



ORIGINAL ARTICLE

The Role of Bone Marrow Aspiration and Bone Marrow Biopsy in Diagnosis of Bone Marrow Metastases

Nour Haaj Mohammad^{1*}, Firas Hussein², Issa Ahmad³

¹Master in Hematology, Tishreen University, Syria

²Associated Prof in Hematology, Alandalus University, Syria

³Associated Prof in Pathology, Alandalus University, Syria

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*Corresponding author:

Nour Haaj Mohammad
Master in Hematology, Tishreen
University
Slayba-22, Latakia-Borsaeed, Syria
Tel: +96 39 44281179
Email: nonahematology@gmail.com

ABSTRACT

Background: Bone marrow is the site of many malignant disorders and it is one of the common places for solid tumors to metastasize. Examination of the bone marrow aspirate and biopsy is a routine procedure performed for assessment of various conditions such as cytopenias, hematologic neoplasms, nonmalignant disorders and metastatic neoplasms.

Methods: The patients were referred to the Hematology Department at Tishreen University Hospital. 236 patients enrolled the study. Both bone marrow aspiration and biopsy were performed for all patients. Bone marrow aspirate was interpreted by the hematologist and the biopsy was examined by a Histopathologist. Moreover, we used immunohistochemical staining of some bone marrow biopsy specimens in cases where more information for diagnosis is required.

Results: Bone marrow metastases was diagnosed in 35 (14.83%) samples. Prostate, breast, stomach, lung and neuromuscular cancers were metastasized to bone marrow in 11, 9, 7, 6 and 2 cases, respectively. Bone marrow biopsy could discover the metastasis in 100% of the involved cases, while only 40% of the cases with bone marrow involvement were diagnosed by bone marrow aspiration. The degree of sensitivity of bone marrow biopsy for diagnosis of bone marrow metastases in comparison to aspiration was statistically significant ($P=0.001$).

Conclusion: Bone marrow Metastases were diagnosed in 14.83% of the patients with malignant tumors. Prostate and breast cancer were the most common. Bone marrow biopsy could diagnose the metastases in all the cases compared to 40% by bone marrow aspiration.

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Introduction

Bone marrow (BM) is among the common sites for many malignant tumors to metastasize. A malignant metastatic tumor in BM usually means an incurable disease, although it is not necessarily fatal. Therefore, it is suggested to exclude BM involvement in any malignancy where the type of treatment is determined by stage of the tumor.¹ Examination of the BMA and BMB is a routine procedure performed for assessment of various

conditions such as cytopenias, hematologic neoplasms, nonmalignant disorders and metastatic neoplasms.^{2,3} BMB is an indispensable adjunct to the study of the blood disorders and may be the only method where the correct diagnosis can be made. BMA and BMB are easy and safe procedures and can be performed in outpatient clinics.⁴ BMA is safer and easier than BMB which may be more associated with pain and bleeding.⁵ BM is one of the most common places where metastatic transplants occur.

However, it is sometimes difficult to diagnose the presence of these metastases within BM for a variety of reasons and even BM involvement may remain undiagnosed until an advanced period of the disease.⁶ Lung, breast, and prostate cancer do often metastasize to bone marrow, so bone marrow studies are essential in determining the tumor stage in these malignancies.⁷ Diagnosis of BM metastases may also contribute significantly to the diagnosis of primary tumors.⁸ As a result, the importance of using sensitive and specific screening methods to detect these metastases is highlighted. The histological and parenchymal study of the BM by BMA and BMB may give an idea of the primary tumor that caused metastasis if the primary tumor is unknown.⁹ As a result, BMA and BMB are complementary in diagnosis.¹⁰ The use of BMB is more important than BMA in the presence of BM fibrosis or infiltrations of tumor cells.^{11,12} BMA has less sensitivity in the detection of solid malignant neoplasms and lymphoma compared with BMB.¹³ BMB is the most reliable method of detecting the presence of infiltration within the BM.¹⁴ BM is a preferred and frequent site for tumor metastases of several types such as breast, prostate and neuroblastoma.¹⁴ In this study, we investigated the sensitivity and value of both BMA and BMB in the diagnosis of BM metastases.

Materials and Methods

236 patients were referred to the Hematology Department at Tishreen University Hospital during the period from Apr 2015 to Sep 2016. Most complaints in the medical records of the patients were isolated anemia or pancytopenia, general fatigue and weakness and a tumoral mass. Both BMA and BMB were performed for all patients. A series of laboratory and radiological examinations were performed as necessary and according to each case. BMA was interpreted by the hematologist and BMB by the Histopathologist. Moreover, we used immunohistochemical staining of bone marrow biopsy when necessary.

SPSS software version 22 was used for analysis. The Shapiro-Wilk test and Pearson correlation coefficient were used. The standard deviation of age was calculated

in the study sample. Statistical significance was calculated at 95% confidence coefficient with statistical importance when the value of alpha was less than 0.05.

Results

The study sample consisted of 236 patients. The number of men was 142 (60.2%). BM metastasis was diagnosed in 35 (14.83%) patients. Prostate cancer was the most common tumor in 11 cases (Figure 1: A, B), breast cancer 9 cases, stomach cancer 7 cases, lung cancer 6 cases, and neuromuscular tumors in two cases (table 1).

Table 1: Distribution of solid tumors that showed a transition to bone marrow

Type	Number	Percentage
Prostate cancer	11	31.4%
Breast cancer	9	25.7%
Stomach cancer	7	20%
Lung cancer	6	17.2%
neuroblastoma	2	5.7
Total	35	100%

BM metastasis was diagnosed in all involved patients by BMB, while only 40% of the cases were diagnosed through BMA (Figure 2 A, B). The percentage of BM metastases diagnosed with lung cancer was 50% and the lowest was in the case of gastric cancer (28.6%). The degree of sensitivity of BMB to diagnosis metastasis in comparison to BMA was statistically significant ($P=0.001$). The results are shown in table 2.

In 9 cases, we could not confirm the presence of malignant cells (metastases) and it was necessary to conduct a bone marrow biopsy to confirm the diagnosis.

Discussion

The study was conducted to determine the importance of BMA and BMB and their usefulness in diagnosing BM metastasis. Infiltration of bone marrow by metastases is known to be common at advanced stages of some malignancies; hence BM could be a probable site for metastasis in solid tumors. BM metastases were often detected much more frequently than routine diagnostic

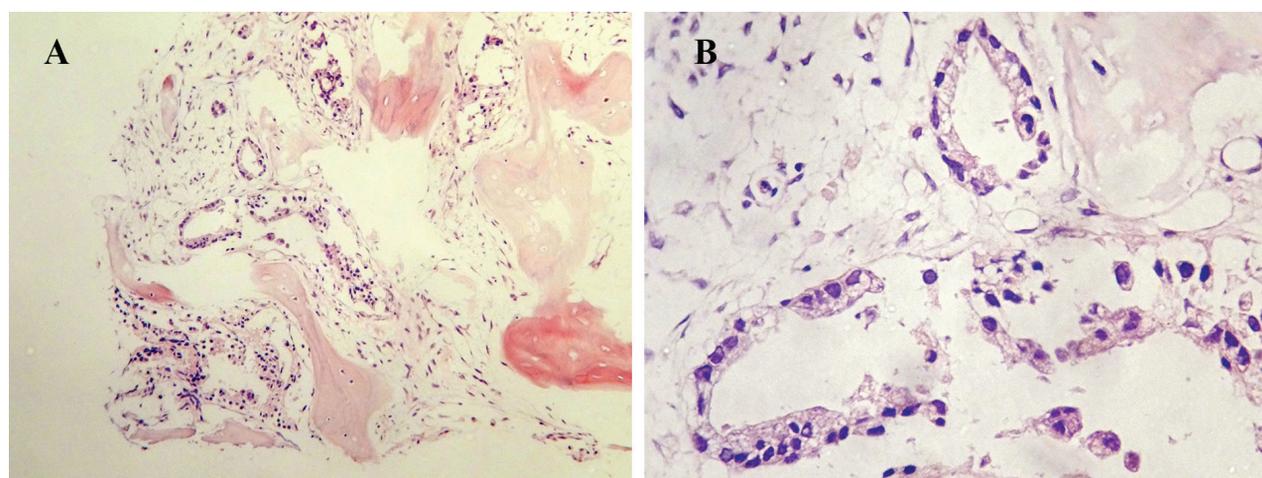


Figure 1: (A, B): The marrow shows extensive fibrosis with deposits of metastatic carcinoma morphologically compatible with metastatic prostatic carcinoma. Normal bone marrow elements are hard to identify.

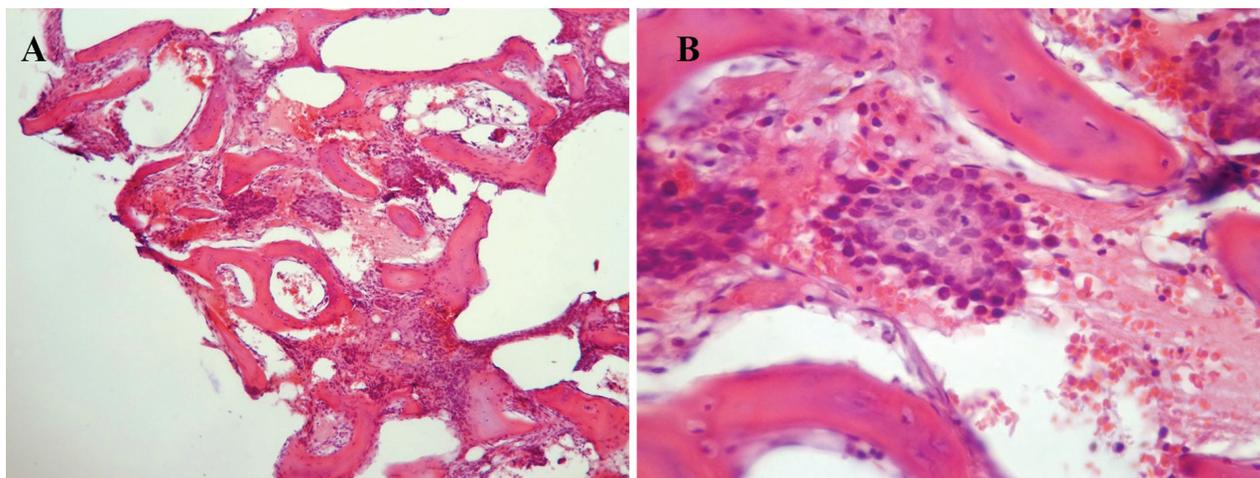


Figure 2: (A, B): Metastatic Carcinoma associated with marrow fibrosis. Normal Hematopoietic Elements are rarely seen.

Table 2: comparison between BMA and BMB in diagnosis of BM metastasis

Malignancy	No	BMB		BMA		P value
		No	Percent	No	Percent	
Prostate cancer	11	11	100%	4	36.6%	0.001
Breast cancer	9	9	100%	4	44.5%	
Stomach cancer	7	7	100%	2	28.6%	
Lung cancer	6	6	100%	3	50%	
neuroblastoma	2	2	100%	1	50%	
Total	35	35	100%	14	40%	

procedures.⁷ Anemia was present in 65.7% of patients, thrombocytopenia in 14.3% and pancytopenia in 17% of the patients. However, there were directed signs and symptoms such as bone pain which was present in 20% of patients and hypercalcemia and high alkaline phosphatase in 22.9% of the cases and the abnormal laboratory tests was anemia with thrombocytopenia and sometimes pancytopenia with the overall hypercalcemia in some cases.¹⁵ BMA is less sensitive to the detection of BM metastasis than BMB.¹⁶ Diagnosis of metastasis in 14.8% of study patients makes it important to conduct a study to compare the sensitivity of BMA and BMB, as it may be key to the diagnosis of primary solid tumors elsewhere in the body.¹⁷ It may be noted that BMB may give an idea of the type of the tumor. This narrowed our search for the primary source of the tumors.⁷ On the other hand, the study of bone marrow has little importance in detection of malignant lesions unless it is associated with other tests that may support the diagnosis such as pancytopenia.¹⁸ Prostate, lung, and breast cancer are tumors that proliferate commonly within the BM.¹⁹ There are also some less invasive tumors in bone marrow such as neuroblastoma, stomach and colorectal cancer.⁷ The superiority of BMB in the diagnosis of BM metastasis makes it important to include it in workup of cases suspicious for BM involvement; however, BMA continues to play its role in the diagnosis or orientation of metastases. Because of the importance of bone marrow studies, combining both procedures of BMA and BMB increases the diagnostic yield of diagnosis of BM involvement¹. All cases in which BMA was positive were associated with positive results in biopsy, which

makes BMA highly sensitive to the diagnosis of BMM, but the value remains low compared to the BMB.

Conclusion

BM metastases were diagnosed in 14.83% of the patients. Prostate and breast cancer were the most common metastatic tumors and the stomach and lung cancer were in decreasing order. BMA could detect metastases in 40% of the involved subjects suggesting a superior role for BMB in the diagnosis of BM metastases. However, BMA continues to play a major role in the diagnosis of BM metastases. Due to importance of diagnosis of bone marrow involvement, combining BMA and BMB increases the diagnostic yield of diagnosis.

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Conflict of Interest: None declared.

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