Indian J Hematol Blood Transfus (Apr-June 2019) 35(2):352–356
https://doi.org/10.1007/s12288-018-1045-7

SHORT COMMUNICATION

Immune Thrombocytopenia is Still the Commonest Diagnosis on Consultative Hematology

Ram V. Nampoothiri[1] · Charanpreet Singh[1] · Deepesh Lad[1] · Gaurav Prakash[1] · Alka Khadwal[1] · Neelam Varma[2] · Pankaj Malhotra[1]

Received: 21 September 2018 / Accepted: 12 November 2018 / Published online: 13 December 2018

Abstract Thrombocytopenia is often a source of concern for physicians and patients alike and is one of the commonest reasons for a hematology consultation. Through this study, we wish to ascertain the different etiologies which should be kept in mind by a hematologist when a consultation for thrombocytopenia is sought. We assessed the etiology & clinical features of thrombocytopenia seen on consultative hematology calls for patients admitted in the general ward of a tertiary care hospital. 88/277 hematology consultations taken over a course of 2 months were for thrombocytopenia. The median age of these patients was 30 years, 62.5% were female, and median platelet of 40,500/μL (1000–112000). Mild, moderate & severe thrombocytopenia was seen in 6.8%, 27.3% and 65.9% respectively. 50% of patients had a primary hematological diagnosis. Immune thrombocytopenia (ITP) was the commonest diagnosis (38.6%). Bleeding manifestations were present in 48.9% patients with 20.5% having a major bleed. One third of hematology consultations in the general ward and emergency of a tertiary care hospital are for thrombocytopenia. Almost in half, the etiology of thrombocytopenia is related to a primary hematological disorder. This information should help in decision making of use of appropriate resources.

Keywords Consultative hematology · Thrombocytopenia · Immune thrombocytopenia · Bleeding manifestations

Introduction

Thrombocytopenia is frequently seen in hospitalized patients and is one of the common reasons for a hematology consultation. Thrombocytopenia has also been linked with the severity of disease, and has been shown to be an independent predictor of mortality in patients admitted in the intensive care unit (ICU) [1].

The hospitalized patients in the general ward for whom a hematology consultation is sought for thrombocytopenia may differ from ICU patients and general population. The pattern and understanding of thrombocytopenia in non-ICU setting would provide important insight to the particular specialty as well as the hematologist on call for appropriate utilization of resources. Thus, we undertook this study to analyze the prevalence, etiology and clinical manifestations of thrombocytopenia among patients seen in general inpatient consultative hematology services in a tertiary care hospital.

Materials and Methods

We conducted a prospective, observational, single institution study to analyze the causes of thrombocytopenia seen on hematology consult over a period of two months from March–April 2016. All adult patients (age more than 12 years) seen on the hematology consult services during this time period were included in the study after obtaining written informed consent from all participants and obtaining institutional ethical committee clearance.

✉ Pankaj Malhotra
hematpgi@gmail.com

[1] Department of Internal Medicine, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

[2] Department of Hematology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Thrombocytopenia was defined as a platelet count below the lower limit of normal (i.e., < 150,000/μL{150 × 10^9/L} for adults). Degrees of thrombocytopenia were further subdivided into mild (platelet count 100,000 to 150,000/μL), moderate (50,000 to 100,000/μL), and severe (< 50,000/μL) thrombocytopenia [2].

A diagnosis of immune thrombocytopenia (ITP) was made in all patients who were treatment naïve with a normal peripheral blood smear with either bone marrow showing features suggestive of ITP (i.e. megakaryocytic hyperplasia with normal morphology of other lineages) or a response (increase in platelet count more than 50,000/μL within 4 weeks) to a trial of steroids (oral prednisolone 1 mg/kg/day) or other immune-suppressants. Pseudothrombocytopenia was diagnosed in patients with no clinical symptoms of thrombocytopenia and with manual platelet count with citrate anti coagulated vial, found to be more than 150,000/μL with or without platelet clumps on the peripheral blood film. A diagnosis of drug induced thrombocytopenia was made in patients with no other apparent cause, and reversal of thrombocytopenia with withdrawal of the inciting drug. Disseminated intravascular coagulation (DIC) was diagnosed as a score of ≥ 5 in the DIC scoring system [3] in patients with an underlying disorder that can be associated with DIC.

A major bleeding episode in a non-surgical patient was defined as fatal bleeding and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome, or causing a fall in hemoglobin level of ≥ 20 g/L (1.24 mmol/L), or leading to transfusion of two or more units of packed red cells [4]. All non major bleeds further differentiated into clinically relevant and non relevant bleeds. A clinically relevant non major bleed was defined as an acute or subacute bleed that did not meet the criteria for major bleed but prompted a clinical response in the form of hospital admission for bleeding or a physician guided medical or surgical treatment for bleeding or a change in anti-thrombotic therapy, including interruption or discontinuation of a drug.

The number of platelet concentrates transfused to the patients were also studied and appropriate transfusions were classified as those given to patients with either 1) Active major bleeding or clinically relevant non major bleeding or 2) Platelet count less than 20,000/μL even with no/non major bleed or 3) Needed to improve platelet count to a specific target before a surgery or interventions, in accordance to the existing guidelines [5].

Results

A total of 88/277 patients (31.7%) aged underwent a consultation from hematology services for various hematological problems during the study period. This cohort had a median age of 30 years (range 22–53 years) with 62.5% (n = 55) females. The median platelet count of all patients with thrombocytopenia was 40,500/μL (range 1000–112,000/μL). Mild, moderate and severe thrombocytopenia was present in 6.8% (n = 6), 27.3% (n = 24) and 65.9% (n = 58) of patients respectively. 22.7% patients (n = 20) were admitted under initial emergency services (before shifting to ICU), while 25% (n = 22), 23.9% (n = 21) and 28.4% (n = 25) were admitted in the medical, surgical and gynecology wards respectively. The maximum number of consultations taken were from the department of gynecology, amounting to 28.41% (n = 25). The frequency of the final etiology of thrombocytopenia in each of these wards is highlighted in Table 1.

On evaluating for the etiology of thrombocytopenia, 50% (n = 44) of patients had a primary hematological diagnosis. ITP constituted the most common diagnosis amongst both the entire cohort, as well as patients with a primary hematological diagnosis, with a prevalence of 38.6% (n = 34). 4 patients were diagnosed with myelophthisis due to infiltration from non hematological primary malignancy. A diagnosis of antiphospholipid antibody syndrome, aplastic anaemia, and myelodysplastic syndrome was made in 2 patients each. Among the patients with a non hematological primary diagnosis (Table 2), DIC was the most common cause of thrombocytopenia, present in 11.4% (n = 10) of patients.

On comparing the different etiologies for thrombocytopenia across the four wards, calls for ITP (p = 0.002) and MDS (p = 0.05) were significantly more prevalent from the emergency department, APLA was most seen in the Medicine wards (p = 0.05), the prevalence of myelophthisis was significantly higher in the surgical ward (p = 0.003), and the gynecology department had a significantly higher number of calls for thrombocytopenia due to DIC (p = 0.028) and due to HELLP syndrome (p = 0.005). Only 4.5% (n = 4; 3—ITP, 1—drug induced) of patients were known to have pre existing thrombocytopenia and 95.5% (n = 84) of patients were newly diagnosed to have thrombocytopenia.

Forty-three (48.9%) patients had active bleeding manifestations at presentation with 18 patients having a major bleed and 21 patients had a clinically relevant non major bleed. All except 2 patients who developed bleeding manifestations had severe thrombocytopenia, while the remaining 2 had moderate thrombocytopenia as highlighted in Table 3. None of the patients with mild

Table 1 Frequency of various etiologies of thrombocytopenia across different wards

Ward	Final diagnosis												Total
	APLA	Aplastic anemia	Chronic liver disease related	Infection related	DIC related	Drug induced thrombocytopenia	Evans syndrome	HELLP	Immune thrombocytopenia	Myelophthisis	Pseudo thrombo-cytopenia	MDS	Unknown cause	
Emergency	0	0	0	2	2	0	0	0	14	0	0	2	0	20
Medical wards	2	0	2	2	0	4	0	0	6	0	4	0	2	22
Surgical wards	0	2	2	0	2	4	0	0	6	4	0	0	1	21
Gynecological ward/Emg	0	0	0	0	6	0	2	4	8	0	4	0	1	25
Total	2	2	4	4	10	8	2	4	34	4	8	2	4	88

APLA Anti Phospholipid Antibody Syndrome, *DIC* Disseminated Intravascular Coagulation, *HELLP* Hemolysis, Elevated Liver enzymes and Low Platelet counts, *MDS* Myelodysplastic Syndrome, *EMG* Emergency

Table 2 Frequency (N) and percentage (%) of the various non hematological causes thrombocytopenia

Diagnosis	N	%
Non hematological causes		
DIC	10	22.7
Drug induced thrombocytopenia	8	18.2
CLD related	4	9.1
Infection associated	4	9.1
HELLP syndrome	4	9.1
Evans syndrome	2	4.5
Pseudo-thrombocytopenia	8	18.2
Unknown	4	9.1
Total	44	

DIC Disseminated Intravascular Coagulation, *CLD* Chronic Liver Diseases, *HELLP* Hemolysis, Elevated Liver enzymes and Low Platelet counts

thrombocytopenia had any bleeding manifestations. The prevalence of bleeding significantly correlated with degree of thrombocytopenia (P = 0.001). 60.2% (n = 53) of patients received platelet transfusions during hospital stay. 58% (n = 51) of patients received random donor platelet (RDP) transfusions and each patient received a mean (± SD) of 2.94 (± 2.9) RDPs. 38.6% (n = 34) of patients received single donor apheresis platelet (SDAP) transfusions, with a mean (± SD) of 0.67 ± 0.82 SDAP transfusions per patient. A total of 7 patients (13.2% of transfusion receiving patients) were retrospectively adjudged to have received transfusions based on treating physicians discretion, not satisfying the transfusion guidelines [6].

Discussion

Consultations taken for thrombocytopenia are usually taken for a variety of reasons- to account for the risk of bleeding, to establish the etiology of the disease (either primary or secondary) and to formulate a treatment plan for the same. Our study found that 31.77% of all hematology consultations in the adult population in a tertiary care centre were for thrombocytopenia. Despite extensive literature review, we could not find any similar published literature which mentions the proportion of thrombocytopenia among all hematology consultations.

The prevalence of thrombocytopenia in hospitalized patients ranges from 0.9 to 6.3% across various studies [7, 8]. In a study conducted by Vaughan et al. [9], retrospective analysis of the laboratory database of full blood counts on seven non consecutive days of the year revealed the presence of thrombocytopenia in 8.6% patients who

Table 3 Frequency of various types of bleeding manifestations across varying severity of thrombocytopenia

	Type of bleed				Total
	No bleed	CNRMB	CRMB	Major bleed	
Severity					
Mild thrombocytopenia	6	0	0	0	6
Moderate thrombocytopenia	22	0	0	2	24
Severe thrombocytopenia	17	4	21	16	58
Total	45	4	21	18	88

CRNB Clinically relevant non-major bleed, *CNRMB* Clinically Non relevant non-major bleed

were being evaluated either in the inpatient or outpatient departments.

Majority of our patients had a primary hematological disease as the cause of thrombocytopenia. This is in contrast to most other studies which evaluated causes of thrombocytopenia among hospitalized patients, where non hematological causes predominate. In a study performed in South Africa by Vaughan et al. [9], sepsis and chemotherapy were the most common causes of thrombocytopenia and were present in around 20% of patients respectively. Similarly, in a study evaluating the etiology of thrombocytopenia among hematology consultations, Boxer et al. [10] found that 35.4% of patients had a primary hematological cause of thrombocytopenia with ITP being the most common hematological cause while liver disease was the single most common cause of thrombocytopenia overall. Although non hematological causes might predominate as the common etiologies of thrombocytopenia in hospitalized patients, most such cases have a degree of thrombocytopenia which might not be severe enough to warrant a hematology consultation. Thus, hematological causes (like ITP), with moderate—severe thrombocytopenia, predominate among those for whom a patients a consultative hematologist's opinion is taken.

13.2% of the patients receiving platelet transfusions in our study were adjudged to have been transfused inappropriately. In a recent single large center audit of platelet transfusions, Mahapatra et al. [11] found that nearly 31% of the total platelet transfusions were inappropriate as per guidelines and are based on the treating physicians discretion. A consultative hematology service would be integral in preventing inappropriate use of blood and blood products.

Conclusion

Consultative hematology can be a challenging task especially when it is for anomalies like thrombocytopenia with such varied etiology, severity and clinical presentation. A structured and methodical approach, with correct application of guidelines will solve the dilemma in most cases. Knowledge about the common etiologies of thrombocytopenia from different settings inside hospital will be of a tremendous help in approaching a case of thrombocytopenia. Our study shows that although hematological causes including ITP are the commonest cause of hematology consultation for thrombocytopenia in a hospital setting, the commonest etiology varies with the department from which the consultation is taken.

Funding No financial grant was obtained for the study from any organization.

Compliance with Ethical Standards

Conflict of interest The authors disclose no conflict of interest.

Ethical Standard All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Hui P, Cook DJ, Lim W, Fraser GA, Arnold DM (2011) The frequency and clinical significance of thrombocytopenia complicating critical illness: a systematic review. Chest 139:271–278
2. Williamson DR, Albert M, Heels-Ansdell D, Arnold DM, Lauzier F, Zarychanski R, Crowther M, Warkentin TE, Dodek P, Cade J et al (2013) Thrombocytopenia in critically ill patients receiving thromboprophylaxis: frequency, risk factors, and outcomes. Chest 144:1207–1215
3. Taylor FB Jr, Toh CH, Hoots WK, Wada H, Levi M, Scientific Subcommittee on Disseminated Intravascular Coagulation of the International Society on T, Haemostasis (2001) Towards definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. Thromb Haemost 86:1327–1330
4. Schulman S, Kearon C, Subcommittee on Control of Anticoagulation of the S, Standardization Committee of the International Society on T, Haemostasis (2005) Definition of major bleeding in

clinical investigations of antihemostatic medicinal products in non-surgical patients. JTH 3:692–694
5. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossetti G, Italian Society of Transfusion M, Immunohaematology Work G (2009) Recommendations for the transfusion of plasma and platelets. Blood Transf 7:132–150
6. Estcourt LJ, Birchall J, Allard S, Bassey SJ, Hersey P, Kerr JP, Mumford AD, Stanworth SJ, Tinegate H, British Committee for Standards in H (2017) Guidelines for the use of platelet transfusions. Br J Haematol 176:365–394
7. Teo CP, Kueh YK (1989) Incidence of thrombocytopenia in an acute care hospital. Ann Acad Med Singap 18:379–381
8. Fountain EM, Arepally GM (2017) Etiology and complications of thrombocytopenia in hospitalized medical patients. J Thromb Thrombolysis 43:429–436
9. Vaughan JL, Fourie J, Naidoo S, Subramony N, Wiggill T, Alli N (2015) Prevalence and causes of thrombocytopenia in an academic state-sector laboratory in Soweto, Johannesburg, South Africa. S Afr Med J 105:215–219
10. Boxer M (2012) Consultation for thrombocytopenia in hospitalized patients. Blood 120:4659
11. Mahapatra S, Ray GK, Paingrahi R, Mishra D, Sahoo B, Parida P (2016) Platelet audit: to weight the rationality between requirement and uses in blood transfusion. Int J Res Med Sci 4:4548–4551. https://doi.org/10.18203/2320-6012.ijrms20163327