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Original research article

A study of clinical profile of fever with thrombocytopenia

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Abstract

Infection is a commonest cause of thrombocytopenia, thrombocytopenia associated with fever helps to narrow differential diagnosis and management of fever. It also helps to know the various complications of thrombocytopenia and its management. 100 patients aged >14 years with fever and thrombocytopenia. Infection was the commonest cause of thrombocytopenia and dengue fever was the commonest infections. Bleeding manifestations were seen in 33% of patients. Among them 67% patients had Petichae/purpura as the commonest bleeding manifestation followed by spontaneous bleeding in 33%. Good recovery was noted in 93% while mortality was 7% Septicemia accounted for 43% of deaths, followed by dengue/VHF 14%. Infections, particularly dengue fever was the commonest cause of fever with thrombocytopenia. In majority of patients thrombocytopenias was transient and asymptomatic but in significant number of cases there were bleeding manifestations. Spontaneous bleeding was noted in platelet count of <20,000 in majority of patients, petichae/purpura was seen in platelet count in range of 20,000-40,000. On treating the specific cause drastic improvement in platelet count was noted during discharge and further follow-up.

Keywords: Infection, malaria, petichae/purpura, spontaneous bleeding, mortality

Introduction

Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is such a common manifestation of illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history [1].

Hippocrates and later during the Roman Empire, physicians gave detailed descriptions of fever and their varied patterns of presentations [1].

With the construction, in the early eighteenth century of an effective thermometer by the Dutch instrument maker Gabrial Daniel Fahreneheit, new interest surfaced in the relationship between body temperature and disease [2].

Modern research had its beginning in 1948 when Dr. Paul Beeson determined that fever is caused by a productof host inflammatory cells. Initially thought to be a product of polymorphonuclear leukocyte, this endogenous pyrogen is generated by mononuclear phagocytes. It is identical or very similar in composition to substances previously identified as lymphocyte activating factor (LAF), mononuclear cell factor and leukocyte endogenous mediator collectively known as interleukin-1 (IL-1). IL-1 has now been shown to have a major role in thermoregulation and fever [3].

Normal body temperature displays a diurnal pattern with lower values in the early morning hours and higher values in the afternoon. Normal ranges are between 35.8 °C (96.5°F) and 37.2 °C (99°F). Fever is superimposed on this pattern and thus temperatures are usually greatest in the afternoon and evening [4].

Fever is defined as an elevation of the body temperature above the normal circadian range as the result of a change in the thermoregulatory center located in the anterior hypothalamus.

An AM temperature of >37.2 °C (98.9°F) or a P.M. temperature of > 37.7 °C (99.9°F) would define fever [1].

Thrombocytopenia is defined as platelet count <150,000/µl. This is due to decreased production, increased destruction (immunogenic and non-immunogenic), increased sequestration in spleen. Of these infections being the commonest cause of thrombocytopenia [2], At times the fever course is prolonged and fever with thrombocytopenia narrows the differential diagnosis of the clinical entity [5].

Septicemia: Infections like malaria, dengue, leptospirosis, typhoid, HIV and military TB are some of the common causes of fever with thrombocytopenia [6].

Therefore a well-organized systemic approach that is carried out with an awareness of causes of fever with thrombocytopenia can shorten the duration of investigations and bring out diagnosis.

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Hence, a need for study to know the causes and complications of fever with thrombocytopenia.

Methodology

We prospectively collected a series of 100 patients with fever and thrombocytopenia.

Inclusion criteria

- The patients of both sexes aged > 14 years.
- Patients admitted with fever and found to have thrombocytopenia are included in the study.

Exclusion criteria

- Patients <14 years are excluded.
- Patients with fever and no thrombocytopenia are not included.
- Patients with thrombocytopenia and no fever are not included.

Once the patients admitted with fever and those who had thrombocytopenia, a careful history was recorded, general physical examination was done. Detailed examination of various systems was done. Routine investigation was done, the specific and special investigations were done as and when indicated.
In whom a final definite diagnosis was reached, were treated for the disease and platelet count was repeated at the time of discharge in all patients and no effort was made to gather follow-up information, if the patient was not followed up in our institution.
Details of history, general physical examination and laboratory and technical investigation reports were noted down from time to time.
Once the specific diagnosis was reached, patients were treated for it specifically and symptomatically.
For bleeding complications platelet transfusions was done if platelet count was <20,000/cumm.
The causes of fever with thrombocytopenia are so numerous, a simple workable classification is presented in-

1. **Viral causes:** CMV; Dengue; Parvo-B19; HSV, HIV, Hantana etc.
2. **Bacterial causes:** Gram +ve and -ve septicemia, miliary tuberculosis, leptospirosis, typhoid etc.
3. **Protozoal causes:** Malaria.
4. **Others:** Leukemia, lymphoma, etc.

Results

Table 1: Distribution of age

Age	Frequency	Percent
15 to 30	57	57.0%
31 to 45	20	20.0%
46 to 60	16	16.0%
Above 60	7	7.0%
Total	100	100.0%

Table 2: Incidence of males and females

Sex	Frequency	Percent
Female	37	37.0%
Male	63	63.0%
Total	100	100.0%

Table 3: Distribution of platelets

Plate count	Frequency	Percent
0 to 20000	13	13.0%
20000 to 50000	23	23%
50000 to 100000	60	60.0%
1 to 1.5 lakh	4	4%
Total	100	100.0%

Table 4: Clinical manifestations of thrombocytopenia

Bleeding	Frequency	Percent
Absent	63	58.0%
present	37	42.0%
Total	100	100.0%

Table 5: Bleeding manifestations

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Bledding manifestations	Frequency	Percent
Petechae	10	10.0%
Petechae/Purpura	6	6.0%
Purpura	8	8.0%
Spontaneous bleeding	13	13.0%
Total	37	37.0%

Table 6: Clinical manifestations of thrombocytopenia in relation to platelet count

Bleeding manifestations	0-20000	20000-50000	50000-1 Lakh
Petechae	0	3	7
Purpura	0	5	3
Petechae/purpura	2	4	0
Spontaneous bleeding	10	3	0

Out of 100 cases, a definitive a diagnosis could be made in all of them.
Among them dengue fever was the major cause accounting for 40 cases and 40% of the total cases. Second major cause was malaria 32 (32%) cases.
In malaria, vivax malaria accounted for 17 cases and 53% of the malaria cases, followed by falciparum malaria accounted for 10 (31%) cases and mixed malaria accounted for 5 (16%). followed by enteric fever 10 (10%), septicemia 9 (9%), and leptospirosis 3 (3%) brucellosis 1 case. 5(5%) cases remain undiagnosed.

Table 7: Incidence of various causes

Diagnosis	Frequency	Percent
Dengue	40	40%
Malaria	32	32%
Typhoid	10	10.0%
Septicemia	9	9%
Leptospirosis	3	3.0%
Brucella	1	1%
Undiagnosed	5	5%
Total	100	100%

Discussion

For a study of fever with thrombocytopenia, patients must satisfy the above mentioned criteria. Prospective case collection is necessary and careful follow up is warranted. These three conditions allow the delineation of a standard study population. The depth and means of exploration are also important but rather difficult to evaluate.
This study was conducted by Nair PS, Jain A, Khanduri U, Kumar V. (2003) at St. Stephen's hospital, New Delhi, for period of one and half years. A total of 109 cases (76 male, 33 female patients) were studied with the same criteria as in our study [7].
Septicemia with 29 cases was the leading cause of fever associated with thrombocytopenia. Second common cause was enteric fever followed by dengue, megaloblastic anaemia, malaria, haematological malignancy with 16, 15, 13, 10, 4 cases respectively [7].
Out of 109 patients 62 patients (56.8%) had platelet count between 50,000-1,00,000 followed by 28 patients (25.7%) had count between 20,000 to 50,000.
Out of 109 patients 45 patients had thrombocytopenic signs accounting for 41.3%. Out of 45 patients spontaneous bleeding was seen in 31 patients accounting for 69% of the bleeding manifestations [7].
During the course of follow up platelets showed increasing trends in 69 patients (63.3%) and continuously decreasing trends in 8 patients (7.3%) [7].
Totally infections represented the most important cause of fever with thrombocytopenia with a relative frequency ranging from 68%-100%.
In our study infections (95%) was the established diagnosis as compared to other study in which along with infection (68%), hematological conditions (15%), was also documented.
This may be due to seasonal and regional variations. But infection was the commonest cause of fever with thrombocytopenia.
Among infections, dengue fever (40%) was the commonest cause as compared to other study in which septicemia (27%) was the commonest cause. This is more likely due to seasonal and regional variations.
In our study septicemia was (9%) was the 4th most common cause of fever with thrombocytopenia, where as dengue (9.2%) was the 3rd common cause in other study.
In our study haematological condition did not present as fever with thrombocytopenia but in other study it accounted for 15%.
In our study malaria (32%) is the 2nd most common cause, where as it was the 5th common cause in other study.

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In our study distribution of platelet count in the range of 50-100 thousands is seen in 60% as compared to 56.8% in other study. Platelet count in the range of 20-50000 was seen in 23% and 25.7% in our study and other study respectively [7].

During the course of follow up platelet count showed increasing trends accounting for 63.3% and continuously falling counts in 7.3% in their study. In our study all the patients were monitored for platelet count on daily basis and except the mortality cases (7%) all other patients showed increasing trend during the hospital stay. Later 34% patients were followed up after 7 days and their platelet counts were within normal range. There was no decreasing trends of platelet count observed [8].

In conclusion our study of fever with thrombocytopenia reveals that infections as the commonest cause, among infections dengue fever was the common cause because of seasonal and regional variations. Definitive increase in platelet count was noted after the underlying cause was treated. Septicemia accounted for 44% of mortality in our study followed by dengue and malaria 22% each.

Infectious diseases group formed the major portion of patients presenting with fever and thrombocytopenia lacking any specific signs. Dengue, Malaria, enteric fever, leptospirosis and other infectious diseases formed the major chunk of this group.

Response to empirical therapy for locally prevalent disease may help the physician for better management of the patients.

Conclusion

- Fever with thrombocytopenia consists of occult presentations of common diseases rather than rare disease.
- Infection is the commonest cause of fever with thrombocytopenia.
- Among infection, dengue was the commonest cause.
- Malaria; typhoid; dengue, still present clinically in atypical and occult forms, making diagnosis difficult and prolonged. So high index of clinical suspicion is needed.
- So they should be investigated with some routine and specific test like rapid spot test for malaria antigen; IgM ELISA and NS1 antigen for dengue, IgM ELISA leptospiral antibodies, etc. for correct diagnosis.
- In majority of patients thrombocytopenia was transient and asymptomatic.
- In significant number of cases thrombocytopenia lead to various bleeding manifestations and influenced the clinical profile of these febrile illness.

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