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Yield of bone marrow evaluation in outpatients with neutropenia

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Abstract
Introduction and Research Problem: Establishing the cause of neutropenia in outpatients can be challanging. Thorough clinical and labortaoy evaluation are required. The yield of assessment of the bone marrow (BM) through BM aspiration and biopsy is not clear.
Materials and Methods: In this retrosepctive chart review investigators reviewed records of all patients who underwent BM assessment in King Adulaziz University Hospital between 1 January 2004 - 31 August 2015 and identfied outpatients who underwent the procedure for investigation of isolated neutropenia or with associated thrombocytoepnia and/or anemia.
Summary of Results: Among 2590 BM assessment procedures, 36 patients underwent the procedure for workup of neutropenia. 5 patients had isolated neutropenia and BM in these patients was either normal or showed mild hypocellulairty. In the 31 remaining patients with neutropenia assoicated with anemia and/or thrombocytopenia, various diseases were identified in BM such as leukemia and myelofibrosis.
Conclusion and Recommendations: None of the patients who had BM assessemnt for isolated neutropenia were found to have a hematologcial malignancy. However,the small sample size does not allow investigators to draw any generlizable conclusions.

Keywords: neutropenia, bone marrow biopsy, bone marrow aspiration, thrombocytopenia, malignancy

Introduction
Neutropenia is a common reason for hematology referrals. Neutropenia can be caused by a large number of diverse disease entities which may be congenital or acquired [1]. Identifying the cause of neutropenia among inpatients is typically a straightforward process, with drugs or malignancies being the commonest causes [2]. On the other hand, the work up in the outpatient setting can be exhausting. Investigations may include a combination of a large number of blood tests, imaging studies, and bone marrow evaluation using bone marrow (BM) aspiration and biopsy.

The research problem
While practicing hematologists recognize that BM aspiration and biopsy are recommended parts of the evaluation of some patients with neutropenia, the yield of these procedure is unclear. There are no published data how many patients among those undergoing BM evaluation will have BM pathology. There are also no data on predictors of abnormal BM findings, which may help the hematologist decide to perform the procedure earlier during the evaluation process.

Research Objectives
1. Identify the percentage of patients who had abnormal BM aspiration and biopsy when performed for investigation of neutropenia in the outpatient setting in King Abdulaziz University Hospital (KAUH).
2. Identify possible predictors of abnormal BM findings among the following data: age, severity of neutropenia, associated anemia or thrombocytopenia, mean corpuscular volume (MCV), and whether lactate dehydrogenase enzyme (LDH) was elevated.

Research Methodology
This was a retrospective chart review. Approval to conduct the study was granted by the Research Ethic Committee (Unit of Biomedical Ethics in KAU). Reference number No 271-15).
Investigators reviewed paper records of all patients who underwent BM aspiration and biopsy procedures between 1 January 2004 until 31 August 2015. Among those, only patients who underwent the procedure in the outpatient (day care) setting for evaluation of neutropenia were included. We also included patients who had neutropenia with associated anemia and/or thrombocytopenia. Electronic and paper patient records were then reviewed to collect demographics, results of complete blood count, LDH levels, results of BM aspiration and biopsy, flowcytometry, cytogenetics, and final diagnosis.

Results and Discussion
Between 1 January 2004 until 31 August 2015, 2590 BM aspiration and biopsy procedures were performed in KAUH. Among those, 36 patients underwent the procedure in the outpatient setting for work up for neutropenia (with or without abnormalities in hemoglobin and platelets). Ages ranged from 3 months to 85 years. Twenty-two patients were males.
Only 5 patients had isolated neutropenia with normal hemoglobin and platelet counts. Their data are summarized in Table 1.

Table 1: Summary of findings in patients who underwent BM evaluation in the outpatient setting in KAUH for evaluation of isolated neutropenia

	Age	Gender	Nadir neutrophil count K/uL	BM findings
1	16 y	M	0.9	Mild hypocellularity
2	50 y	F	0.39	Mild hypocellularity
3	49 y	F	0.6	Normal
4	15 y	M	1.3	Marked hypocellularity
5	43 y	M	Not available	Normal

Among the remaining 31 patients, all had accompanying thrombocytopenia and 30 had anemia.

Results of LDH testing were only available for 11 patients and were normal in all cases except in a patient who had hemophagocytic lymphohistiocytosis (HLH).

Findings of bone marrow evaluation in these patients are summarized in Table 2.

Table 2: Summary of findings in patients who underwent BM evaluation in the outpatient setting in KAUH for evaluation of neutropenia associated with anemia and/or thrombocytopenia.

BM findings	Number of patients	Age range	Comments
Normal	6	6-62 years	2 patients had splenomegaly
Hypocellular BM	10	2-53 years	3 patients were previously diagnosed with BM disorders (Aplastic anemia, Diamond-Blackfan anemia and red cell aplasia)
Acute leukemia	3	3-73 years	
Myelofibrosis	2	46-66 years	
Megaloblastic anemia	1	28 years	
HLH	2	3-7months	
Chronic myeloid leukemia	1	28 years	
Plasma cell dyscrasia	1	66 years	
Inconclusive	5	2-85 years	

Conclusion

Mild BM hypo cellularity was the most common finding in patients who had BM evaluation as part of the work up for isolated neutropenia in the outpatient setting. No malignancies were identified in this patient group. On the other hand, a variety of diagnoses were identified when outpatients had BM aspiration and biopsy procedures for work up of neutropenia associated with anemia or thrombocytopenia. BM hypo cellularity was the commonest abnormality but a number of patients with malignancies were identified.

The small sample size and the lack of some data limit our ability to draw any practice-changing recommendations or identify predictors that may allow physicians to safely abandon performing BM aspiration and biopsy procedures in this patient population.

Perspectives

Until further data are available, BM aspiration and biopsy should continue to be part of the evaluation for most patients with neutropenia if other investigations fail to identify an alternate cause for the hematological findings.

References

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