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STUDY OF PLATELET FUNCTION DEFECTS IN CASES OF CHRONIC MYELOID LEUKAEMIA

Haematology

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ABSTRACT

AIM: Chronic myeloid leukaemia (CML) is one of the chronic myeloproliferative disorders. The emerging data overwhelmingly suggests that study of platelet defects in CML would be useful for comprehensive management of CML. This study was conducted to identify the platelet function defects and to correlate the results with clinical symptoms in cases of CML.

METHODS: Clinical and laboratory data of CML patients, diagnosed and managed at a tertiary centre from January 2018 to September 2019 were analyzed. Patient's platelet rich plasma was subjected to platelet function tests (PFT) with Chronolog Dual Channel Platelet Aggregometer using arachidonic acid, epinephrine, adenosine diphosphate (ADP) and ristocetin as agonists.

RESULTS: Most cases of CML (30%) were from age range of 51 to 60 years and 83% of cases were male. Splenomegaly was seen in 97% of cases. Median haemoglobin was 13 g/dl and median total WBC count was 6.315 x 10^3/µL. About 64% of all cases showed the total platelet count of 201-300 x 10^3/µL. Median platelet distribution width (PDW) was 10.7 and median value of mean platelet volume (MPV) was 9.4. There was significant association between platelet aggregation response with ADP and bleeding manifestations. In 98% of cases showing normal platelet aggregation responses with ADP, bleeding manifestation were absent.

CONCLUSION: The present study suggests that platelet function defects are seen in CML. Platelet aggregation study can be useful especially in those patients exhibiting bleeding manifestations with normal or increased platelet counts. This would enable a comprehensive management in cases of CML.

KEYWORDS

Chronic myeloid leukaemia, Platelets, Aggregation defects, Haematology

INTRODUCTION

Chronic Myeloid Leukaemia (CML) is one of the chronic myeloproliferative disorders.[1] It is a clonal stem cell disorder characterized by reciprocal translocation of chromosome 9 and 22, t(9; 22)(q34;q11) resulting in the fusion of BCR/ABL gene observed on the derivative chromosome 22 called Philadelphia chromosome.[2, 3] The incidence of CML usually increases with age, with men being affected more often than women (3:2).[4] The aetiology of CML is unknown in most cases, although it may develop after radiation exposure.[5] One of the complications of CML is thrombotic and haemorrhagic diathesis.[6] They are correlated with the qualitative disorders of platelets.[7] Although there is no clear explanation for the absence of the relationship between thrombocytosis and haemorrhage in patients with CML[8], it is important to realize that the appearance of thrombocytosis in a CML patient may be of some prognostic significance, but does not constitute a medical emergency. Overall, emerging data overwhelmingly suggest that study of platelet defects in CML will be useful for comprehensive management of CML.[9] The present study was conducted to analyse platelet functions and to correlate the platelet function analysis with the clinical symptoms in cases of chronic myeloid leukaemia.

MATERIALS AND METHODS

The study was conducted at the Department of Pathology of a tertiary care hospital. The duration of study was from January 2018 to September 2019. A total of 100 cases of chronic myeloid leukaemia were included and the inclusion criteria were first 100 consecutive cases of CML diagnosed and managed in the Department of Pathology and Haematology during the time period of January 2018 to September 2019. The patients with platelet count less 100 x 10^9 /L in peripheral blood were excluded from the study. After obtaining the informed consent, the blood samples from patients who met the inclusion criteria were collected and platelet functional analysis was done with Chronolog Dual Channel Platelet Aggregometer. The agonists used for platelet function analysis were adenosine diphosphate (ADP), arachidonic acid, epinephrine and ristocetin.

Analysis of data

The data were analyzed using IBM SPSS statistics for Windows, version 22.0, New York: IBM Corp and Microsoft Excel for Windows, Version 2010: Washington: Microsoft Corp.

RESULTS

The minimum value of PDW was 7.5 and maximum value was 16.2. PDW value of 10.1 to 13 was most commonly seen in 64% of cases followed by 7.1 to 10 found in 23% of the cases. Regarding mean platelet volume (MPV), minimum value of MPV was 7.6 fL and maximum value was 11.8 fL. MPV value of 9.1-10 fL was most commonly seen viz. in 45% of cases.

For platelet function analysis, the agonists used were ADP, arachidonic acid, epinephrine and ristocetin, and the forms of aggregation tracing were analyzed. Responses were classified into normal and abnormal responses. Abnormal response included absent and decreased responses. Out of total 100 cases of CML, 95 cases showed normal platelet aggregation responses to all agonists. The two cases showed absent response with arachidonic acid, one case showed decreased response with arachidonic acid, two cases showed absent response with epinephrine, three cases show decreased responses with epinephrine, two cases showed decreased responses with ADP and one case showed absent response with Ristocetin. (Table 1)

Table (1) Platelet aggregation responses to different agonists in CML patients

Type of Responses	Numbers of patients with various response with four agonists			
	With Arachidonic Acid	With Epinephrine	With ADP	With Ristocetin
Normal	97	95	98	99
Absent	2	2	0	1
Decreased	1	3	2	0

In this study, platelet aggregation function analysis was compared with clinical features of CML including splenomegaly, symptoms of anemia like fatigue and weakness, and bleeding manifestations (table 2).

Table (2) Comparison between platelet aggregation responses and various parameters

Platelet Aggregation Responses		Spleno-megaly		*P* value	Fatigue and Weakness		*P* value	Bleeding Manifest-ations		*P* value
Agonists	Response	+	-		+	-		+	-	

Arachidonic acid	Normal	94	3	1	19	78	1	1	96	1
	Abnormal	3	0		0	3		0	3	
Epinephrine	Normal	92	3	1	19	76	0.58	0	95	0.05
	Abnormal	5	0		0	5		1	4	
ADP	Normal	95	3	1	19	79	1	0	98	0.02*
	Abnormal	2	0		0	2		1	1	
Ristocetin	Normal	96	3	1	19	80	1	1	98	1
	Abnormal	1	0		0	1		0	1	

* A significant association between platelet aggregation response with ADP and bleeding manifestations was seen with Fisher exact test *P* value being 0.02.

DISCUSSION

Various studies have assessed various forms of platelets aggregation responses in CML to determine the relevance of these abnormalities and infer whether these observations were of diagnostic importance.[10]

In our study the median MPV was 9.4 and median PDW was 10.7 whereas in the study by Yan K, et al., the median MPV was 11.4 and median PDW was 14.7.[11]

Our study showed that the commonest defect in platelet aggregation was with epinephrine, followed by arachidonic acid, ADP and ristocetin, which was similar to a study on abnormalities of platelet aggregation in chronic myeloproliferative disorders by Avarum *et al*., done in Romania.[12] There was no significant association between platelet aggregation responses and splenomegaly and symptoms of anemia such as fatigue and weakness in our study.

No significant association was detected between platelet aggregation responses with arachidonic acid, epinephrine, ristocetin and bleeding manifestations. But there was significant association between platelet aggregation responses with ADP and bleeding manifestations. Platelet aggregation function was compared with total platelet count, but no significant association was seen. This was in accordance with a study done by Fabris F *et al*. in which the platelet aggregation response did not appear to be related to circulating platelet number in cases of myeloproliferative disorders including CML.[13] In comparison between platelet aggregation responses with MPV, significant association was not detected. A study by Abdel Salam Ibrahim Bashier on abnormalities of platelet aggregation function in classic myeloproliferative neoplasm also showed no significant association between platelet aggregation abnormalities with MPV.[10] Furthermore, this study showed no significant association between platelet aggregation responses and platelet distribution width (PDW).

CONCLUSION

There was significant association between platelet aggregation response with ADP and bleeding manifestations. In our study, the platelet aggregation abnormalities were detected in cases of chronic myeloid leukaemia and therefore, the platelet aggregation study can be useful especially in those cases where the patient exhibit bleeding manifestations with normal or increased platelet counts. Since the platelet number is not the only factor that controls the thrombotic or hemorrhagic diathesis in CML, studying platelet function is important. Larger scale studies involving more number of patients and long-term follow-up are needed to identify and analyze platelet function defects in cases of chronic myeloid leukaemia. Hence, we recommend platelet function tests for comprehensive management of CML cases.

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Competing interests
None declared.

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