

Pattern of Bone Marrow Involvement by Solid Tumors: Experience from a Tertiary Care Center from South India

Abstract

Background: Bone marrow involvement by solid tumor implicates advanced disease and dismal prognosis. Bone marrow aspiration and biopsy are routinely performed as staging workup for certain small round cell tumors and also for unexplained cytopenia in other solid tumors. It is important to rule out bone marrow involvement before planning for curative treatment. **Materials and Methods:** This was a retrospective observational study. The aim of our study was to evaluate the pattern of bone marrow involvement by different solid tumors and their correlation with the hematological abnormalities. We retrospectively evaluated bone marrow aspirations and biopsy performed in past 3 years. **Results:** At our institution, bone marrow examinations were performed in 440 patients during past 3 years for solid malignancies. Out of 440, 206 were pediatric cases and 234 were adult cases. Bone marrow was involved in 56 (12.7%) patients. Among the pediatric cases, bone marrow involvement was present in 30 (12.8%) cases, and in adult cases, bone marrow was involved in 26 (11.1%) cases. Neuroblastoma (40%) was the most common malignancy, which involved the bone marrow among pediatric cases, followed by retinoblastoma (26.6%) and Ewing's sarcoma (20%). Among adult patients, neuroendocrine carcinoma (23%) was at the top of the list of tumors involving bone marrow, which is followed by Ewing's sarcoma (19.2%) and nasopharyngeal carcinoma (11.5%). **Conclusion:** Neuroblastoma and neuroendocrine carcinoma are the major cause of bone marrow involvement among the solid malignancies in pediatric and adult population, respectively. Use of immunohistochemistry markers on bone marrow biopsies may result in higher detection rate.

Keywords: Bone marrow and solid tumor; metastasis to bone marrow; pattern of bone marrow involvement

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Introduction

Bone marrow involvement is commonly seen in hematopoietic disorders, but solid tumors too rarely involve bone marrow through hematogenous spread. Detection of bone marrow involvement by solid tumor is important for accurate staging, for prognostication and treatment.^[1] Sometimes, bone marrow involvement may be the first evidence of disease manifestation. Rohr and Heggin studied sternal aspirates of 75 patients with cancer and found marrow involvement in 11 of 13 patients with bone marrow metastases.^[2] The metastasis can be reported by the examination of bone marrow aspiration only, but the bone marrow biopsy may be the more accurate procedure for detecting metastasis by solid tumors.^[3] The purpose of bone marrow assessment in the solid tumor is either for

staging purpose or as a reflex procedure on suspicion of marrow involvement, such as anemia, leukocytopenia, and/or thrombocytopenia.^[4]

This study was undertaken to comprehensively analyze bone marrow metastasis in nonhematological malignancies diagnosed at a single tertiary care center in South India over the period of 3 years (2014–2016).

Materials and Methods

In this retrospective observational study, we reviewed the results of bone marrow aspiration and biopsy carried out for solid tumor at Kidwai Cancer Hospital, Bengaluru, India, between January 2014 and December 2016. Diagnosed cases of lymphoma were not included in this study.

For all patients, bone marrow aspiration and biopsy were performed from the

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posterior iliac crest using Jamshidi needle. Slides were prepared from bone marrow aspiration, imprint smears, and peripheral smears and stained by Romanowsky stains, either by Giemsa or Leishman. Bone marrow biopsies after standard processing were stained with hematoxylin and eosin and reviewed by hematopathologist. Patient's name, age, sex, diagnosis, and purpose for performing the bone marrow assessment were recorded. Pediatric age was defined as a patient with age <14 years. The bone marrow was considered to be "involved by the tumor" if tumor cells were detected in bone marrow aspirate, biopsy, or both.

Results

A total of 440 cases of solid tumors were evaluated for bone marrow assessment either for staging workup or on suspicion of bone marrow involvement. Bone marrow was involved in 56 patients (12.7%). Out of 440, 206 were pediatric cases and 234 were adult cases. In pediatric cases, bone marrow involvement was present in 30 (12.8%) cases, and in adult cases, bone marrow was involved in 26 (11.1%) cases [Table 1].

Pediatric cases

Male-to-female ratio was 1.2:1. Neuroblastoma (40%) was the most common malignancy, which involved the bone marrow, followed by retinoblastoma (26.6%), Ewing's sarcoma (20%), rhabdomyosarcoma (6%), and Wilms tumor (6%) [Table 2].

Adult cases

Male-to-female ratio was 1.5:1. Neuroendocrine carcinoma (23%) was at the top of the list of tumors involving bone marrow, which is followed by Ewing's sarcoma (19.2%), nasopharyngeal carcinoma (11.5%), medulloblastoma (7.6%), rhabdomyosarcoma (7.6%), breast carcinoma (7.6%), prostate cancer (7.6%), colon cancer (7.6%), stomach cancer (3%), and urinary bladder cancer (3%) [Table 3].

Peripheral blood examination

Hematological abnormalities as a result of bone marrow involvement lead to anemia in 38 (67.85%) patients, while the neutropenia and thrombocytopenia were detected in 13 (23.2%) patients and 33 (58.9%) patients, respectively. Pancytopenia was found in 10 (17.8%) patients. Around one-fifth of the patients had normal blood picture, indicating hematological abnormality may not be present when bone marrow is involved.

Discussion

Bone marrow involvement in nonhematological solid tumors is a rare phenomenon and almost reported with all solid malignancies with variable frequency. Cells, which are disseminated from the primary solid tumor, are considered to be the cause of metastases to bone marrow.

Table 1: Distribution of bone marrow involvement among all patients

Subgroup	Total number of cases assessed	Number of positive cases (%)
Pediatric cases	206	30 (12.8)
Adult cases	234	26 (11.1)
Total	440	56 (12.7)

Table 2: Distribution of bone marrow involvement among pediatric patients

Primary tumor histology	Number of cases (%)
Neuroblastoma	12 (40)
Retinoblastoma	8 (26.6)
Ewing's sarcoma	6 (20)
Rhabdomyosarcoma	2 (6.7)
Wilms tumor	2 (6.7)
Total	30 (100)

Table 3: Distribution of bone marrow involvement among adult patients

Primary tumor histology	Number of cases (%)
Neuroendocrine carcinoma	6 (23)
Ewing's sarcoma	5 (19.2)
Breast cancer	3 (11.5)
Prostate cancer	2 (7.6)
Rhabdomyosarcoma	2 (7.6)
Nasopharyngeal carcinoma	2 (7.6)
Medulloblastoma	2 (7.6)
Colon cancer	2 (7.6)
Cancer urinary bladder	1 (3)
Gastric carcinoma	1 (3)

Detection of metastatic tumor in the bone marrow is of great importance. It is used not only for staging purpose in certain tumor but also it has prognostic value. The survival of patients with bone marrow involvement is poor.^[5]

Morphological examination of the bone marrow aspiration is much less sensitive than the other methods such as immunohistochemistry, flow cytometry, and PCR techniques, but still, it remains the easiest, cheapest, and least time-consuming procedure for the diagnosis of clinically suspected bone marrow involvement.^[6]

Many studies have shown that bone marrow involvement is more common in small round cell tumor, breast, prostate, and lung.^[7,8] In pediatric cases, neuroblastoma is responsible for the majority of cases. In a retrospective study, Mohanty and Dash reported that, in children, neuroblastoma was the most common primary tumor involving bone marrow, while in adult patients, breast and prostate cancers are common histologies.^[8]

In this study, we also found the neuroblastoma as the most common malignancy metastasizing to bone marrow among

pediatric cases, comprising around 40% of all patients. Neuroblastoma was followed by retinoblastoma (26.6%), Ewing's sarcoma (20%), rhabdomyosarcoma (6%), and Wilms tumor (6%).

Among adult patients, neuroendocrine carcinoma is the main histology with a propensity to affect bone marrow, followed by Ewing's sarcoma (19.2%) and nasopharyngeal carcinoma (11.5%). The possible reason for this discrepancy from other studies^[7,8] may increase the utilization of immunohistochemistry markers for diagnosis of primary histology. Earlier the neuroendocrine carcinoma was diagnosed as poorly differentiated carcinoma and treated as metastasis from an unknown primary. However, after the availability of immunohistochemistry markers, these tumors are increasingly diagnosed. Our institute is a referral tertiary care center; the immunohistochemistry markers are used more often. When bone marrow was done for abnormal blood pictures, the anemia was the most common manifestation.

The major drawback of this study was that the bone marrow involvement was based only on morphology. We know that immunohistochemistry markers increase the detection rate if performed on bone marrow biopsy specimen like in lymphoma. Hence, the use immunohistochemistry markers will definitely increase the detection rate and will have great therapeutic implication in the management.

Conclusion

Neuroblastoma and neuroendocrine carcinoma are the major causes of bone marrow involvement among the solid

malignancies in pediatric and adult population, respectively. Use of immunohistochemistry markers on bone marrow biopsies may result in higher detection rate.

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Conflicts of interest

There are no conflicts of interest.

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