Indian Journal of Pathology and Oncology 2020;7(3):374–377

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Indian Journal of Pathology and Oncology

Journal homepage: www.ipinnovative.com

Original Research Article

Reactive thrombocytosis in malignancy- Can it be a strong predictor for IT

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ARTICLE INFO

Article history:
Received 28-01-2020
Accepted 18-03-2020
Available online 19-08-2020

Keywords:
Malignancy
Predictor
Thrombocytosis

ABSTRACT

Background: An increased platelet number may be secondary to many conditions. Malignancies are known to induce thrombocytosis in some cases. In patients with malignancies, thrombocytosis has previously been related to disease stage, histological type, and survival. Studies have shown that thrombocytosis is associated with a poor prognosis in various malignancies such as carcinoma ovary, cervical cancer, endometrial cancer, breast cancer and lung cancer. The aim of this study was to analyze the etiology and prevalence of thrombocytosis in malignancy and to assess whether platelet count can be used as a predictor of malignancy in the cases diagnosed as cancer at the time of its first diagnosis.
Materials and Methods: This descriptive study was done on 500 patients with platelet count > 450,000/ μl with the cause being termed reactive.
Result: The most common cause of reactive thrombocytosis was Infections (28.8%), Tissue damage (16.4%), Iron deficiency anemia (16.2%), Malignancy (9.6%) and Inflammation (9.4%). Among malignancies, carcinoma oral cavity (20.8%) was found to be more commonly associated with thrombocytosis; with only (4.2%) cases being less than 18 years, rest (95.8%) cases were above 18 years.
Conclusion: Thrombocytosis is associated with various neoplasms, therefore it can be used as a diagnostic clue for malignancy in an undiagnosed patient presenting with reactive thrombocytosis and associated symptoms of the disease thus indicating poor outcomes and mortality.

1. Introduction

Thrombocytosis refers to a platelet count above the normal value with the widespread use of electronic cell counters and the subsequent availability of a platelet count as part of a 'routine' blood count, thrombocytosis is more often observed as an unexpected finding. Thus, an elevated platelet count has become an important clinical problem for differential diagnosis. The association of thrombocytosis with malignancies has been known for more than 100 years.[1] Secondary thrombocytosis associated with malignancy, chronic infection, iron deficiency or chronic inflammatory diseases may persist for a longer time. Thrombocytosis was reported in patients with lung,[2] colon,[2] renal cell carcinomas,[3] cervical cancer,[4,5] ovarian cancer[6] and vulval cancers.[7]

2. Materials and Methods

The study was conducted over a period of 16 months in a tertiary care hospital. A total of 500 patients who had come to OPD or admitted patients having reactive thrombocytosis were taken up for the study. All the samples which were received by the Central Diagnostic Laboratory, with requisition form for investigations from the respective OPD's or wards and were found to have accidental thrombocytosis were taken. The cause for thrombocytosis was found to be reactive after taking the clinical details from the consulting physicians or surgeons. The information was collected and compiled in the master chart & further subjected to statistical analysis. Statistical analysis was done using the Cross tabulations for categorical data & correlation for continuous data in the SPSS ver.19 programme. Following parameter were included in my study: HISTOGRAM- The sample was run on the

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https://doi.org/10.18231/j.ijpo.2020.075

automated blood cell counter (Sysmex KX-21, K-1000) to know the platelet count, WBC, and MPV

2.1. Inclusion criteria

All patients who had come to the OPD and patients admitted in hospital (booked or emergency) having reactive thrombocytosis (platelet count >450,000/μl).

2.2. Exclusion criteria

Patients having platelet count more than 4.5 lakh/μl, but this was normal for their age as in paediatrics. Patient having thrombocytosis due to Myeloproliferative disorders (polycythemia vera, chronic myeloid leukaemia, chronic idiopathic myelofibrosis, essential thrombocytosis). Patient having thrombocytosis which is autonomous (primary) and not reactive (secondary).

3. Results

A total of 500 patients with the platelet count >450,000/ul was observed during the study period. Majority of the cases were between 38-56 years (31%) and 19-37 years (26%) (Table 1). Almost equal numbers of cases were studied in both the genders, males (50.8%) and females (49.2%) (Figure 1).

Causes of reactive thrombocytosis were as follows: infections (28.8%), tissue damage (16.4%), iron deficiency anemia (16.2%), malignancy (9.6%) and inflammation (9.4%), diabetes mellitus (6.4%), tuberculosis (6.0%), poisoning (2.0%), haemolytic anemia (1.8%), post splenectomy(1.0), hemorrhage (0.8%), myocardial infarction (0.4%), benign tumours(0.4%) low birth weight, megaloblastic anemia, CCF and drug reaction (0.2%) each respectively.

In malignancy, carcinoma oral cavity 20.8%, carcinoma breast 14.6% and carcinoma lung 14.6% were found to be more commonly associated with reactive thrombocytosis (Table 2). Only (4.2%) cases were studied in paediatric age group rest of the cases (95.8%) were adults (Table 3).

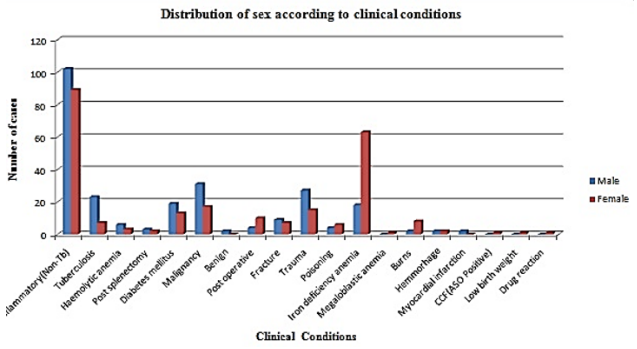

Fig. 1: Distribution of sex according to clinical conditions

Almost equal number of cases was studied in both the genders, males (50.8%) and females (49.2%).

4. Discussion

Given the importance of platelets, thrombocytosis serves as a pathological clue to diagnosis. In the present study the most common cause of reactive thrombocytosis was found to be infection 28.8% and malignancy accounted for 9.6% cases.

Among the malignant lesions, carcinoma oral cavity 20.8%, carcinoma breast 14.6% and carcinoma lung 14.6% were found to be more commonly associated with reactive thrombocytosis. This was similar to the study conducted by Levine S P et al[8] which showed that malignancy of lung and breast were more frequently associated with reactive thrombocytosis.

Our study examined the correlation between neoplasm and reactive thrombocytosis. Although there are several studies suggesting that platelets increase in various organ cancers, there were also some studies suggesting no change in platelet count in colon cancer, breast carcinoma, and gastric cancer.[9–11]

The relation between platelets and cancer progression suggests a possible role that extends beyond their hemostatic function. Platelets secrete cytokines and growth factors such as transforming growth factor-β, vascular endothelial growth factor (VEGF), matrix metalloproteinase-2, platelet factor-4, and platelet-derived growth factor which in turn induce hallmarks of cancer progression such as epithelial–mesenchymal transition, angiogenesis, cell migration, and/or proliferation and also facilitate the retention of tumor emboli in microcirculation.[12] Platelets also stimulate the release of pro-inflammatory cytokines (interleukin 1, 3, and 6) by cancer cells.[13] Thus, platelets are essential and have a multifunctional role in cancer development.

4.1. Thrombocytosis and oral cavity carcinoma

In my study carcinoma oral cavity was most commonly associated with reactive thrombocytosis, as it is the most common malignancy in India due to tobacco chewing. Association of reactive thrombocytosis with carcinoma oral cavity was also studied by Kannar V, Raja V, Suresh TN et al.[14]

Thrombocytosis and lung carcinoma

In an almost similar study done by Patel A, Abdeen Y, et al[15] the predictive role of thrombocytosis in identifying patients with advanced lung carcinoma in an urban medical center was studied.Thus concluding that accidental reactive thrombocytosis can be used as a diagnostic clue as well as predicator of malignancy.

In the present study 14.6% cases of breast malignancy having reactive thrombocytosis were found. A similar

Table 1: Number of cases in relation to age group

S. No.	Age in years	No. of cases	Percentage%
1.	0 - 18 years	105	21.0
2.	19 - 37 years	129	25.8
3.	38 - 56 years	155	31.0
4.	57 - 75 years	97	19.4
	76 - 94 years	14	2.8
Total		500	100.0

Table 2: Types of malignant lesion causing reactive thrombocytosis

S. No.	Disease	No. of cases	Percentage%
1.	Carcinoma oral cavity	10	20.8
2.	Carcinoma breast	7	14.6
3.	Carcinoma lung	7	14.6
4.	Carcinoma cervix	2	4.1
5.	Carcinoma maxilla	2	4.1
6.	Carcinoma oesophagus	2	4.1
7.	Carcinoma of post cricoid region	2	4.1
8.	Hepatocellular carcinoma	1	2.1
9.	Adenocarcinoma of ampulla of vater	1	2.1
10.	Borderline metaplastic brennertumor	1	2.1
11.	Carcinoma penis	1	2.1
12.	Carcinoma stomach	1	2.1
13.	Carcinoma testis	1	2.1
14.	Extraskeletal Ewing's sarcoma of left popliteal region	1	2.1
15.	Hodgkin's Lymphoma of right cervical lymph node	1	2.1
16.	Leiomyosarcoma	1	2.1
17.	Malignant small round cell tumor of chest wall	1	2.1
18.	Metastasis carcinoma to left level IIA lymph node	1	2.1
19.	Metastasis of poorly differentiated Carcinoma	1	2.1
20.	Metastasis of poorly differentiated SCC, in frontal lobe	1	2.1
21.	Squamous cell carcinoma of genital region	1	2.1
22.	Transitional cell carcinoma of bladder	1	2.1
23.	Unknown primary malignancy	1	2.1
Total		48	100

Table 3: Showing comparison of causes of reactive thrombocytosis in paediatrics and adults in malignancy

S. No	Causes	0 -18years		>18years		Total	
		No.	%	No.	%	No.	%
1.	Neoplastic a) Malignant	2	4.2	46	95.8	48	100
	b) Benign	2	100	0	0	2	100

correlation between platelet count and breast neoplasms was found by Harano K, Kogawa T et al,[16] who studied platelet count as a prognostic factor in breast carcinoma.

Thus thrombocytosis appears to be a universal marker of adverse outcomes in cancer. Its association with worse oncologic outcomes has been also reported in early and advanced breast cancer,[17,18] ovarian cancer,[19,20] genitourinary cancers[21,22] and several other types of cancer.[23,24]

5. Conclusion

Thrombocytosis is observed in many types of malignancies and many studies have indicated that an elevated platelet count may help in giving a clue for diagnosis and prognosis of malignancy. The prevalence of thrombocytosis associated with various cancers portrays a worse survival, independent of other clinical or biochemical factors. With further studies, this single independent prognostic factor may provide a simple approach to improved risk stratification of patients in future clinical trial protocols. Utility of platelet indices in diagnosis of cancer, determination of recurrence and in follow-up treatment, needs to be evaluated by further studies conducted on a larger population.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Garg B. Reactive thrombocytosis in malignancy- Can it be a strong predictor for IT. *Indian J Pathol Oncol* 2020;7(3):374-377.