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Bone marrow metastasis of solid tumors: Clinicopathological evaluation of 73 cases

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ABSTRACT

The aim of this study was to investigate the clinical characteristics of adult patients with BM metastases of solid tumors diagnosed by bone marrow (BM) aspiration. In this retrospective study, we reviewed the results of 3842 BM aspirations carried out in the Medical Oncology Unit in Hacettepe University between January 1993 and December 2004. Basic clinical characteristics of patients as well as sites of metastases and complete blood counts were obtained from the hospital records. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows version 10.0. Seventy-three patients (1.9%) had evidence of involvement of the BM by a solid tumor. Thirty-six patients were male (49.3%) and 37 were female (50.7%). Mean age was 49±13 (min: 17, max: 77). Breast cancer (28.8%) and lung cancer (23.3%) were the most common cancers associated with a BM metastasis. At the time of diagnosis, 68.5% of patients were found to have anemia, 58.9% thrombocytopenia, and 23.3% neutropenia. The most common site of metastasis associated with BM involvement was bone (n=51, 70.8%). Median survival after the diagnosis of BM metastasis was found to be 5 months and one-year survival was 28%. Patients with thrombocytopenia had significantly shorter median survival than patients with normal thrombocyte counts (1 month vs. 13 months, respectively; p <0.0001). BM involvement by solid tumors carries a poor prognosis, especially when thrombocytopenia is present. [Turk J Cancer 2007;37(3):85-88]

KEY WORDS:

Solid tumor, metastasis, bone marrow, aspiration

INTRODUCTION

Though bone marrow (BM) involvement is most commonly seen with myeloid or lymphoid hematological malignancies, solid tumors may also spread to the BM via the hematogenous route. Presenting signs and symptoms are usually related to cytopenias and include fatigue, dizziness, orthostatic hypotension, bleeding and infections. The latter two are known to result in substantial morbidity and even mortality in this group of patients. Therefore, BM metastasis is almost universally a poor prognostic factor (1). Imaging techniques like radionuclide bone scan, magnetic resonance and computed tomography are usually ineffective and BM aspiration and biopsy remain the procedures of choice to document BM involvement (2,3). BM aspiration can be carried out in a matter of minutes, and histomorphological examination by Wright or Giemsa stain can be completed in an additional hour. It therefore is the fastest, easiest and cheapest method to search for metastatic foci in the BM. In this report, we have investigated the clinical characteristics of seventy-three adult patients with BM metastases of solid tumors diagnosed by BM aspiration.

PATIENTS AND METHODS

We reviewed the results of BM aspirations carried out in the Medical Oncology Unit in Hacettepe University between January 1993 and December 2004. This unit is one of the largest medical oncology centers in Turkey, and all kinds of solid tumors as well as hematological malignancies are diagnosed and treated. In the daily practice, BM aspirations are performed from the posterior iliac crests and are accompanied by trephine biopsies, unless deemed clearly unnecessary. Aspiration specimens are stained with Wright stain and at least 3 smears are examined by experienced hematooncologists.

In this retrospective study, the results of 3842 BM aspirations were examined. Those with involvement of hematological malignancies were excluded and those with metastases of solid tumors were recorded. Confirmation by histopathological examination of trephine biopsies was also required. Basic clinical characteristics of patients as well as sites of metastases and complete blood counts were obtained from the hospital records. Anemia was defined as Hb value ≤12 gr/dL thrombocytopenia as platelet count below 150,000/mm^3 and neutropenia as white blood cell count (WBC) lower than 3500/mm^3. The central tendency of numerical variables like age, hemoglobin, thrombocyte and WBC counts are given as mean±standard deviation (SD). Overall survival following the diagnosis of BM metastasis was calculated using the Kaplan-Meier method. The comparison of the survival of subgroups was carried out by the log-rank test. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows version 10.0.

RESULTS

We reviewed the results of 3842 BM aspirates carried out in our institute from January 1993 to December 2004. Seventy-three patients (1.9%) had evidence of involvement of the BM by a solid tumor. Thirty-six patients were male (49.3%) and 37 were female (50.7%). Mean age was 49±13 (min: 17, max: 77). Clinical characteristics of the patients are summarized in table 1.

Breast cancer (28.8%) and lung cancer (23.3%) were the most common cancers associated with a BM metastasis, followed by gastric cancer (9.7%), prostate cancer (6.8%), and Ewing sarcoma (6.8%). No primary tumor site could be detected in 7 patients (8.2%) with BM metastasis. Less frequent sites included soft tissue sarcoma (2.7%), nasopharyngeal carcinoma (2.7%), malignant melanoma (2.7%), medulloblastoma (1.4%), and cancers of the larynx (1.4%), bladder (1.4%), rectum (1.4%), endometrium (1.4%), and testis (1.4%). The diagnosis of BM metastasis coincided with the diagnosis of the primary tumor in 35 patients (47.9%). Histopathological diagnoses of the patients are given in table 2.

Table 1
Clinical characteristics of the patients

Age (Mean±SD)	49.4±12.9	
	n	**%**
Sex		
Male	36	49.3
Female	37	50.7
Other sites of metastasis		
Bone	55	75.3
Liver	10	13.7
Brain	7	9.7
Lung	7	9.7
Adrenal glands	5	6.8
Other	5	6.8

Table 2
Primary diagnoses of the patients

Diagnoses	**n**	**%**
Breast cancer	21	28.8
Lung cancer	17	23.3
Gastric cancer	7	9.6
Unknown primary tumor	6	8.2
Prostate cancer	5	6.8
Ewing sarcoma	5	6.8
Soft tissue sarcoma	2	2.7
Nasopharyngeal carcinoma	2	2.7
Malignant melanoma	2	2.7
Laryngeal carcinoma	1	1.4
Bladder cancer	1	1.4
Rectum cancer	1	1.4
Endometrial cancer	1	1.4
Testicular cancer	1	1.4
Medulloblastoma	1	1.4
Total	**73**	**100.0**

Table 3
Hematological parameters of the patients at the time of diagnosis

Blood count findings	n	%
Normal	10	13.9
Anemia	50	68.5
Neutropenia	17	23.3
Thrombocytopenia	43	58.9
Bicytopenia		
Anemia + neutropenia	20	27.4
Anemia + thrombocytopenia	2	2.7
Neutropenia + thrombocytopenia	1	1.4
Pancytopenia	13	17.8

At the time of diagnosis, 68.5% of patients were found to have anemia, 58.9% thrombocytopenia, and 23.3% neutropenia. Blood counts were normal in 13.7% of patients, while 17.8% had pancytopenia. Anemia and thrombocytopenia were present in 23.3% of patients, while only 2.7% had anemia and leukopenia and 1.4% had leukopenia and thrombocytopenia. Mean hemoglobin level was 10.5±2.5 g/dl (min: 5.8, max: 16.5), WBC 7,900±6,600/mm³ (min: 2,200, max: 44,800), and platelet 180,000±163,000/mm³ (min: 9,000, max: 837,000). The hematological parameters of the patients at the time of diagnosis are summarized in table 3.

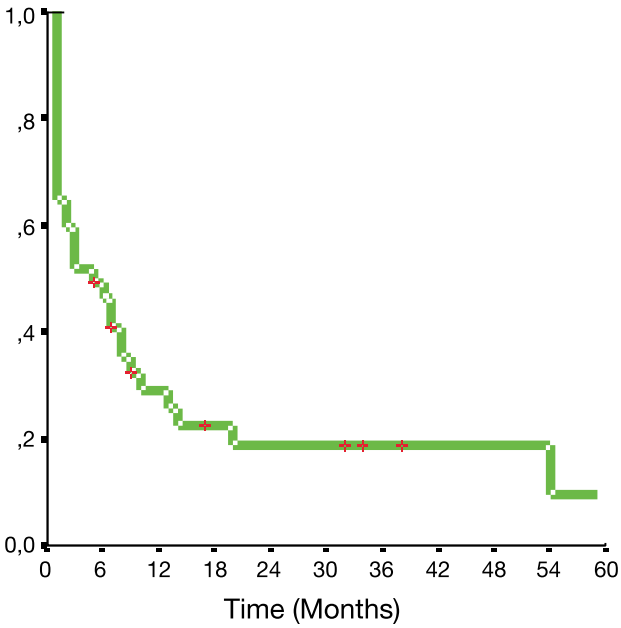

Fig 1. Overall survival in patients with bone marrow metastasis

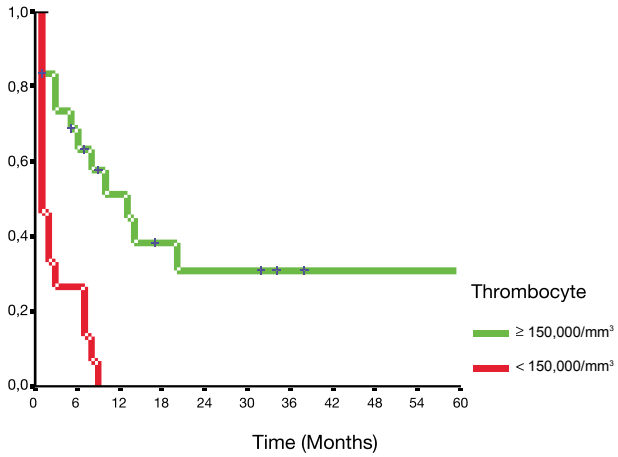

Fig 2. Overall survival of patients with thrombocytopenia

The most common site of metastasis associated with BM involvement was bone (n=51, 70.8%). Other sites included liver (16.7%), brain (9.5%), lungs (9.5%), adrenal glands (5.5%), soft tissues (2.7%), orbita (1.4%), kidney (1.4%) and breast (1.4%). Other sites of metastasis associated with BM involvement are summarized in table 1. Median survival after the diagnosis of BM metastasis was found to be 5 months (95% CI: 1.0-9.0) and one-year survival was 28% (Figure 1). Patients with thrombocytopenia had significantly shorter median survival than patients with normal thrombocyte counts (1 month vs. 13 months, respectively; $p<0.0001$) (Figure 2).

DISCUSSION

Though not very frequent, BM is one of the important sites of metastasis of solid tumors. The involvement of the BM is not only a sign of diffuse hematogenous spread of the tumor; it also results in cytopenias that increase the risk of bleeding and infection. Cytopenias also hinder the delivery of effective anti-neoplastic treatment, as almost all chemotherapeutics have at least some degree of hematotoxicity. All these factors add up to yield a worse prognosis for the patient who has BM metastasis.

Magnetic resonance imaging can give some clues on the involvement of BM and the definitive diagnosis depends on histopathological examination of BM biopsies. Immunohistochemical studies as well as molecular techniques like polymerase chain reaction have enabled us to detect metastatic cells in the BM, even if they are in minute quantities (4). Though these methods are gaining popularity, they require much more effort, time and money than the conventional techniques. The clinical significance of microscopical involvement of the BM also remains to be established.

Morphological examination of the BM aspiration is much less sensitive than the latter methods, yet it remains the easiest, cheapest and least time consuming procedure for the diagnosis of clinically suspected BM involvement.

Theoretically, all tumors can metastasize to the BM, however, cancers of the breast, prostate and lung are the most frequently encountered ones in adults (5-7). In pediatric cases, neuroblastoma is responsible for the majority of cases. In a retrospective study, Mohanty et al. (6) showed that prostate cancer (47.8%) was the most common tumor among adults, followed by breast cancer (28.2%). In this series, all pediatric cases had neuroblastoma. In another study, these findings were confirmed: Neuroblastoma was the most common primary tumor in children, followed by breast and prostate cancers in adults (8).

In our study, we reviewed the results of 3842 patients who had a BM aspiration. We found 73 cases with BM metastasis of solid tumors. Breast and lung cancers were the most commonly encountered tumors. In contrast to the literature, we had only 5 cases of prostate cancer (6.8%). Though this may at least in part be due to a lower incidence of prostate cancer in our country than in more developed countries, it probably results from the small number of patients followed in our clinic, as most prostate cancer patients are treated by urologists in our country.

Patients with BM involvement could have normal blood counts, some disturbances in one or more series or they could be pancytopenic. Though severe anemia can be life-threatening, the complications of neutropenia and thrombocytopenia result in more morbidity and mortality. Pancytopenic patients are known to have a higher complication risk than the others. In a study, the authors have reported six cases with tumors metastatic to the BM (8). Of these, 4 patients (67%) had anemia, 5 (83%) had thrombocytopenia and 3 (50%) had leucopenia. In our study, the figures that we have observed are somewhat smaller: Anemia was observed in 68.5%, leukopenia in 23.3% and thrombocytopenia in 58.9% of the patients, while 17.8% of patients had pancytopenia, 37.4% bicytopenia, and %13.9 had normal counts. These findings suggest that in our institution, bone marrow aspiration is done in patients with less profound hematological disturbances.

Median survival of the patients with thrombocytopenia was significantly shorter than those without thrombocytopenia. This finding may be related to amount of bone marrow involvement, long lasting recovery of thrombocytopenia that leads to hemorrhagic complications and death.

The four parameters, which are strongly correlated with marrow involvement, were the leukoerythroblastic blood pattern, a serum lactic dehydrogenase over 500 IU/liter, a platelet count under 100,000/microliter, and bone pain (9).

BM involvement by solid tumors carries a poor prognosis, especially when thrombocytopenia is present. Aspiration of the BM provides an easy and quick way of detecting involvement, however, biopsy with immunohistochemical and/or molecular techniques may be needed in case of microscopical tumor burden.

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