Original Article

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Morphological Spectrum of Bone Marrow Lesions in Various Hematological Diseases

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Abstract

Aim: This investigation was carried out to examine the diagnostic utility and value of bone marrow aspirate and biopsy in different hematological illnesses, as well as the part that both procedures play an important role in obtaining an accurate diagnosis when carried out in tandem.

Methods and Material: In order to link the results of bone marrow aspiration and biopsy in diverse hematological disorders, the pathology department at BGS GIMS undertook the current prospective investigation. Bone marrow evaluation using both marrow biopsy and bone marrow aspirate was performed on 106 participants in this study. Cases without or with insufficient bone marrow aspirate for an opinion were not included in the analysis.

Results: The age range of 31 to 40 years old was the most frequently observed, with a male majority. The most frequent finding was nutritional anemia, among those with nutritional anaemia, the most frequent finding was megaloblastic maturation (33.9%), micronormoblastic maturation (13.2%), and megaloblastic and micronormoblastic maturation (15.2%). Acute leukemia was 1.8% and chronic leukemia was 2.8%. Twelve cases (11.32%) of plasma cell dyscrasia were found in our study. Aplastic anemia, prostatic adenocarcinoma carcinoma metastasis, immune thrombocytopenic purpura (ITP), hematolymphoid malignancy, and myelofibrosis were among the other cases.

Conclusion: Both the bone marrow biopsy and aspiration are complementary procedures that aid in the identification of a range of haematological disorders. When combined with a clinical examination and auxiliary tests, bone marrow examination is a valuable diagnostic tool for the diagnosis of a variety of haematological illnesses.

Keywords: Megaloblast; Multiple myeloma; Myelofibrosis; Aplastic anemia and Idiopathic Thrombocytopenic purpura.

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INTRODUCTION

Both hematological and non-hematological illnesses can be diagnosed with the help of a bone marrow examination. One of the fundamental diagnostic pillars of hematological practice is the examination of bone marrow. It might also be crucial in diagnosing different storage and infiltrative illnesses and in the evaluation of patients with pyrexia of unknown cause (PUO). A bone marrow aspiration and a needle biopsy of the bone and surrounding marrow are two distinct but related specimens that are typically used in bone marrow examinations.[1]

In general, bone marrow aspirate smears are crucial for assessing the fine details of individual cells. However, it is impossible to accurately determine how different cell types relate to the cellularity of the marrow since aspiration destroys cell cohesion. An appropriate bone marrow core biopsy adds these crucial data. A bone marrow biopsy is necessary in the event of a "blood tap" or "dry tap." Therefore, in an effort to reach a more definitive diagnosis, we tried to link both of these factors.

In a wide range of clinical circumstances, including both hematological and non-hematological ones, bone marrow examination is the foundation for diagnosis and treatment. Two distinct but related techniques are required for a complete marrow evaluation. The cytological assessment of aspirated and smeared cells is the initial step. This makes it possible to differentiate counts and visualize cell morphology in high quality. The other method involves taking a bone marrow sample by percutaneous needle biopsy, which enables a histological evaluation of cellularity, fibrosis, infections, infiltrative disease, and disorders affecting the bone and its cells.

MATERIALS AND METHODS

Study design: Descriptive and prospective study

Study period: The present study was conducted from January 2020 - December 2022

Study settings: The present study was conducted in department of pathology at BGS GIMS from 2020-december 2022.

The physical examination, pertinent hematological, biochemical, and radiological studies, and other clinical data were documented.

The most favored location for both aspiration and biopsy was the posterior superior iliac spine. Under local anesthetic, 2% injection-plain lignocaine was used for the procedure.

Giemsa and Leishman stains were applied to bone marrow aspiration slides, and bone marrow biopsy fragments were allowed to decalcify for a full day before being processed and stained with hematoxylin and eosin stains. For the purpose of evaluating the iron stores in all anemia cases, aspiration smears and biopsy samples were stained with prussian blue. When necessary, additional specific stains such as Zeil Neilson stain, Periodic Acid Schiff, and Reticulin were applied.

Statistical methods were used to evaluate the data, including the Chi-square test and SPSS software version 22.0.

Ethical clearance was taken from institutional ethics committee (Ref: BGSGIMS/IEC/App/Dec/2023/006). Informed consent was obtained from all individual participants included in the study.

RESULTS

A total of 106 aspiration and biopsy cases were included in our investigation. We could determine the final diagnosis or offer suggestions for the course of the illness in 100 cases. Only minor erythroid hyperplasia was found in 6 instances, and no other substantial pathology was found. 60 men and 46 women were among the 106 instances that were examined. (Table 1) the range of ages was three to seventy years.

Table 1: Sex distribution of all cases that underwent bone marrow examination

Sex	No. of cases	Percentage
Males	60	56%
Females	46	44%
Total	106	100%

The age range of 31 to 60 years old, were 69 cases (65%; Table 2), accounted for the majority of the cases. In this investigation, there were several indications for undergoing bone marrow aspiration and biopsy. Pancytopenia was the most frequent cause, accounting for 46 cases (43.3%), followed by anemia under assessment in 20 instances (18.8%), patient investigation for probable myeloma in 10 cases (9.4%), acute leukemia in 10 cases (9.4%), and severe thrombocytopenia in 10 cases (9.4%) (Table 3). Aplastic anemia, probable myelodysplastic syndrome, and persistent leukemias were other indications.

Table 2: Age distribution of all the cases for whom bone marrow examination was done

Age	Number of cases	Percentage of cases
0 – 10 yrs	02	1.8%
11 – 20 yrs	06	5.6%
21- 30 yrs	19	17.2%
31 – 40 yrs	29	25.4%
41 – 50 yrs	21	20%
51 – 60 yrs	19	18%
61 – 70 yrs	10	9.4%
Total	106	100%

Table 3: Indication for bone marrow biopsy/aspiration

Indication	No. of cases	Percentage
Pancytopenia	46	43.39%
Anemia under evaluation	20	18.90%
Suspected acute leukemia	10	9.43%
Suspected chronic leukemia	5	4.71%
Severe thrombocytopenia	10	9.43%
Suspected multiple myeloma	10	9.43%
Suspected myelodysplastic syndrome	5	4.71%
Total	106	100%

Non-neoplastic lesions accounted for 81% of the lesions in the 106 instances in the current study, while neopalstic lesions made for 19%. (Table 4)

Table 4: Distribution of non neoplastic and neoplastic lesions

Diseases	No. of cases	Percentage
Non neoplastic	86	81%
Neoplastic	20	19%
Total	106	100%

The majority of bone marrow findings in the 106 patients in the current investigation were megaloblastic maturation in 36 cases during aspiration, and comparable results on biopsy were detected in 35 cases (Table 5). One case had a sparsely distributed biopsy. Megaloblasts, which are big cells with an elevated N:C ratio and sieve-like or stippled open chromatin that affect all phases of erythroid precursors, were discovered in these 35 cases of megaloblastic maturation. The leucopoiesis revealed the presence of band formations and large metamyelocytes. In fifteen of the cases, there was a decline in megakaryocytes. Prussian blue staining of the erythroid precursors in these cases revealed an increase in the quantity and size of iron granules. All 36 cases had deficiencies, according to a biochemical study of vitamin B12 and folic acid assay results.

Table 5: Distribution of bone marrow cases according to diseases

Bone marrow findings	Bone marrow aspirate	Bone marrow biopsy
Megaloblastic maturation	36 (33.9%)	35 (33.01%)
Micronormoblastic maturation	14 (13.2%)	14 (13.2%)
Megaloblastic and Micronormoblastic maturation	16 (15.09%)	16 (15.09%)
Erythroid hyperplasia with normoblastic maturation	8 (7.54%)	8 (7.54%)
Idiopathic thrombocytopenic purpura (ITP)	10 (9.4%)	10 (9.4%)
Aplastic anemia	1 (0.94%)	1 (0.94%)
Plasma cell dyscrasia	12 (11.32%)	12 (11.32%)
Acute Leukemia	2 (1.8%)	2 (1.8%)
Chronic Myeloid Leukemia	3 (2.8%)	3 (2.8%)
Hematolymphoid malignancy	2 (1.8%)	2 (1.8%)
Myelofibrosis	–	1 (0.94%)
Metastatic deposit	–	1 (0.94%)
Fragmented biopsy	–	1 (0.94%)
Total	106	100%

The current investigation included 14 examples of micronormoblastic maturation, which demonstrated erythroid hyperplasia and smaller micronormoblasts with fraying cytoplasmic borders, indicating a lack of hemoglobinization. Nuclear budding and karyorrhexis, two characteristics of dyserythropoiesis, were also noted. Megakaryopoiesis and myelopoiesis were both normal. Iron particles were almost completely absent, as shown by Prussian blue staining. In the majority of these instances, serum iron tests indicated an iron deficit.

Megaloblast and micronormoblastic maturation were both present in 16 instances. These instances' biochemical analyses revealed iron, vitamin B12, or folic acid deficiencies. In the present study total of 65 cases of nutritional anemia were identified.

Our analysis revealed 7.54% of erythroid hyperplasia with normoblastic maturation on aspiration and there was 100% concordance on biopsy.

There were 10 patients (9.4%) of idiopathic thrombocytopenic purpura who presented with thromcytopenia. bone marrow aspiration and biopsy revealed elevated hypo-lobated megakaryocytes (Fig. 1), which was consistent with peripheral platelet destruction; antiplatelet antibody levels were then correlated to confirm the diagnosis of Idiopathic thrombocytopenic purpura.

In this investigation, two cases (1.8%) of acute leukemia were found, with 80% of the blast on bone marrow aspiration and biopsy replacing the marrow components. One example was a 35-year-old male patient who had significant splenomegaly and pancytopenia. The peripheral smear revealed 50% blasts, which was subsequently confirmed by flow cytometry and a bone marrow investigation. In the second instance, a one-year-old girl baby had hepatosplenomegaly and recurring fever.

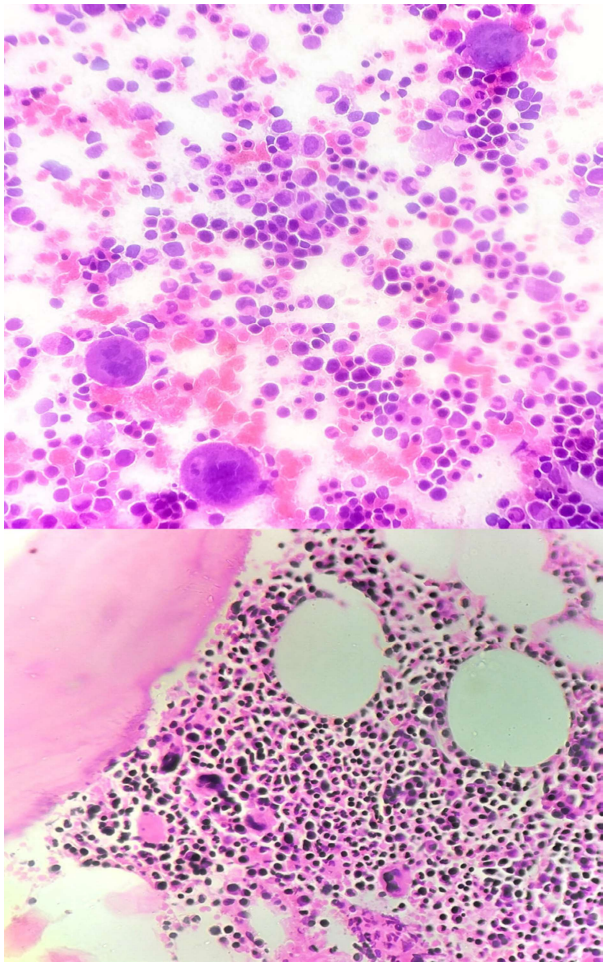

Fig. 1: Megakayocytic Hyperplasia In immune thrombocytopenic purpura; Aspiration (Upper) and Biopsy (Lower) Showing Increased Megakaryocytes MGG,X100 and Biopsy (H&E,X400)

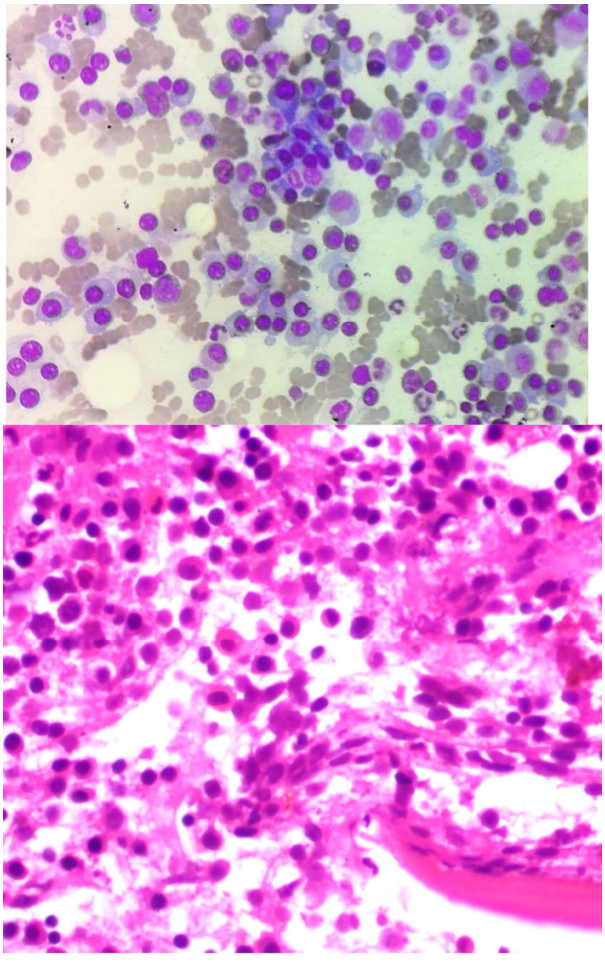

Fig. 2: Multiple myeloma: aspiration smears (upper) and trephine biopsy (lower) section showing sheets of plasma cells with few binucleated forms (MGG, H and E, 400X)

The peripheral smear revealed an 80% blasts, which was later confirmed by bone marrow examination and flow cytometry.

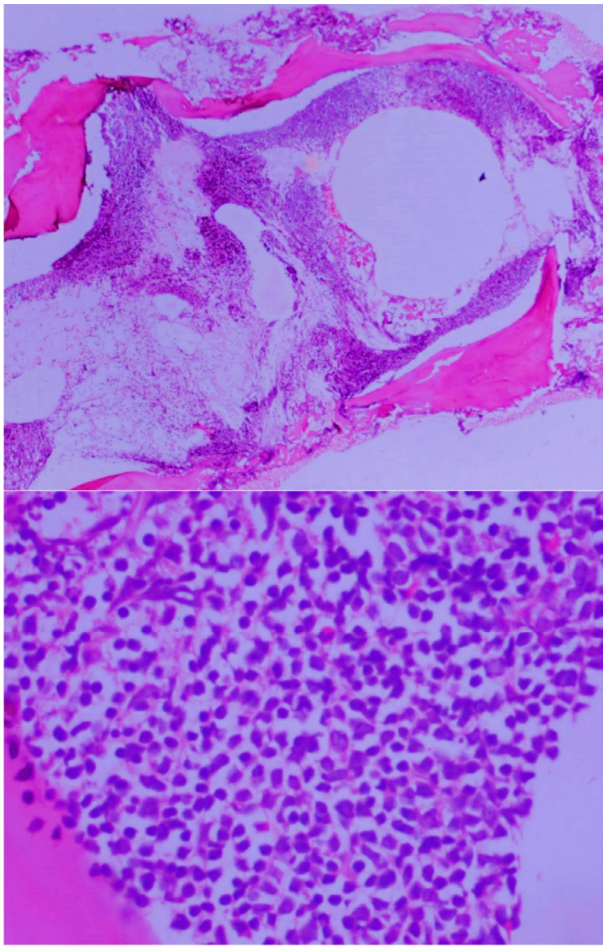

Fig. 3: Small lymphocytic lymphoma showing nodular & diffuse interstitial pattern in (H and E, 10x and 400x)

Two cases (1.8%) of chronic myeloid leukemia with 100% biopsy concordance were found in our investigation.

Twelve cases (11.32%) of plasma cell dyscrasia were found in our study. In each of these patients, we found a link between the bone marrow aspiration and the biopsy. It was recommended to use serum electrophoresis with immunofixation, and all instances demonstrated a M spike that was compatible with multiple myeloma.

In our investigation, one case of hematolymphoid cancer was identified. The results of the biopsy were consistent with aspiration, and the bone marrow was entirely replaced by a series of lymphoid cells.

A single case of myelofibrosis was noted in the investigation; a bone marrow biopsy was used to confirm the diagnosis after a dry tap resulted from bone marrow aspiration.

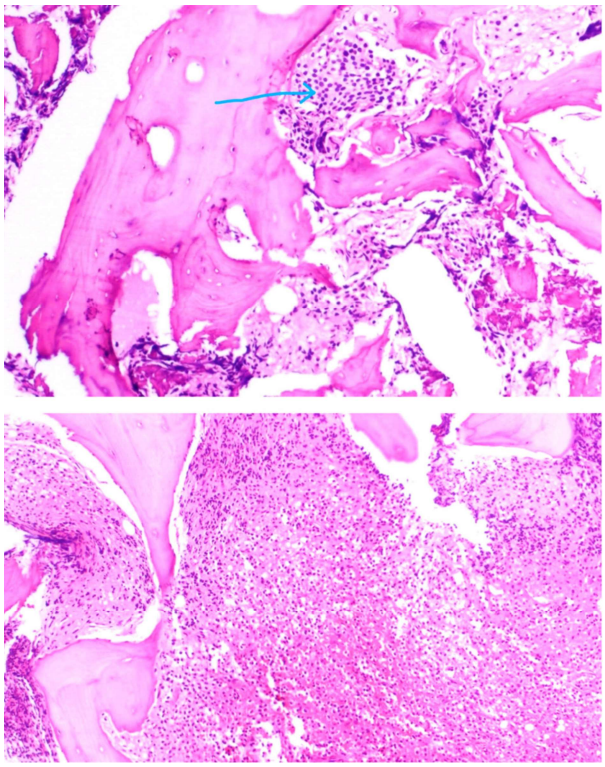

Fig. 4: Metastatic Prostatic Carcinoma: Trephine Biopsy Section Showing Metastatic Deposits of Prostatic Adenocarcinoma (H And E, 400x)

Three cases (2.8%) of chronic myeloid leukemia were observed in the current investigation, with 100% agreement between aspiration and biopsy findings.

DISCUSSION

The preferred technique for extracting bone marrow for diagnostic reasons is often vacuum aspiration of bone marrow particles using a wide-bore needle placed into the bone marrow cavity.

The benefits of this kind of method include the ability to practically immediately study films made from aspirated material and a higher level of morphological information than that found in histological sections of core biopsies collected by the trephine procedure. On the other hand, the bone marrow trephine shows some abnormalities such neoplastic cells or fibrotic material that may not be removed from the marrow cavity by suction and offers a more accurate indicator of the cellularity of hematopoietic elements.

Because each technique yields information that is cumulative, the total data have a higher diagnostic value than the information obtained from each procedure alone.

The most common locations for aspiration and biopsies in adults are the iliac crest and the body of the

sternum; in children younger than one year of age, the medial aspect of the proximal part of the tibia is the recommended location; in older children, the iliac crest should be used.

While the sternal bone marrow is thought by some to be more cellular, the operator chooses a different place for adults, and the iliac crest is preferred as it is not visible for the patient. and thus causes less anxiety.

We looked at 106 cases in our study, 46 of which were male and had a male to female ratio of 1.3:1. Similar results about the preponderance of men were noted by Kaur *et al.* and Shubhangi Agale *et al.*[2–3] The patients' ages range from 3 to 70 years old, with the age group between 31 and 50 years old being the most prevalent. Mehra *et al.* observed similar results.[4] The most common age group observed by Kaur *et al.*[3] is between 10 and 30 years old.

Similar to what Kaur *et al.* found, pancytopenia was the most frequent reason for a bone marrow examination in the current investigation.[3] Unexplained anemia was the most prevalent indication in a research by Shubhangi Agale *et al.*[2]

According to this study, both aspiration and biopsy results for 61.3% (65 patients) revealed signs of nutritional anemia. In their research, Shubhangi Agale *et al.*[2], Atla *et al.*[5], and Gohil *et al.*[6] found that, respectively, 52.4%, 50%, and 52.21% of the participants displayed signs of nutritional anemia. In 98% of these cases, there was concordance with the biopsy results. 70% concordance was reported by Shubhangi Agalle *et al.*[2] and 100% of cases showed positive correlation with bone marrow biopsy, according to Mehra *et al.*[4] We had micronormoblastic maturation at 13.2%, megaloblastic maturation at 33.9%, and a combination of megaloblastic and micronormoblastic maturation at 15%. 38% of megaloblastic and micronormoblastic maturation, 11.9% of micronormoblastic maturation, and 7.1% of megaloblastic maturation were noted by Shubhangi Agale *et al.*[2]

Compared with Shubhangi Agale *et al.*[2], our studied had predominantly megaloblastic maturation (33.9%). Kaur *et al.*[3] and Shubhangi Agale *et al.*[2] had 32% and 38.1% of megaloblastic and micronormoblastic maturation respectively while our study had 15.09% cases lower when compared to the above studies.

Our analysis revealed 7.54% of erythroid hyperplasia with normoblastic maturation on aspiration and there was 100% concordance on biopsy. Nearly identical to the findings of the current study, Shubhangi Agale *et al.*[2] reported 9.5% of normoblastic maturation in their investigation.

This study included two instances (1.8%), with acute leukemia, with 80% of the blast on bone marrow aspiration and biopsy replacing the marrow components. Similar to the current study, Shubhangi Agale *et al.*[2] reported 2.3% of cases of acute leukemia in their investigation. Our study's 100% aspirate and biopsy concordance in diagnosing acute leukemia was close to that of Shubhangi Agale *et al.*[2] but less so than that of Mehra *et al.*[4], who reported 28% of their cases to be leukemia.

In this investigation, three instances (2.8%) with chronic myeloid leukemia were found to have 100% concordance on both aspiration and biopsy. Tilak *et al.*[7] and Shubhangi Agale *et al.*[2] reported similar results.

12 cases (11.32%) of plasma cell dyscrasia were found in our investigation; this is more than what Shubhangi Agale *et al.*[2], Atal *et al.*[6], and Mehra *et al.*[4] reported. In every one of these patients, we found that bone marrow aspiration and biopsy correlated, as reported by Shubhangi Agale *et al.*[2], Chauhan *et al.*[8], and Charles *et al.*[9] Serum electrophoresis revealed the M band in each of these instances, and bone marrow plasmacytosis of over 60% of the plasma cells was seen. (Fig. 2) On presentation, six instances exhibited lytic bone lesions. We used the most recent criteria revised by the International Myeloma Working Group (IMWG) to diagnose plasma cell myeloma. The most notable observation made in each of these cases was the formation of a rouleaux on the peripheral smear. Combined, radiographic findings, bone marrow examination, and peripheral blood smear examination allowed the diagnosis of plasma cell myeloma.

In our analysis, two cases of hemato lymphoid cancer were identified. A 75-year-old female patient was assessed for pancytopenia after presenting with the condition. After bone marrow aspiration, over 80% of the lymphocytes proliferated, along with 10% of the prolymphocytes and just a small number of hematopoietic components. The results of the biopsy were consistent with aspiration, and the bone marrow was entirely replaced by a series of lymphoid cells. (Fig. 3) Subsequent analysis revealed numerous lymphadenopathy on the PET scan. Three cases of chronic lymphoid leukemia were reported by Shefali Verma *et al.*[10], which was more than what our analysis found.

The study included one case of myelofibrosis; a bone marrow biopsy was used to confirm the diagnosis after a dry tap resulted from bone marrow aspiration. Comparable results were noted by Vijayamohanan *et al.*[12], Thakur S. *et al.*[11], and Gilotra *et al.*[13]

In this investigation, one instance of metastatic

deposit was noted. The 78-year-old male patient was a confirmed case of prostatic carcinoma. Tumor cells were found to be invading in sheets and nodule patterns in both the aspiration and biopsy results. Thakur *et al.*[11] noted similar results.

Nevertheless, we only had one example of a fragmented biopsy, whereas Shubhangi Agale *et al.*'s study2 had two cases.

Bone marrow examination aspiration and biopsy are complementary methods for diagnosing hematological disorders. Aspiration offers high-quality cell information and is useful for diagnosing the majority of illnesses. Biopsies are helpful in determining cellularity, topography, aberrant infiltration, and fibrosis. Additionally, a biopsy is highly helpful if the aspiration produces diluted or dry tap marrow.

CONCLUSION

A bone marrow aspirate and biopsy are essential tests for the diagnosis of several haematological disorders. Despite being an intrusive operation, the benefits are timely, cost-effective, and mutually beneficial. In order to analyze cell features, architectural patterns, and arrangement to provide a definitive diagnosis with IHC and special stains done when necessary, aspiration and biopsy should always be performed in tandem.

Conflicts of Interest: Nil

Funding information: Nil

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