Original Article

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Clinicopathological Evaluation of Metastatic Carcinomas of Bone Marrow Presenting as Cytopenia

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ABSTRACT

Background: Metastatic carcinomas can involve bone marrow and may lead to subsequent marrow fibrosis and failure. The Bone marrow examination is important in patients diagnosed or patients on chemotherapy for cancer, who presented with peripheral cytopenia. The metastasis of bone marrow by these tumors is a sign of advanced stage of disease with poor prognosis.

Methods: Our study is a retrospective study, in which we reviewed a total of 702 bone marrow procedures, out of which 118 bone marrow procedures done in patients with a diagnosis of cancer or patients on chemotherapy presented as cytopenia in Great Eastern Medical College and Hospital during a period of 10 years.

Result: During this study period, among 118 malignancies reported in histopathology, 32 cases show bone marrow metastasis. Out of 118 patients 74 males and 44 females. Peripheral smear examination of these cases show anaemia in 24 cases (75%), which was the commonest presentation, thrombocytopenia in 18cases (50%), bleeding manifestations in 10 cases(31.2%), Pancytopenia in 9 cases (28.1%), bi-cytopenia in 4cases (12.5%).Out of these 32 cases of bone marrow metastasis 17.1% were carcinoma breast, 25% were carcinoma stomach 33.3% were Carcinoma prostate and carcinoma urinary bladder, 23.5% were SCC carcinoma lung, all cases of Ewing's sarcoma; neuroblastoma and poorly differentiated carcinoma show bone marrow metastasis.

Conclusion: Bone marrow examination is valuable tool in the diagnosis and staging of hematologic and nonhematological disease, as well as in the assessment of overall bone marrow cellularity, pattern of marrow involvement in metastatic carcinomas.

Keywords: *Metastatic Carcinoma, Cytopenia, Pancytopenia, Bone Marrow Studies*

Introduction

Multiple lineage cytopenia in association with cancer warrants consideration of bone marrow metastasis . Metastatic carcinoma can involve bone marrow and may lead to subsequent marrow fibrosis and failure. Bone marrow metastasis occurs in fewer than 10% of patients with metastatic disease, and are more common in patients with lung, breast, or prostate carcinoma. The precise mechanism for poor outcomes is unknown; studies suggest that tumors that secrete more pro-angiogenic and pro-inflammatory cytokines may be more likely to metastasize to the bone marrow. [1]

Total marrow replacement by tumor is rare, and only a small percentage of marrow may be needed to support normal peripheral blood counts, as indicated by the observation that normal blood counts are often found in normal older adults with hypocellular marrows. [1-5] Cytopenia results from the release of substances such as cytokines that suppress hematopoiesis destroy stem progenitor and stromal cells. With the disruption of normal bone marrow architecture by infiltrating cells, the marrow some time releases immature hemopoietic cells into the peripheral blood. [2]

Bone marrow Aspirate and where ever necessary bone marrow biopsies have numerous advantages in determining the degree of cellularity, metastatic deposits and degree of fibrosis (in biopsy samples). In this study we studied the bone marrow in patients diagnosed with cancer or in patients on chemotherapy presented with cytopenia. [3] Some of the studies have reported that diagnosing the tumor cells in marrow may be the primary manifestation of malignant solid tumors.[4]

Materials and Methods

This study is performed at tertiary care hospital in the department of pathology Great eastern medical college and Hospital during the period of May 2010-June 2020. A total of 702 Bone marrow procedures were done during this period. The patients with a diagnosis of cancer or patients on chemotherapy presented as cytopenia (such as hemoglobin <8mg/dl not responding to medication, platelets count <50000/mm^3 or patients with platelets <100000/mm^3 having bleeding manifestations, neutropenia <500 cells/mm^3, leucopenia <4000 cells/mm^3 were included in the study.

Data necessary for study has been retrieved from the histopathology records in our department. 118 bone marrow aspirations and biopsies were performed in patients with cytopenia. 32 cases were diagnosed with bone marrow metastasis. Site preferred was iliac crest by using Jamshidi needle. Peripheral blood picture and bone marrow studies were studied. 0.5-1.0 ml of bone marrow aspirates were taken and slides prepared according to the standard protocols.

Bone marrow smears prepared were stained with Geimsa stain. Bone marrow biopsy done where ever necessary and fixed in formalin or Bouin's fluid, then decalcified, stained with hematoxylin and eosin. Special stains were done where ever necessary.

Results

In this study of 118 patients 74 (62.7%) were males and 44 (37.2%) were females.

Peripheral smear examination of the cases with metastatic marrow showing, 24 out of 32 (75%), cases present with anemia, which was the commonest clinical presentation. Others were, thrombocytopenia in 18 (50%), bleeding manifestations in 10 (31.2%) cases, Pancytopenia in 9 (28.1%) of cases, bi-cytopenia in 4 (12.5%) of cases (Table 1).

During this study period, among malignancies reported in histopathology,

41 (34.7%) were carcinoma breast, 20 (16.9%) carcinoma stomach, 18 (15.2%) carcinoma prostate, 17 (14.4 %) SCC carcinoma lung, 6 (5.1%) carcinoma urinary bladder, 4 (3.4%) carcinoma Cervix, 3 (2.16%) Ewing's sarcoma, 2 (1.7%) cases of each neuroblastoma and poorly differentiated carcinoma and 5 (4.2 %) with unknown primary site (Table 2). Bone marrow metastasis was found in 32 out of 118 (27.1%) malignancies (Table 3).

Discussion

The bone marrow being the origin of primary hematological malignancies and is also commonly involved by metastatic tumors. Many studies have shown

Table 1: Peripheral blood picture of metastatic carcinomas of bone marrow.

S. No	Peripheral blood / Clinical picture	Total no. of cases	Percentage (%)
1	Anemia	24	75
2	Thrombocytopenia	16	50
3	Bleeding manifestations	10	31.2
4	Pancytopenia	09	28.1
5	Bi-cytopenia	04	12.5

Table 2: Number and percentage of malignancies reported in Histopathology.

S. No	Type of primary malignancy	No of cases reported in Histopathology (n = 118)	Percentage of cases reported in Histopathology (%)
1	Carcinoma Breast	41	34.7
2	Carcinoma Stomach	20	16.9
3	Carcinoma Prostate	18	15.2
4	SCC carcinoma lung	17	14.4
5	Carcinoma urinary bladder	06	5.1
6	Carcinoma Cervix	04	3.4
7	Neuroblastoma	02	1.7
8	Ewing's sarcoma	03	2.6
9	Poorly differentiated carcinoma	02	1.7
10	Unknown primary	05	4.2

Table 3: Number and percentage of malignancies reported in Histopathology.

S. No	Type primary malignancy	No of cases reported in Histopathology (n = 118)	Number of cases of metastasis to Bone marrow (n=32)	Percentage of diagnosed cases metastasis to Bone marrow (%)
1	Carcinoma Breast	41	07	17.1
2	Carcinoma Stomach	20	05	25
3	Carcinoma Prostate	18	06	33.3
4	SCC carcinoma lung	17	04	23.5
5	Carcinoma urinary bladder	06	02	33.3
6	Carcinoma Cervix	04	00	0
7	Neuroblastoma	02	02	100
8	Ewing's sarcoma	03	03	100
9	Poorly differentiated carcinoma	02	02	100
10	Unknown primary	05	01	20

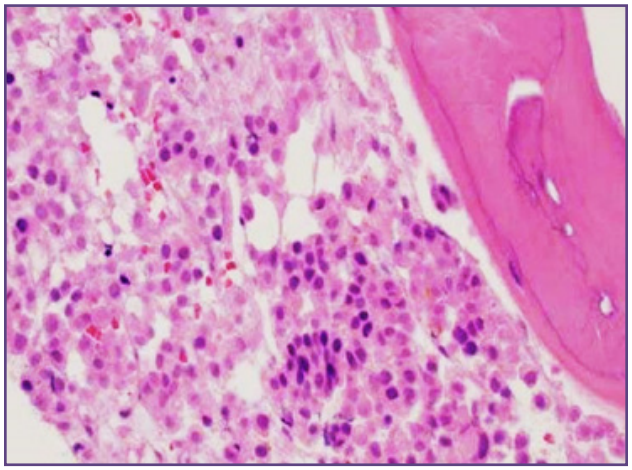

Fig. 1: Bone marrow biopsy showing carcinoma breast deposits (H&E X400).

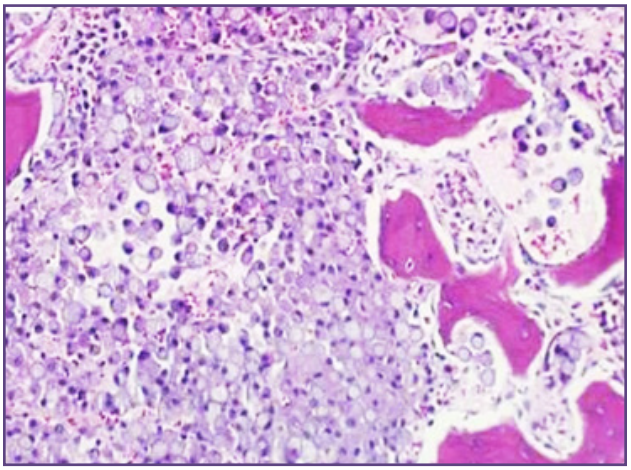

Fig. 2: Bone marrow biopsy showing carcinoma stomach deposits (H&E X200).

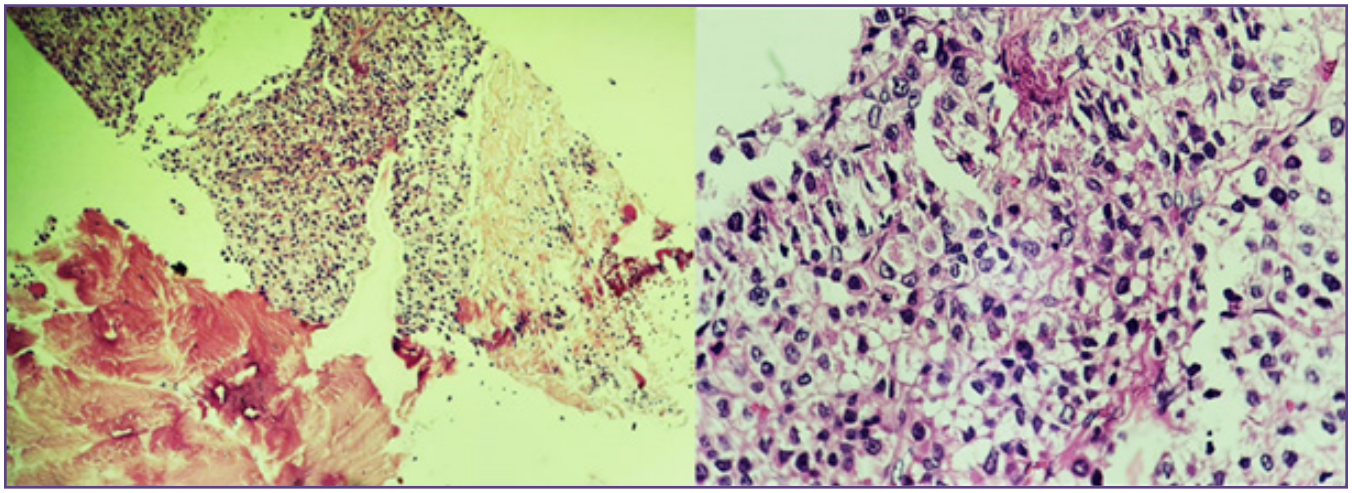

Fig. 3: Bone marrow biopsy showing carcinoma prostate deposits (H&E 100x and 400x).

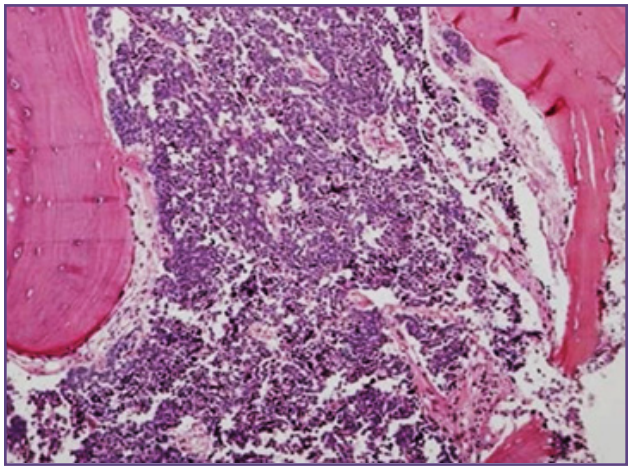

Fig. 4: Bone marrow biopsy showing Neuroblastoma deposit (H&E 100X).

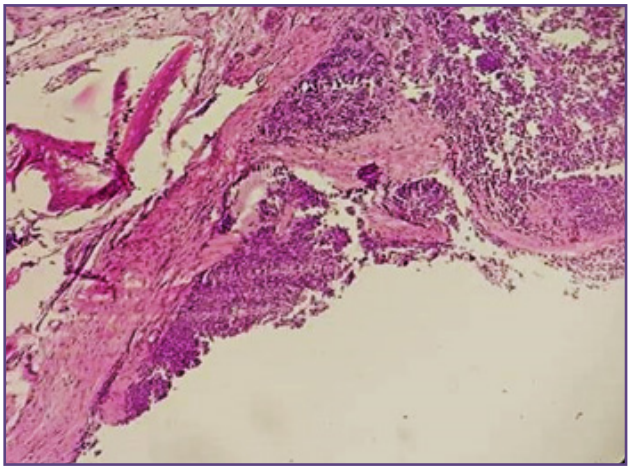

Fig. 5: Bone marrow biopsy showing Ewing's sarcoma deposit (H&E 100X).

that bone metastasis can be the first manifestation in some tumors. Bone marrow examination by aspiration and biopsy are well known procedures to diagnose hematological malignancies. Bone marrow examination is a tool for staging and prognosis of solid tumors. [5, 15] The malignancies of prostate, breast, lungs, kidney, thyroid and gastric in adults and neuroblastoma and rhabdomyosarcoma in children are the primary tumors which frequently involve bone marrow. [6-12]

Prostate, lung and breast malignancies are the common tumor metastasizing to bone marrow. Marrow infiltration by tumor cells is related to the amount of fibrosis. Fibrosis is more marked in carcinoma lung, prostate, stomach and breast.[13] In our study bone marrow fibrosis MF-0, MF-1 are seen in 4 cases with 2 cases each carcinoma stomach and breast.

The fibrosis is due to release of cytokines which leads to cytopenia. Sometimes the morphology of the tumor cells at metastatic site may not reveal exact site of origin, so always it is advisable to correlate the morphology of metastatic tumor cells with the clinical presentation and histopathological findings of the tumor to get final diagnosis.

The advanced and sensitive diagnostic procedures like *Bone scan, Radiographs like CT, MRI, Positron emission tomography* (PET) are better modalities to assess the bone marrow metastasis [15] but they are expensive and available only at advanced medical centers. While the bone marrow aspiration and biopsy are cost effective and easy procedures for staging of the solid tumors, but less useful in diagnosis of solid tumors.

In our study anemia is the most common presentation (75%) which is correlated with the study done by Kritichauhan.[14]

Cancers of the breast, prostate and lung are more frequently seen in adults, in pediatric cases; neuroblastoma is responsible for the majority of cases. In a study, by Mohanty et al. showed that prostate cancer (47.8%) was the most common tumor among adults, followed by breast cancer (28.2%). [7]

The overall percentage of bone marrow metastasis in our study is only 27%, was much lower than studies reported from different countries. Bone marrow metastasis occurs in advanced stages and the procedure in our institution might be done earlier before the metastasis could occur. Beside these there are many molecular mechanisms that cause bone marrow metastasis. The metastasis from carcinoma breast in the present study was not as high as reported in the study done by Mohanty and Dash, 2003. No bone marrow metastasis was observed in carcinoma cervix. Metastasis is found in all cases of Neuroblastoma and Ewing's sarcoma.

Conclusion

Bone marrow examination is valuable tool in the diagnosis and staging of hematologic and non-hematological disease, as well as in the assessment of overall bone marrow cellularity, pattern of marrow involvement. Bone marrow aspiration with biopsy is very useful in all cases of Pancytopenia to evaluate the cause. Our study reflects that, for staging of all solid tumours, bone marrow examination is necessary, as it is cost effective and minimal invasive procedure.

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Competing Interests

None declared

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