



Original Research Article

Bone Marrow Study In Malignant Disorders: Marrow Trepine Biopsy Versus Marrow Magnetic Resonance Imaging

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ABSTRACT

Bone marrow involvement in malignant disorders is central to both staging and treatment, therefore extremely important. Histopathologic examination for bone marrow involvement is the best diagnostic method, but it can be sometimes misleading in patients with focal involvement while Magnetic Resonance Imaging (MRI) presents more global view of bone marrow and is highly sensitive. The aim of this study was to assess and compare the efficacy of MRI with bone marrow biopsy in evaluation of bone marrow infiltration in various malignant diseases. This study included 100 patients with known malignancies who underwent complete evaluation on both MRI and bilateral bone marrow biopsy. Out of 100 patients, only 45 showed bone marrow involvement. All these 45 cases were positive on MRI but only 39 on bone marrow biopsy. Six cases showed marrow involvement on MRI but their bone marrow biopsy did not show any marrow infiltration but certain secondary changes were present in the form of increase in eosinophils, prominence of lymphocytes, mild fibrosis, or reactive plasmacytosis in various malignant disorders respectively. Thus we conclude that both bilateral iliac crest bone marrow biopsies and marrow MRI are important in establishing bone marrow involvement in cancer patients. This study also indicates that sensitivity of marrow MRI in detecting marrow infiltration is higher as compared to bone marrow biopsy especially when marrow is involved focally which may show secondary changes only on marrow biopsy.

Keywords: bone marrow biopsy, Magnetic resonance imaging, malignant disorders, Marrow infiltration.

INTRODUCTION

Bone marrow biopsy is still the examination of choice not only in hematologic malignancies but also for tumors that metastasize into the marrow. The definitive diagnosis of primary and metastatic hematopoietic malignancies traditionally requires microscopic examination of marrow aspiration or

trepine biopsy because it provides direct evidence of the presence and the nature of the disease. [1] When marrow aspiration leads to dry tap in such situations, evaluation of bone marrow cellularity and abnormal architecture patterns and detection of structures other than hematopoietic cells within the marrow are best achieved by bone marrow biopsy. [2] The trephine biopsy has

the advantage that, because of the possibility of assessing tissue structure and applying histochemical stains, it may be possible to predict the tissue of origin of metastatic tumor – e.g. breast or prostatic gland. [3] Multiple biopsy specimens obtained from different sites may also increase the diagnostic yields. [2]

Accurate documentation of the bone marrow status is critical in choosing the appropriate therapeutic strategy. A means of improving the detection of marrow infiltration would therefore have important therapeutic implications. In order to detect and evaluate the extent of bone marrow infiltration, there are some other diagnostic tests such as bone marrow scintigraphy, flow cytometric analysis of marrow aspirate and Magnetic Resonance Imaging (MRI) of bone marrow. [4] Bone marrow contains a large proportion of mobile protons in fat and water, in cellular haemopoietic and stromal tissue. It is therefore, ideally suited for study with MRI. MRI provides a non invasive means to evaluate a large proportion of marrow and detecting marrow lesions, as it provides information at the level of cellular and chemical composition. MRI can be used to provide more accurate diagnosis- for initial staging, to guide treatment and to follow therapy related changes. [5] MRI of the bone marrow is more sensitive than specific for detecting a variety of marrow disorders like metastatic disease, multiple myeloma, leukemia and various subtypes of lymphomas. [6]

The specimens obtained by blind bone marrow aspirates and biopsies from the posterior iliac crests are tiny compared with the entire marrow space and focal involvement elsewhere can be easily missed due to sampling error. [7] MRI clearly demonstrates soft tissue extensions and skip areas of bone tumors. It is better than other modalities, including biopsy, especially

when tumor involvement is patchy and not diffuse. [1]

The aim of this study was to assess and compare the efficacy of MRI with bone marrow biopsy in evaluation of bone marrow infiltration in various malignant diseases.

MATERIALS AND METHODS

The present study was carried out in Postgraduate department of Pathology, Govt. Medical College (GMC), Jammu. The study extended over a period of one year and a total of 100 patients with various malignant disorders were studied. The patients of both sexes belonging to different ages who were admitted in the GMC hospital and associated hospitals of this college and also all those patients referred to this institution from district hospitals and peripheral health centers.

The patients suffering from hematologic and non-hematologic malignancies were taken up for the current study.

Among hematologic malignancies the patients studied included multiple myeloma, non-Hodgkin's lymphoma and Hodgkin's disease.

Patients suffering from non-hematologic malignancies suspected of marrow involvement (having bone pain; fever not responding to the treatment) were taken up for the study.

Our study also included those cases that were diagnosed as metastatic carcinoma directly on Bone Marrow examinations and their primary malignancies were not known and they presented with Generalized Weakness, Pallor, Bone pains or Fever not responding to treatment and some of them were evaluated for Anemia and Leukoerythroblastosis.

The research project was explained to these patients and their attendants and a

proper consent was taken from them for conduct of this study.

A detailed clinical history, general physical and systemic examination was done. All those patients who were taken up for the study were subjected to a set of investigations like Complete blood count (CBC), Bleeding time (BT), Clotting time (CT), Erythrocyte sedimentation rate (ESR) and Peripheral blood film (PBF). All the patients were subjected to bilateral bone marrow trephine biopsy and the methods of preparation and staining of marrow sections used were those mentioned in Lewis.^[8]

Procedure for Bone Marrow Trephine Biopsy

Bone marrow trephine biopsy was performed by using the Jamshidi needle from posterior iliac spine taking all aseptic precautions.

Skin, subcutaneous tissue and periosteum overlying the selected site was infiltrated with 2% xylocaine. Trephine specimen, was obtained by inserting the biopsy needle into the bone and using to and fro rotation to obtain a core of tissue. Imprint smears were taken before the specimen was transferred into the fixative. The bony core was gently dabbed or rolled across the slide, which was then fixed and stained with MayGrunwald Geimsa (MGG) stain to prepare imprint smears. Bone marrow trephine biopsies were studied for;

- Bone marrow architecture.
- Cellularity.
- Proportion of cells of all hematopoietic series.
- Foci of malignant cells/infiltration especially in paratrabeular areas.
- Assessment of lymphocyte number and their distribution- lymphocyte nodules in the intertrabeular space and presence of lymphocyte along the paratrabeular area.
- Necrosis.

- Stromal fibroblastic reaction.
- New bone formation.
- Reactive plasmacytosis
- Reticulin stain assessment of reticulin fiber density and thickness.

All the patients were subjected to Magnetic Resonance Imaging (MRI) of bone marrow of pelvis, spine, and bilateral femoral bones. It was done on 1.5 tesla Magnetic Resonance (MR) machine, Siemens Magnetom symphony. Imaging was done in all the planes coronal, axial, and sagittal planes.

MRI sequences that were used included T1, T2, T1FS, Short Tau inversion recovery (STIR) imaging and Heavy T2 imaging. Repetition Time (TR) exceeding 3,000ms and Echo Time (TE>90ms). Contrast MR was also done wherever needed.

The MRI was considered positive for marrow infiltration when the lesion on T1 W1 image showed markedly decreased intensity compared with normal adult marrow; on STIR images, lesions were considered present when their intensity was greater than muscle and much greater than normal marrow; on T2 W1 images abnormal lesions were hyper-intense.

The positive (abnormal) findings on marrow MRI were categorized as follows:

Focal pattern, characterized by focal areas of fatty marrow replacement with a signal intensity that was lower on T1 W1 SE images (higher on STIR images) than that of muscles;

Scattered pattern, characterized by multiple scattered foci of marrow replacement on a background of uninvolved marrow; and

Diffuse pattern, characterized by diffuse replacement of fatty marrow.

OBSERVATIONS AND ANALYSIS

During this period, all those patients suffering from hematologic and non-hematologic malignancies, who were

admitted in the GMC hospital, associated hospitals of Jammu and also all those patients who were referred to this institution

from other peripheral healthcare centers were taken up for the study.

Table No. 1: TYPES OF MALIGNANT DISORDER IN 100 PATIENTS

HEMATOPOETIC MALIGNANT DISORDERS	Number of patients	Percentage
MULTIPLE MYELOMA (MM)	19	19
NON HODGKIN LYMPHOMA (NHL)	12	12
HODGKIN LYMPHOMA (HL)	4	4
NON HEMATOPOETIC MALIGNANT DISORDERS		
BREAST CANCER	10	10
RESPIRATORY TRACT CANCER	11	11
GASTROINTESTINAL TRACT CANCER	11	11
HEPATOBIILIARY TRACT CANCER	05	05
GENITOURINARY TRACT CANCER	20	20
THYROID CANCER	04	04
PERIPHERAL NEUROECTODERMAL TUMOR (PNET)	01	01
SARCOMA	03	03
TOTAL	100	100

A total of 100 patients underwent complete evaluation for Bone Marrow involvement on both MRI and bilateral Bone Marrow Biopsy. Among these 100 patients Genitourinary tract cancer (20%) and Multiple myeloma (19%) were the most common malignant tumors followed by Non-Hodgkin lymphoma (12%), Respiratory

tract cancer (11%), Gastrointestinal tract cancer (11%), Breast cancer (10%), Hepatobiliary tract cancer (5%), Hodgkin lymphoma (4%), Thyroid cancer (4%), Synovial sarcoma (3%), and Peripheral neuroectodermal tumor (1%) (*Table no. 1*).

Table No. 2: MALIGNANT DISORDERS WITH MARROW INVOLVEMENT

Type of Malignant disorders	Total cases	No. of cases With Marrow involvement	MRI +ve	BM Biopsy +ve
Hematopoietic	35	25	25	22
Non-Hematopoietic	65	20	20	17
Total	100	45	45	39

Out of 100 patients with malignant disorders, 45 showed Bone Marrow involvement. All these 45 cases were positive on MRI but only 39 on bone marrow biopsy. All 39 cases who showed marrow infiltration on bone marrow biopsy were also MRI positive while the 45 cases that showed abnormal findings on MRI, only 39 had positive biopsies. Of these 45

patients with various malignant disorders, 25 were of hematopoietic malignancy and 20 of non-hematopoietic malignancy. Among hematopoietic malignancies 25 were positive on MRI and 22 on BM biopsy but in non-hematopoietic malignancies 20 showed positivity on MRI and 17 on bone marrow biopsy (*Table no.2*).

Table No. 3: HEMATOPOETIC MALIGNANT DISORDERS WITH MARROW INVOLVEMENT

HEMATOPOETIC MALIGNANT DISORDERS	Number of cases=25	Percentage
MULTIPLE MYELOMA	19	76
NON HODGKIN LYMPHOMA	05	20
HODGKIN LYMPHOMA	01	04
TOTAL	25	100

Out of 35 cases of Hematopoietic Malignant disorders, 25(71.14%) showed bone marrow involvement, among these 25, 19 were constituted by Multiple Myeloma, 05 by Non-Hodgkin lymphoma and 1 by Hodgkin lymphoma respectively (*Table No.3*).

Table No. 4: NON-HEMATOPOETIC MALIGNANT DISORDERS WITH MARROW INVOLVEMENT

NON-HEMATOPOETIC MALIGNANT DISORDERS	Number of cases – 20	Percentage
BREAST CANCER	03	15
RESPIRATORY TRACT CANCER	02	10
GASTROINTESTINALTRACT CANCER	03	15
HEPATOBIILIARYTRACT CANCER	01	05
GENTOURINARY TRACT	08	40
THYROID CANCER	01	05
PNET	01	05
SARCOMA	01	05
TOTAL	20	100

Out of 65 cases of Non-Hematopoietic Malignant disorders 20(30.76%) cases showed Bone Marrow involvement. Among these 20 cases 8 were constituted by Genitourinary tract cancer, 3 by Breast cancer, 3 by Gastrointestinal tract cancer, 2 by Respiratory tract cancer, 1 by Hepatobiliary tract cancer, 1 by Thyroid cancer, 1 by Peripheral neuroectodermal tumor and 1 by Synovial sarcoma respectively (*Table No.4*).

TableNo.5: FREQUENCY OF ABNORMAL FINDINGS ON MRI IN PATIENTS WITH BONE MARROW INVOLVEMENT (number of cases=45)

PATTERN	Number of cases	Percentage
FOCAL	07	15.55
SCATTERED	11	24.44
DIFFUSE	27	60
TOTAL	45	100

These patients ranged in age from 8 years to 80 years (median, 57 years) and majorities (42.22%) of cases were in the age group of 51 to 60 years and males constituted 62.23% of cases.

Frequency of abnormal findings on MRI (Table No.5):

Forty five cases showed presence of abnormal findings on MRI on both T1-weighted SE and STIR images out of hundred. Frequency was 45 %.

Frequency of abnormal findings on bone marrow biopsy:

Bone marrow trephine biopsy was studied for architecture, cellularity, proportion of cells of all hematopoietic series, frequency of marrow infiltration (Hematopoietic and non-hematopoietic) and frequency of other abnormal findings like fibrosis; new bone formation; necrosis and reactive plasmacytosis.

Out of 45 patients who showed abnormal MRI findings, bone marrow biopsy revealed marrow infiltration with fibrosis in 23 cases, marrow infiltration with fibrosis and plasmacytosis in 4 cases, marrow infiltration with fibrosis, osteosclerosis and necrosis in 2 cases, marrow infiltration with fibrosis and osteosclerosis in 5 cases, marrow infiltration with fibrosis and necrosis in 1 case, marrow infiltration alone in 4 cases, isolated fibrosis without marrow infiltration in 1 case, fibrosis and reactive plasmacytosis without marrow infiltration in 1 case, fibrosis with osteosclerosis and necrosis without marrow infiltration in 1 case, mild eosinophil prominence without marrow infiltration in 1 case and mild lymphocyte prominence without marrow infiltration in 2 cases. Thus, among these 45 cases 39 (86.6%) cases exhibited marrow infiltration on BM biopsy and these comprised of 19 cases of multiple myeloma, 3 of Non-Hodgkin lymphoma, 6 of genitourinary tract cancer, 3 of gastrointestinal tract cancer, 2 of Breast cancer, 2 of Respiratory tract cancer, 1 of Hepatobiliary tract cancer, 1 of Thyroid cancer, 1 of peripheral neuroectodermal tumor and 1 case of Synovial sarcoma. As shown in *Table no. 6*, Fibrosis was seen in 38 (84.44%) cases; all grades of fibrosis were seen, from mild to moderate to marked

increase in density and thickness of reticulin fibers. This was the most frequently associated secondary change in the presence of marrow infiltration. New bone formation (osteosclerosis) was seen in 8 (17.77%) cases, Necrosis in 4 (8.88%) and Reactive plasmacytosis in 5 cases (11.11%)

Table No.6: FREQUENCY OF ABNORMAL FINDINGS ON BONE MARROW TREPINE BIOPSY IN PATIENTS WITH BONE MARROW INVOLVEMENT (number of cases=45)

ABNORMAL FINDINGS ON BM BIOPSY	Number of cases	Percentage
MARROW INFILTRATION	39	86.6%
FIBROSIS	38	84.44%
NEW BONE FORMATION	8	17.77%
NECROSIS	4	8.88%
REACTIVE PLASMACYTOSIS	5	11.11%

Correlation of MRI and Bone marrow histology (biopsy) in patients with malignant disorders: As shown in Table No. 7, patients were analyzed in relation to pathologic diagnosis. All the patients with abnormal bone marrow biopsy showed abnormal findings on MRI. Negative bone marrow biopsy results despite positive MR imaging

were observed in six patients with various malignant disorders [2 patients(16.6%)with Non-Hodgkin lymphoma,1 patient(25%) with Hodgkin's Lymphoma,2 patients(10%) with Genitourinary tract cancer, 1 patient(10%)with Breast cancer]. 39 patients with various malignant disorders showed positive results both on MRI and bone marrow biopsy 19 patients(100%) with multiple myeloma, 3 patients (25%) with Non-Hodgkin lymphoma, 2 patients(20%) with infiltrating ductal carcinoma of breast, 2 patients (18%) with small cell lung cancer, 3 patients (27%) with gastrointestinal malignancy, 1 patient (20%) with Hepatobiliary malignancy, 6 patients(30%) with genitourinary tract cancer, 1 patient (25%) with thyroid cancer, 1 patient (100%) with Peripheral neuroectodermal tumor and 1 patients(33%) with Synovial sarcoma. Out of 100 patients, 55 were negative for marrow infiltrations on both MRI and bone marrow biopsy. There was a good correlation between marrow MRI and bone marrow histology.

Table No.7: CORRELATION OF MARROW MRI AND MARROW BIOPSY IN PATIENTS WITH MALIGNANT DISORDERS (number of cases=100)

MALIGNANT DISORDERS	MRI/BIOPSY			
	*	¥	#	£
	-/-	-/+	+/-	+/+
MULTIPLE MYELOMA (n=19)	0	0	0	19
NON HODGKIN LYMPHOMA (n=12)	7	0	2	3
HODGKIN LYMPHOMA (n=4)	3	0	1	0
BREAST(n=10)	7	0	1	2
RESPIRATORY TRACT(n=11)	9	0	0	2
GASTROINTESTINAL(n=11)	8	0	0	3
HEPATOBIILIARY(n=5)	4	0	0	1
GENITOURINARY(n=20)	12	0	2	6
THYROID(n=4)	3	0	0	1
PERIPHERAL NEUROECTODERMAL TUMOR (n=1)	0	0	0	1
SARCOMA(n=3)	2	0	0	1

* -/-, Normal MRI/negative BM biopsy
 ¥ -/+, Normal MRI/positive BM biopsy
 # +/-, positive MRI/ negative BM biopsy
 £ +/+, positive MRI/ positive BM biopsy
 n number of cases

Sensitivity of MRI for detecting marrow involvement in malignant diseases:

In our study MRI showed a higher ability to detect marrow infiltration than bone marrow

biopsy. As shown in *Table No. 8*, the number of true positive cases for MRI was 45 and true negative 55, there were no false

positive and false negative cases. Thus, the sensitivity of MRI was 100% in our study.

Table No. 8.COMPARATIVE RESULTS OF MARROW MRI AND BM BIOPSY IN 100 PATIENTS

TOTAL CASES	MRI RESULT		BIOPSY RESULT	
	POSITIVE	NEGATIVE	NEGATIVE	POSITIVE
NORMAL(55)	55	0	55	0
ABNORMAL(45)	0	45	6	39
100	55	45	61	39

The number of true positive cases for bone marrow biopsy was 39; true negative 55, false positive 0 and false negative 6 out of total 100. Thus, the Sensitivity of bone marrow biopsy in this study was 86.66%.

DISCUSSION

Bone marrow (BM) involvement in malignant disorders has an adverse effect on the prognosis and is an important factor in the choice of treatment modality. Histopathological examination for BM involvement is the best diagnostic method, but it can sometimes be misleading in patients with focal involvement. Moreover, bone marrow biopsy has some disadvantages. It is an invasive technique, may need anesthesia, and does not reflect the whole body. Unilateral and even bilateral iliac crest bone marrow biopsies have low sensitivity for BM infiltration, while MRI presents more global view of BM [9] and is highly sensitive. [10]

A total of 100 patients with known malignant disorders were studied during the study period. Among these 100 patients Genitourinary tract cancer (20%) and Multiple myeloma (19%) were the most common malignant tumors followed by Non-Hodgkin lymphoma (12%), Respiratory tract cancer (11%), Gastrointestinal tract cancer (11%), Breast cancer (10%), Hepatobiliary tract cancer (5%), Hodgkin lymphoma (4%), Thyroid cancer (4%), Sarcoma (3%), and Peripheral neuroectodermal tumor (1%). Among these

100 patients 55 cases were negative for marrow infiltration on both MRI and bone marrow biopsy, whereas 45 cases showed bone marrow involvement. Brunning et al. [11] reported bone marrow metastasis in 26 % (14/54) of cases which is very close to our study. Ringenberg et al. [12] stated that depending on the primary site, up to 25% of patients with cancer (other than lymphoma) will have metastases on BM biopsy specimen examination. According to Yun et al. [13] incidence was 11.9% (111/932) and in the study by Kilickap et al. [14] it was 1.9% (73/3842). The high incidence of bone marrow metastasis in our study may be because of less number of patients studied.

These 45 patients with bone marrow infiltration ranged in age from 8-80 years (Median, 57 years) and majority (42.22%) was in the age group of 51-60 years. Males constituted 62.23% and Females 37.77%. Generalized weakness and bone pains were the most common modes of presentation followed by weight loss, fever, bleeding manifestation and pathological fracture. Pallor due to Anemia was the most frequently observed sign along with Bony tenderness. Majority of cases with bone marrow involvement were anemic having Hemoglobin level $\leq 11\text{gm}\%$. Tsunoda et al. [15] in their study of 56 patients observed a median age of 58 years (range of 13-86 years). Males constituted 59% and females 41%. Male to female ratio was 1.43:1.

Of 45 patients with various malignant disorders 25 were of

Hematopoietic malignancy and 20 were of Non-Hematopoietic malignancy in our study. Out of 25 cases of Hematopoietic malignant disorders, 19(76%) comprised of Multiple Myeloma, 5(20%) Non Hodgkin Lymphoma and 1(4%) Hodgkin Lymphoma. Out of 20 cases of Non-Hematopoietic malignant disorders, 8(40%) comprised of Genitourinary tract cancer, 3(15%) Breast cancer, 3(15%) Gastrointestinal Tract, 2(10%) Respiratory Tract, 1(5%) Peripheral neuroectodermal tumor and 1(5%) Synovial sarcoma [Figure 1a and b]. In our series the most frequent primary sites of non-hematopoietic malignancies were genitourinary tract (40%), Breast cancer (30%) and

gastrointestinal tract cancer (27%). Francis and Hutter emphasized that any cancer can metastasize to bone. [16] Contreras et al. [17] reported most frequent primary sites as Breast (30%), Prostate (28%), Genitourinary (10%) and Gastrointestinal (10%). In the present study the frequency of marrow involvement detected by BM biopsy in patients with focal, scattered, and diffuse patterns on MRI was 42%, 81%, and 100%, respectively. Similarly, Tsunoda et al. have seen abnormal 'positive' images in 29 of the 56 patients (52%) which are very close to our study. The frequency of marrow involvement detected by focal, scattered, and, diffuse patterns was 0%, 52%, and 100%, respectively. [15]

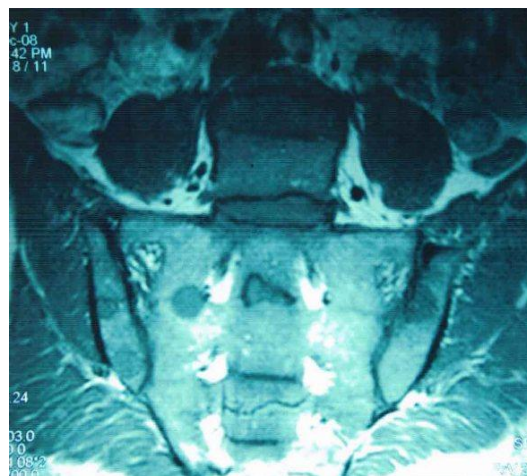
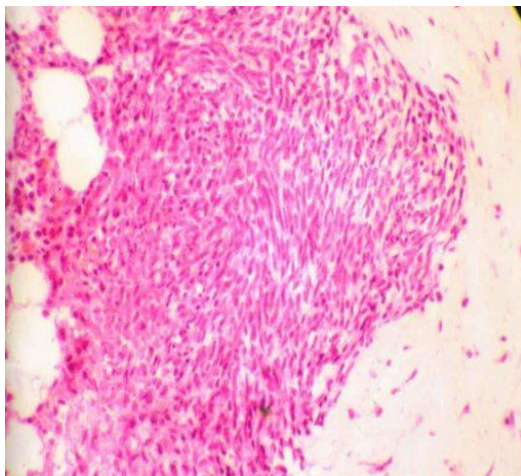


Figure 1a Bone marrow trephine biopsy showing Metastatic deposits in a case of synovial sarcoma (H&E X 400)
Figure 1b MRI of pelvis showing multiple focal patterns of abnormal marrow in a case of synovial sarcoma

Comparison of Frequency of Abnormal patterns on MRI in patients with marrow involvement

94% of cases showed good correlation between MRI and BM histology in the present study; similar findings were also reported by Dohner et al. in 26(86.66%) of cases while 4(13.33%) cases showed discordant results. [6] In our study discordant results between MRI and BM biopsy was seen in 6 (6%) of cases. The frequency of abnormal findings on BM biopsies was 39% (39/100) in the present

study. In our series malignant marrow infiltration was seen in 86.66% (39/45) of cases on BM trephine biopsy. Contreras et al. and SC NG et al. reported frequency of marrow infiltration in their studies as 94 % (94/100) and 83.33% (10/12) respectively. [17, 18]

The abnormal appearance of MRI in bone marrow disease appears to be related to the change that occurs in marrow once it has become infiltrated. Cohen et al. [19] emphasized the fact that images obtained are mainly those of fat located within the

marrow space. Normal bone marrow has high signal intensity at both T1 and T2 scan sequences due to its fat content. Any process that alters or replaces marrow fat will decrease the T1 signal. The T2 signal strength will depend on the type of tissue that replaces a normal marrow. Necrotic tissue, hematoma and inflammatory debris will have higher T2 signals than neoplastic tissue. Fibrotic or sclerotic tissue has low signal on both T1 and T2 weighted sequences. Our study indicates that MRI is a sensitive method for detecting areas of malignant marrow infiltration and it showed a sensitivity of 100%. We had no false positive or false negative cases in both hematopoietic and non-hematopoietic malignant disorders. Our findings are also supported in the prospective study by Daffner et al.; the sensitivity of MRI in detecting malignant infiltration was 100% in 50 patients with bone marrow metastasis, whereas radionuclide bone scans showed a 20% (10/50) false positive rate. In the same study MRI showed an accuracy of 100% in 30 patients with multiple myeloma, in contrast with the (10/30) false negative rate of radiography. [20]

Linden et al. reported sensitivity and specificity of MRI in bone marrow involvement to be 100% and 80% respectively. Their study included 107 adult patients with malignant lymphoma. [21]

These six cases that were negative for marrow infiltration on bone marrow biopsy (but showed marrow involvement on MRI) in our study however showed secondary changes [Figure 2a, 2b and 2c] in the bone marrow like increase in eosinophils (Hodgkin Lymphoma), mild prominence of lymphocytes (Non-Hodgkin Lymphoma), mild fibrosis (Infiltrating ductal carcinoma of breast), mild fibrosis and reactive plasmacytosis (Renal cell carcinoma) and hypo-cellular bone marrow with marked fibrosis, osteosclerosis and

focal area of necrosis (Carcinoma Cervix). These secondary changes in the marrow in such patients should be considered indirect evidence of marrow infiltration and all such patients should be subjected to MRI.

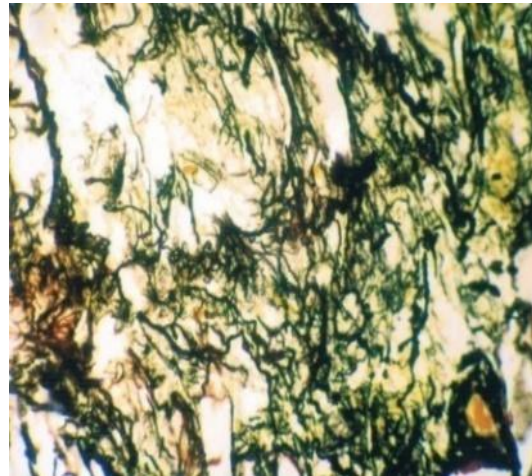


Figure 2a Bone marrow biopsy showing increase in reticulin density and thickness in a case of Carcinoma Cervix (reticulin stain $\times 400$)

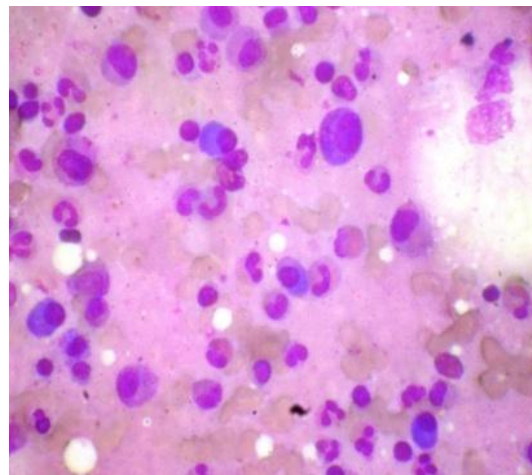


Figure 2b Bone marrow imprint smears showing reactive plasmacytosis in a case of renal cell carcinoma (MGG $\times 100$)

However, the sensitivity of bone marrow biopsy increased to same level when the secondary changes like fibrosis, necrosis, plasmacytosis, mild prominence of eosinophils in Hodgkin lymphoma and mild lymphocytosis in Non-Hodgkin lymphoma along with bone pains/tenderness, fever and Leukoerythroblastic blood picture were

considered as a consequence of marrow involvement.

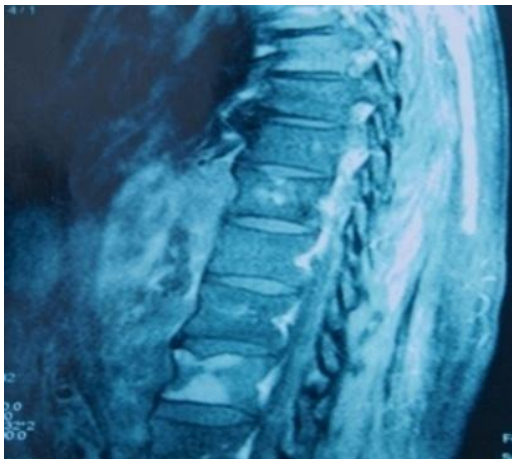


Figure 2c MRI of spine showing scattered pattern of abnormal marrow in a case of renal cell carcinoma which is negative on bone marrow biopsy

The sensitivity of MRI was 100% and the sensitivity of bone marrow biopsy was 86.66% for detection of marrow infiltration.

CONCLUSIONS

The current study shows that both bilateral iliac crest bone marrow biopsies and marrow MRI are important in establishing bone marrow involvement in cancer patients. The study also indicates that sensitivity of marrow MRI in detecting marrow infiltration is higher as compared to bone marrow biopsy especially when marrow is involved focally. The study also concludes that when bone marrow biopsy is negative for abnormal cells/foreign cells on light microscopy in such patients then secondary changes like fibrosis, necrosis, plasmacytosis associated with fever, bone pains/tenderness, severe anemia, and leukoerythroblastic blood picture should be suspected of consequences of marrow infiltration and these cases should be confirmed on marrow MRI.

Informed consent: “Informed consent was obtained from all individual participants included in the study.”

Compliance with Ethical Standards

Ethical approval: “All procedures performed in studies involving human participant were in accordance with the ethical standards of the institutional ethical committee.”

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