally for their ability to visualize me-

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TABLE 1. COMPARISON OF RESULTS OF BONE SCINTIGRAM AND SKELETAL SURVEY FOR THE DETECTION OF BONE METASTASES IN 40 CHILDREN WITH NEUROBLASTOMA

	Both studies abnormal	Skeletal survey abnormal bone scintigram normal	Skeletal survey normal bone scintigram abnormal	Total
Metastases present on initial presentation	7 (64%)	1 (10%)	3 (26%)	11
New or recurrent metastases seen during followup (previous studies normal)	6 (35%)	1 (6%)	10 (59%)	17
Persistent or increase of known metastases	13 (76%)	0 (0%)	4 (24%)	17
Total	26	2	17	45

tastases in follow-up of a child with previously diagnosed metastases.

Results of the bone-marrow and bone scans were also compared.

RESULTS

Of the 40 patients studied, 19 were male and 21 female. The age at the time of initial presentation was less than 1 yr in 13 cases, 1 yr in nine, 2 yr in ten, and more than 2 yr in eight cases. Four of the 40 patients were stage I, seven stage II, six stage III, 21 stage IV, and two were stage IV S.

In the 40 patients a total of 189 bone scans, 86 marrow scans and 203 skeletal surveys were performed.

A total of 124 skeletal surveys and bone scans were performed within 14 days of each other. On 79 occasions both studies were normal. The 45 occasions on which one or both studies were abnormal are analyzed in Table 1.

Marrow scans and bone scans were performed within 14 days of each other on 69 occasions. The results comparing these two modalities are summarized in Table 2.

DISCUSSION

Bone metastases in neuroblastoma are common (*2*). It is important to identify these metastases reliably as they may be the only site of metastasis in the stage IV disease. Accurate identification of bone metastases in the initial evaluation of a new patient is particularly important since it may contraindicate laparotomy in those cases with a positive node or marrow biopsy.

Most prior series report bone scanning to be more sensitive than radiography (*1–4*). In one series, however, the bone scans missed metastases identified by radiographs in 12 patients (*5*). Our study was done because of this discrepancy, because several of the series were small (<14 patients), and because none of the previous series evaluated marrow scanning.

In our 40 patients, bone scans proved far more sensitive than skeletal survey for the diagnosis of metastasis from neuroblastoma. On only two occasions did the bone scan miss metastases—these were focal destructive lesions. It is not clear why Kaufman et al. (*5*) had substantially more false-negative scans, especially since their imaging technique was very similar to ours in most instances. In some cases they seemed to have relied on whole-body images, which certainly have poorer resolution than multiple spot views. As stated earlier, we paid particular attention to the ends of the long bones, including the shapes of the epiphyses. We have also noted that the metastases can be symmetrical and may have uptake only slightly more than the normal bone.

Because of cost (a total of $73,000 was spent on

TABLE 2. COMPARISON OF RESULTS OF BONE SCAN AND MARROW SCAN IN SEARCH FOR METASTASIS FROM NEUROBLASTOMA*

Both normal	Both abnormal	Bone normal, marrow abnormal	Bone abnormal, marrow normal	Total
42	17	7	3	69

* In each patient both studies were performed within 14 days of each other.

skeletal surveys and bone and marrow scans in our 40 patients) and radiation dose, both scans and skeletal surveys should not be done on all occasions. Although skeletal survey has been recommended as the test to look for bone metastases in the initial evaluation of neuroblastoma (*6*), bone scan, as it is far more sensitive (*1*,*2*,*7*), should always be the first test done. Abnormal areas seen on the scan may be radiographed to exclude nonmetastatic causes for positive scans, if clinically indicated. If the diagnosis of metastasis is confirmed, radiographs of the rest of the skeleton are usually not required in most cases. Demonstration of additional metastases would not alter patient management.

If the bone scan is negative, the skeletal survey is not routinely justified, because of the very low incidence of false-negative scans. In selected situations where major management decisions are to be made, we recommend a skeletal survey following a negative bone scan. The situations would be in patients not already known to be stage IV (e.g., by evidence of node or marrow metastasis), in whom initial or second-look surgery is being contemplated (i.e., a major management decision dependent on the results of the investigation). We do not agree with the use of routine skeletal surveys (*2*,*5*,*8*).

Bone-marrow scan may be very helpful. It is not recommended as the initial study because it may miss metastases. Marrow scans were normal in three patients with bone metastases. They were positive, however, on seven occasions in five patients in whom the bone scans and skeletal surveys were normal. Three of the patients had confirmatory marrow biopsies.

Marrow metastases do not occur at the same sites or at the same time as bone metastases. If other metastases have already been located, then marrow scans are not recommended as routine. If no bone metastases are found on the bone scan or skeletal survey, then the marrow scan is valuable, as it may be positive even when these other studies are negative. It may also be useful to identify a favorable site for marrow biopsy when this procedure is being contemplated.

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