

THE ROLE OF THE BONE MARROW ASPIRATION AND TREPINE BIOPSY IN THE DIAGNOSIS OF HEMATOLOGICAL DISORDERS PRESENTING WITH PANCYTOPENIA

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ABSTRACT

Background: Pancytopenia is defined by reduction of all three formed elements of blood below the normal reference. It can be a manifestation of a wide variety of disorders, yet there is a few reported studies of the frequencies of various etiologies, and these frequencies exhibit substantial geographic variation. Bone marrow aspiration and biopsy evaluation along with good clinical correlation is of utmost importance to evaluate the causes of pancytopenia. **Aim of study:** The present study was a prospective clinicohaematological study under taken to analyze the various causes of pancytopenia by evaluating bone marrow aspiration and biopsy and correlating with clinical findings, complete blood counts and peripheral blood picture. The present study was under taken to evaluate the accuracy of the bone marrow aspiration and biopsy in the diagnosis of hematological disorders presenting with pancytopenia. **Methods:** This was prospective study Conducted in Tishreen academic hospital in Lattakia city, Syria, over a period of one year. A total of 70 patients (32 female, 38 male) with the diagnosis of pancytopenia were enrolled in the study, Written consent was obtained from patients to participate in the study. A detailed medical history, full physical examination, complete blood count with peripheral film, erythrocyte sedimentation rate, liver function tests and serology for viral hepatitis, ultrasonography of abdomen. Bone marrow aspiration and bone marrow biopsy have been done for all patients. Perl's stain, immune-histochemistry and reticulin were done wherever necessary. **Results:** The majority of cases were encountered in the age group of more than sixty years old. Infiltration disorders were the commonest cause (35.71%) followed by viral infections (25.71%), megaloblastic anemia (10%), aplastic anemia (10%), myelodysplasia (7.14%), myelofibrosis (7.14%) and leishmaniasis (4.28%). bone marrow biopsy was superior in the diagnosis of infiltrative lesions (100% versus 33-50%), in aplastic anemia (100% versus 0%) myelofibrosis (100% versus 0%) and myelodysplasia (100% versus 20%), while bone marrow aspiration was superior in the diagnosis of infectious lesions such as leishmaniasis (66.66% versus 33.33%). Bone marrow aspiration was diagnostic of in 100% of cases in megaloblastic anemia the bone marrow aspiration alone was conclusive in only 20 patients (25.71%), while the bone marrow biopsy procedure alone was conclusive in 50 patients (71.42%), and when the aspiration and biopsy were performed together, the diagnostic rate increased to 84.2% (59/70) patients. **Conclusion:** This study concluded that most common cause of pancytopenia is infiltration disorders followed by infections. The advantages of bone marrow aspiration and biopsy differ; both are complimentary to each other and should be performed simultaneously for a complete bone marrow work up and evaluation. Elaborate hematological investigations and bone marrow examination, both, in correlation with clinical findings are vital for the diagnosis of pancytopenia.

KEYWORDS: Pancytopenia. Bone marrow aspiration, Trepine biopsy.

BACKGROUND

The spectrum of disorders affecting the bone marrow may manifest with pancytopenia, which is defined as reduction in all the three formed elements of blood below

the normal reference range. The presenting symptoms are often due to either anemia or thrombocytopenia and leukopenia, which develops subsequently. Various disorders manifest with features of pancytopenia.^[1-3] The

mechanisms of pancytopenia include, decrease in hematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, in effective hematopoiesis with cell death, defective cell formation, antibody mediated sequestration or destruction of cells in a hypertrophied and overactive reticuloendothelial system.^[4] Bone marrow examination is an indispensable diagnostic tool in the evaluation of various hematological disorders, non-hematological malignancies, pyrexia of unknown origin and infective diseases.^[5] Clinical history, physical examination, primary hematologic investigations coupled with bone marrow aspiration is helpful in diagnosing underlying pathology in most of the patients with Pancytopenia. Bone marrow trephine biopsy provides overall cellularity, detection of focal lesion and infiltration. Flow cytometry may be needed in typing of leukemia.^[6-7]

Methods

This was prospective study conducted in Tishreen academic hospital in Lattakia city, Syria, over a period of one year from May 2016 to May 2017. A total of 70 patients (32 female, 38 male) with the diagnosis of pancytopenia were enrolled in the study, written consent was obtained from patients to participate in the study. Inclusion criteria (Hemoglobin < 9 g/dL, Leucocyte count < 4×10⁹/L and Platelet Count < 100×10⁹/L). A detailed medical history, full physical examination, complete blood count with peripheral film, erythrocyte sedimentation rate, liver function tests and serology for viral hepatitis, ultrasonography of abdomen, bone marrow aspiration and bone marrow biopsy have been done for all patients. Perl's stain, immune-histochemistry and reticulin were done wherever necessary. Various causes of pancytopenia were studied based on aspiration and biopsy findings. Significant parameters like etiology, age, gender, clinical features, hematological parameters, peripheral blood film, bone marrow aspiration and bone marrow biopsy findings in different cases of pancytopenia were compared with various studies published in literature.

RESULTS

70 patients (32 female, 38 male) with the diagnosis of pancytopenia were enrolled in the study. Patients' ages ranged from 14-90 years, with the mean age of the patients (50, 37) years, that 40% of the patients were over 60 years old as shown in (Figure 1).

We have studied the causes of pancytopenia in the study sample as shown in (Table 1,2), the study showed that Infiltration disorders were the commonest cause (35.71%) followed by viral infections (25.71%), megaloblastic anemia (10%), aplastic anemia (10%), myelodysplasia (7,14%), myelofibrosis(7,14%) and Leshmaniosis (4,28%).

We studied the accuracy of both bone marrow biopsy and bone marrow aspiration in diagnosis of pancytopenia, where bone marrow biopsy was superior in the diagnosis of infiltrative lesions (100% versus 33-50%), in aplastic anemia (100% versus 0%) myelofibrosis (100% versus 0%) and myelodysplasia (100% versus 20%), while bone marrow aspiration was superior in the diagnosis of infectious lesions such as Bone marrow aspiration was diagnostic of in leishmaniasis (66.66% versus 33.33%). 100% of cases in megaloblastic anemia without the necessity to bone marrow biopsy as an invasive procedure, as shown in (Table 3).

We studied the correlation between bone marrow aspiration and bone marrow biopsy in the diagnosis of pancytopenia in the study sample (70 pts.).(Table 4). where we found that the bone marrow aspiration alone was conclusive in only 20 patients(25.71%), while the bone marrow biopsy procedure alone was conclusive in 50 patients (71.42%), and when the aspiration and biopsy were performed together, the diagnostic rate increased to 84.2%(59/70) patients. It was observed through the study that bone marrow biopsy was conclusive in 50% of patients with conclusive bone marrow aspiration (9/18 patients) and in 64% with oriented bone marrow aspiration (16/25 patients) and in 92.59% of patients with non-conclusive bone marrow aspiration (25/27 patients). This study demonstrated the superiority of bone marrow biopsy in the diagnosis of pancytopenia compared to bone marrow aspiration and it increase the diagnostic value in the case of non-conclusive Bone marrow aspiration. On the other hand, bone marrow aspiration was diagnosed at (9/20 patients) non-conclusive biopsy (45%), which leads us to say that there is an Important positive association relationship between bone marrow aspiration and bone marrow biopsy in the diagnosis of pancytopenia and that they complement each other and conduct them together raises the accuracy of the diagnosis to more than 84%.

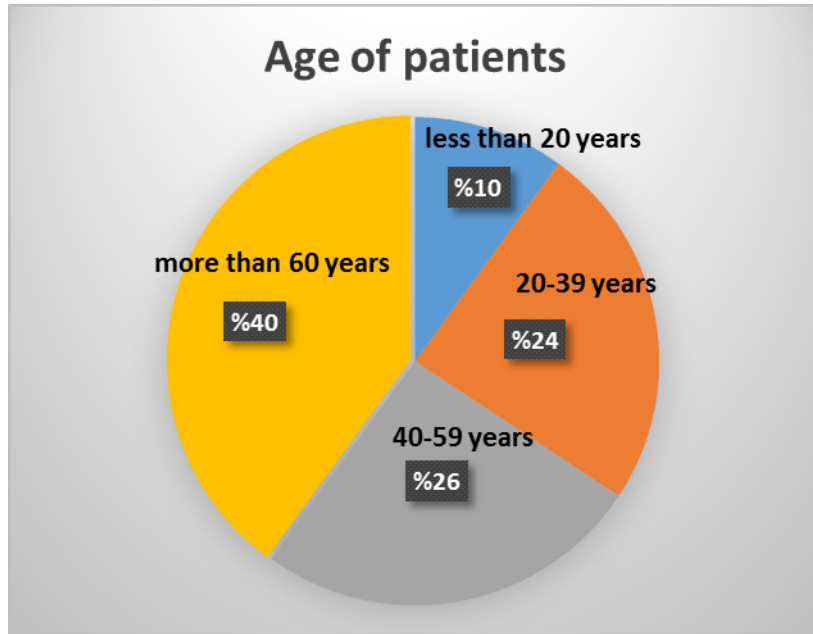
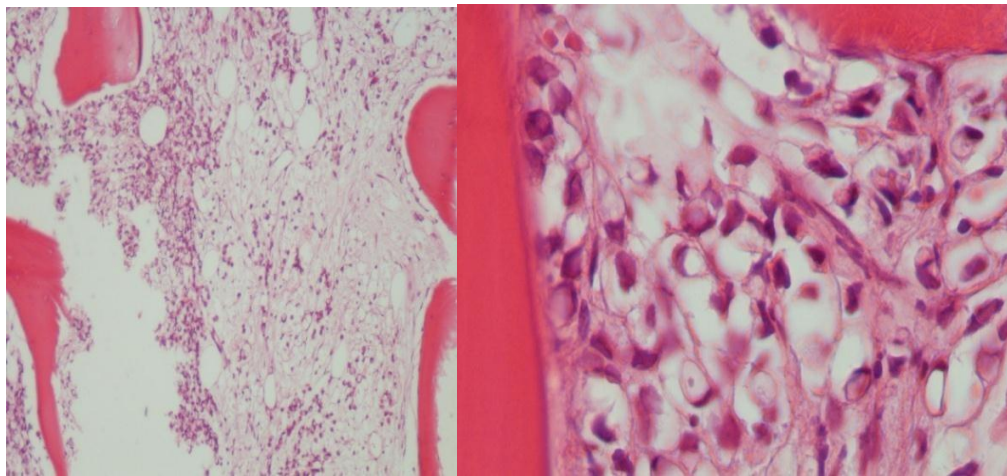
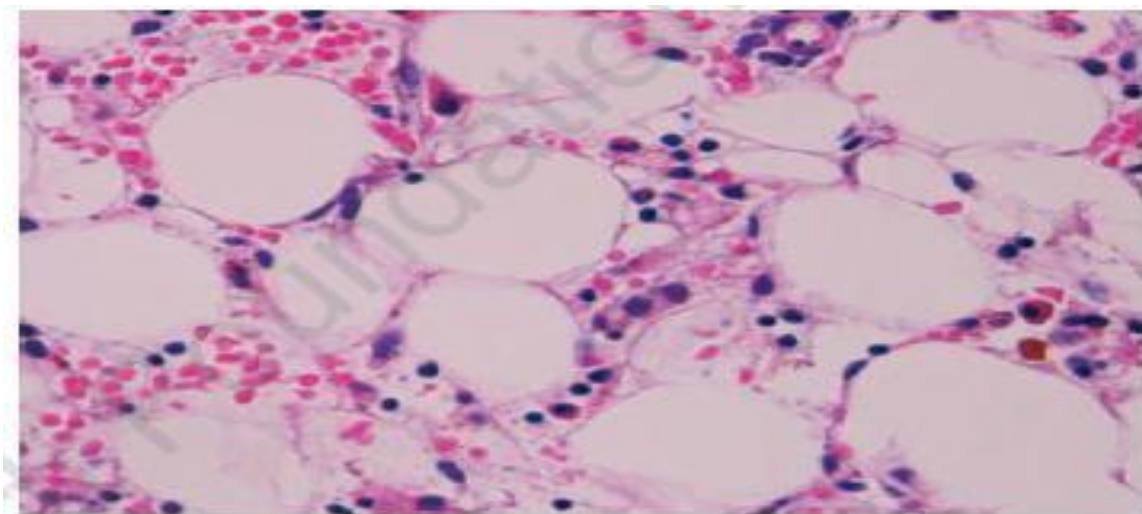


Figure 1



(A)

(B)



(C)

Figure (2): A and B: Bone marrow biopsy showing bone marrow infiltration with adenocarcinoma, C: hypocellular marrow with 90% fat in aplastic anemia.

Table (1):

Diagnosis		N	%
Infiltrations 25 Cases 35,71%	metastases	8	11,42%
	AML	6	8,57%
	ALL	4	5,71%
	HCL	4	5,71%
	NHL	3	4,28%
Viral infections		18	25,71%
Aplastic anemia		7	10%
Megaloblastic anemia		7	10%
Myelofibrosis		5	7,14%
Myelodysplasia		5	7,14%
Leshmaniosis		3	4,28%
Total Cases		70 pts	100%

Table (2):

Final diagnosis of pancytopenia						
diagnosis		BMA			BMB	OTHER
		N	Conclusive	oriented	Non conclusive	
Infiltrations 23 cases	Metastases	8	4	2	2	8
	ALL	4	2	0	2	4
	AML	6	2	2	2	6
	HCL	4	0	2	2	4
	NHL	3	0	2	1	3
Viral infections		18	0	9	9	0 serology
Aplastic anemia		7	0	4	3	7
Megaloblastic anemia		7	7	0	0	7
Myelofibrosis		5	0	0	5	5
Myelodysplasia		5	1	3	1	5
Leshmaniosis		3	2	1	0	1
Total cases		70 pts	18	25	27	50

Tablet (3):

Accuracy of bone marrow aspiration and biopsy in diagnosis in pancytopenia patients								
Diagnosis		N	%	conclusive BMA	%	BMB	%	p-value
Infiltrations 25 Cases 35,71%	metastases	8	11,42%	4	50%	8	100%	
	ALL	4	5,71%	2	50%	4	100%	
	AML	6	8,57%	2	33,33%	6	100%	
	HCL	4	5,71%	0	0%	4	100%	
	NHL	3	4,28%	0	0%	3	100%	
Viral infections		18	25,71%	0	0%	0	0%	
Aplastic anemia		7	10%	0	0%	7	100%	
Megaloblastic anemia		7	10%	7	100%	7	100%	
Myelofibrosis		5	7,14%	0	0%	5	100%	
Myelodysplasia		5	7,14%	1	20%	5	100%	
Leshmaniosis		3	4,28%	2	66,66%	1	33,33%	
Total cases		70pts	100%	18	25,71%	50	71,42%	

Tablet (4):

Correlation between bone marrow aspiration and biopsy in pancytopenia patients					
		Biopsy		Total numbers of aspirations	P-VALUE
		Conclusive	Non conclusive		
Bone marrow aspiration	conclusive	9	9	18	0,001
	oriented	16	9	25	
	Non conclusive	25	2	27	
Total of biopsies		50	20	70 pts.	

DISCUSSION

Pancytopenia is a common hematological finding with variable clinical presentations. It often creates diagnostic challenge to physician and the knowledge of accurate causes of this condition is crucial in the management of the patient.^[8-9] Bone marrow examination is a useful test in reaching the final diagnosis.^[10] Bone marrow examination is extremely helpful in evaluation of pancytopenia. Bone Marrow Aspirate Cytology (BMA), Touch Imprint Cytology (BMI) and Trepine Biopsy (BMB) are the three main basic preparations for bone marrow evaluation. Marrow aspiration is assessed for cytology and trephine biopsy provides overall cellularity, detection of focal lesion and infiltration. The severity of pancytopenia and underlying pathology determines the management and prognosis of patients.^[11]

Our study concluded that most common cause of pancytopenia is infiltration disorders followed by infections. There is an important positive association relationship between bone marrow aspiration and bone marrow biopsy in the diagnosis of pancytopenia and that they complement each other and conduct them together raises the accuracy of the diagnosis to more than 84%.

Sudha Horakereppa Metikurkea et al.^[12] found megaloblastic anemia was the commonest cause of pancytopenia. Clinical history and bone marrow examination is critical in arriving at the diagnosis. There was a positive correlation of 75.8% between BMA and BMB. Both the procedures were complimentary to each other and should be performed simultaneously. Rajesh H Chandan et al.^[13] Confirmed the same conclusion as the main causes of pancytopenia was Megaloblastic anemia (37%) followed by Nutritional anemia (31%), aplastic anemia (9%) and Leukemia (1.75%). Majority (79%) of the patients had hypercellular bone marrow followed by hypo cellular (13%) and normal cellular marrow (8%). hematological investigations and bone marrow examination, both, in correlation with clinical findings are vital for the diagnosis of pancytopenia. Bone marrow Aspiration and Trepine biopsy complement each other in diagnosis of challenging cases. Subuh Parvez Khan1 et al (14), found that the commonest cause of pancytopenia was megaloblastic anemia seen in 103 cases (30.8%) followed by dual deficiency anemia seen in 69 cases (20.7%). 37 cases (11%) were of acute leukemia. Aplastic anemia was seen in 35 cases (10.5%). Other causes of pancytopenia were myelodysplastic syndrome, multiple myeloma, iron deficiency anemia and hypersplenism. We note that most studies agree that megaloblastic anemia is the most important cause of pancytopenia, while our study showed that infiltrative lesions are the most common cause, and this may be due to different dietary habits, geographical distribution, and genetic predisposition to tumor lesions. Our study confirmed that the sensitivity of bone marrow biopsy is up to 100% in diagnosing aplastic anemia, myelofibrosis, and infiltrative lesions, and this is consistent with the

study conducted by Chauhan et al,^[15] where his study showed a high sensitivity of bone marrow biopsy of reaches up to 84% in the diagnosis of hematological and non-hematological lesions and considered it the golden means for diagnosing infiltrative lesions and aplastic anemia. As shown in **Figure 2**.

CONCLUSION

Our study confirmed that in patients with pancytopenia it is preferable to perform both bone marrow aspiration and bone marrow biopsy because this increases the rate of diagnosis.

Abbreviations: "Not applicable"

Declarations

Ethics approval and consent to participate

Written consent was obtained from patients to participate in the study, written informed consent was obtained from a parent for participants under 16 years old. Our study was approved by our institutional ethics committee in the faculty of medicine- Tishreen University

Consent for publication: written consent to publish this information was obtained from study participants.

Availability of data and materials: All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Competing interests: no conflict of interest.

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Authors Contributions: Corresponding author analyzed and interpreted the patient data.

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