



Routine funduscopy in immune thrombocytopenic purpura—is it really necessary?

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Abstract

Immune thrombocytopenic purpura (ITP) is a common cause of symptomatic thrombocytopenia in children, most of whom present with cutaneous and mucosal bleeding. Complications, such as intracranial hemorrhage and occult hemorrhage from various sites, are rare, and retinal hemorrhage is exceptionally rare. Our institutional clinical practice guidelines for managing ITP in the pediatric emergency department (PED) include routine funduscopy. The aim of this retrospective case series is to provide evidence-based recommendations for a tertiary care PED work-up of ITP, with special emphasis on the guidelines for funduscopy. The medical records of all pediatric patients diagnosed with ITP over a 4-year period (2013–2016) who had a platelet count $< 50,000/\text{mm}^3$ were retrieved and reviewed. Seventy-five patients with thrombocytopenia (platelet count $< 50,000/\text{mm}^3$) were diagnosed as having ITP in the PED. Sixty-one (79%) of these patients underwent funduscopy and retinal hemorrhage was ruled out in all of them, indicating that retinal hemorrhage as a complication of ITP is very rare.

Conclusion: Our data suggest that funduscopy should not be performed routinely on pediatric ITP patients, but rather be reserved for those who present with concurrent anemia or visual complaints.

What is Known:

• Many internal institutional protocols in Israel call for retinal hemorrhage bleeding surveillance in work up of ITP. Our study found no case of ITP with retinal bleeding.

What is New:

• Many internal institutional protocols in Israel call for retinal hemorrhage bleeding surveillance in work up of ITP. Our study found no case of ITP with retinal bleeding.

Keywords Funduscopy · Immune thrombocytopenic purpura · Occult bleeding · Retinal hemorrhage

Abbreviations

CBC Complete blood count
ICH Intracranial hemorrhage
ITP Immune thrombocytopenic purpura
PED Pediatric emergency department

PICU Pediatric intensive care unit
SD Standard deviation

Introduction

Immune thrombocytopenic purpura (ITP) is an acquired thrombocytopenia caused by autoantibodies that target platelet antigens, leading to platelet destruction [6]. It is a common cause of symptomatic thrombocytopenia in children, with an annual incidence between 1.9 to 6.4 cases per 100,000 children [6]. In the pediatric population, ITP typically presents as a sudden-onset petechial rash, bruising, or bleeding in an otherwise healthy child. Most commonly, children experience an antecedent viral illness, but other causes, such as recent measles, mumps, and rubella vaccination, can be present as well [12]. Children usually feel and appear well, and mucocutaneous bleeding is often the sole clinical finding. Systemic

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symptoms, such as fever, anorexia, bone or joint pain, and weight loss, are typically absent, and their presentation may suggest an alternative underlying pathology [12].

While most children with ITP present with cutaneous bleeding, up to 40% also have mucosal bleeding typically involving the nasal passages and buccal and gingival surfaces [6]. Patients with platelet counts $< 10,000/\text{mm}^3$ are more likely to have mucosal bleeding and, less commonly, intracranial hemorrhage (ICH) [12]. Nonetheless, these complications are rare, with only ~3% of patients experiencing serious hemorrhage that requires hospitalization and/or blood transfusion, and ~1% exhibit ICH [10]. Three bleeding scores [9] confirm that most children with ITP do not have serious bleeding problems despite very low platelet counts.

One complication of ITP other than overt bleeding is occult hemorrhage at various sites, one of them is retinal hemorrhage [2]. Little is known about the frequency and significance of clinically unapparent or occult hemorrhage in ITP [2]. Ophthalmic involvement in ITP is rare [2]; however, varying grades of anemia might accompany ITP with resultant ocular manifestations [5]. Although the basic underlying pathophysiology of ITP has been known for years [4, 5], reports in the literature indicate that the investigation and management of patients with thrombocytopenia vary widely [6]. It is not well established whether testing for occult bleeding should be part of standard care in ITP patients. According to the evidence-based practice guidelines of the American Society of Hematology [8], funduscopy is not a part of a standard ITP evaluation, and the only mandatory tests for ITP pediatric patients are a complete blood count and a blood smear. Our institutional clinical practice guidelines for managing ITP in the pediatric emergency department (PED) include routine urine microscopy and funduscopy.

The objective of this study was to provide detailed relevant information on all pediatric patients diagnosed with ITP in our PED who underwent funduscopy over a 4-year period (January 2012 and December 2016), and to explore the frequency of occult retinal hemorrhage on presentation to the PED in a cohort of children with ITP. Our goal is to provide evidence-based recommendations for refining a PED work-up of ITP.

Materials and methods

We retrospectively reviewed the medical charts of all patients between 0 and 16 years of age who were diagnosed at our PED as having ITP with a platelet count $< 50,000/\text{mm}^3$ during the study period. The medical records were reviewed, and data on the reason for referral, work-up, treatment, disposition, and follow-up were collected. Severe anemia was defined as hemoglobin levels $< 7 \text{ mg/dL}$ [11].

Results

During the 4-year study period, a total of 322 patients with thrombocytopenia presented to the PED, 295 of whom had a platelet count $< 50,000/\text{mm}^3$. We excluded 76 oncology patients, 26 patients with a diagnosis other than ITP (such as thrombocytopenia secondary to a known viral illness and congenital thrombocytopenia), and 108 repeat visits. Ten charts were illegible and those children were also excluded from the study. The remaining 75 patients with thrombocytopenia $< 50,000/\text{mm}^3$ who were diagnosed with ITP in the PED comprised the final study group. The demographic and clinical characteristics of these patients are presented in Table 1.

Table 1 Characteristics of the study population

	Patients ($n = 75$)
Median age (range), years	2.5 (0.5–16)
Male gender, n (%)	42 (56)
Platelets count, range (mm^3)	1000–50,000
Patients with platelet number $< 30,000/\text{mm}^3$, n (%)	63 (84%)
$= < 10,000/\text{mm}^3$	32 (42.6%)
10,000–30,000/ mm^3	31 (41.3%)
Reason for referral to PED	
Ecchymosis	47 (62.6%)
Thrombocytopenia on routine CBC	20 (26.6%)
Bleeding	6 (8%)
Fever	1 (1.3%)
Failure to bear weight	1 (1.3%)
Other manifestations	
Epistaxis	1 (1.3%)
Hematuria	1 (1.3%)
Severe anemia	1 (1.3%)
Funduscopy performed	61 (81.3%)
Disposition	
Admission to PICU	1 (1.3%)
Admission to pediatric ward	70 (93.3%)
Extended stay in PED	1 (1.3%)
Discharge	1 (1.3%)
Long-term follow-up	
Chronic ITP	11 (14%)
Lupus	1 (1.3%)
Funduscopy examination	61 (81.3%)
Funduscopy results:	
Normal	60 (89%)
Optic neuropathy (unilateral)	1 (1.6%)
Papilledema	0 (0%)
Retinal hemorrhage	0 (0%)

SD standard deviation, *PED* pediatric emergency department, *CBC* complete blood count, *PICU* pediatric intensive care unit, *ITP* immune thrombocytopenic purpura

Their median age was 2.5 years (range 0.5–16 years), and there was a slight male predominance (56%).

The mean platelet count of the study group on presentation was $15,400/\text{mm}^3$ (range $1000/\text{mm}^3$ – $50,000/\text{mm}^3$). There were 63 patients with a platelet count $< 30,000/\text{mm}^3$: 32 of them had a platelet count $\leq 10,000/\text{mm}^3$ and 31 had a platelet count between $11,000/\text{mm}^3$ – $30,000/\text{mm}^3$. Most of the patients (62%) were evaluated in the PED due to ecchymosis. Another prominent reason for PED referral (26.6%) was thrombocytopenia, which had been identified on a routine blood count. One patient had severe anemia with a hemoglobin count of 4 mg/dL.

Sixty-one (81%) patients underwent funduscopy (Table 1), and retinal hemorrhage was ruled out in all of them. One of those 61 patients was diagnosed with optic neuropathy. All funduscopies were completed either in the ED or during day 1 of admission to the regular pediatric ward. All 75 patients were followed-up after their PED stay to ensure that a final diagnosis of ITP had been made. The diagnosis of thrombocytopenia was later corrected in 12 children when their follow-up data were reviewed: 11 were diagnosed as having chronic ITP and one had systemic lupus erythematosus and was excluded from the study.

Discussion

Retinal hemorrhage without symptoms is known as “occult retinal hemorrhage,” and it represents a rare complication of ITP. None of the pediatric ITP patients in our current study were diagnosed with retinal hemorrhage, and only one patient had optic neuropathy that was diagnosed by funduscopy. Thrombocytopenia alone, even when it is severe (i.e., a platelet count $< 10,000/\text{mm}^3$), is rarely enough to cause significant retinal hemorrhage [5]. However, while thrombocytopenia combined with anemia is a known risk factor, retinal hemorrhage in association with ITP has only been reported to occur with concurrent severe anemia [1, 3]. For example, Carraro et al. observed that retinopathy is a frequent finding in severe anemic (hemoglobin [Hb] < 8 g/dL) and thrombocytopenic (platelet count $< 50,000/\text{mm}^3$) patients [1].

There are no large case series on the spectrum of fundoscopic findings in patients with ITP. The literature contains mostly single case reports [1, 3] on adult patients and includes vitreous hemorrhage, massive subretinal hemorrhages, and vitreous hemorrhage [1, 3]. Moreover, all the patients in these case reports had anemia combined with thrombocytopenia, and the anemia in most of them was severe. Goel et al. described a unique case of a 21-year-old woman who initially presented with decreased vision and vitreous hemorrhage, and was finally diagnosed as ITP with severe anemia [3]. The proposed mechanism was that the same antiplatelet antibodies can act similarly against the membrane protein of the blood

vessel endothelium, and that this damage can lead to macular exudate and exudates among the retinal vessels [3].

There are several series in the literature on retinal findings in other hematological diseases. In 1969, Holt et al. defined the incidence of retinopathy in various disorders of the blood, aiming to determine whether the lesions were of any diagnostic importance, and to identify abnormalities in the blood counts and associated prognosis [5]. Those authors concluded that retinal abnormalities were rarely of diagnostic significance, but that they reflected the severity of the anemia [5]. They did not detect retinal hemorrhage when the sole abnormality in the peripheral blood was thrombocytopenia. Mansour et al.’s recent study on ocular manifestations of idiopathic aplastic anemia demonstrated retinal hemorrhage in 37% of their subjects [7].

The physiological mechanism that explains retinal bleeding in aplastic anemia and other hematological diseases is completely different from that of ITP. Retinal bleeding in other hematological diseases is attributed to the anemia and lack of oxygen delivery to the tissue, leading to bleeding diathesis inside the eye [5] and to paradoxical hypercoagulability, resulting in a disseminate intravascular coagulopathy state [7]. We cannot conclude that the same ocular manifestations in aplastic anemia and other hematological diseases will occur in patients with ITP, who should not be anemic unless they have a severe bleeding due to thrombocytopenia [8]. Only one of our study patients had severe anemia, and he was finally diagnosed as having pernicious anemia. The results of his funduscopy were normal. One patient was diagnosed with optic neuropathy, but we assumed this was an incidental finding, and not related to the acute presentation of ITP. Moreover, there is no evidence in the literature regarding optic neuropathy in patients with ITP or other hematological diseases.

Our current findings confirm that retinal hemorrhage as a complication of ITP is very rare. We therefore recommend that funduscopy be reserved for patients with ITP who have visual complaints and for patients with concurrent severe anemia.

Authors’ contributions Tali Capua and Neta Cohen contributed significantly and equally to the planning of the study and the study design, performed statistical analysis and did major manuscript preparation. Adi Anafy and Dana Greisman collected data. Dror Levin contributed for manuscript expertise. Ayelet Rimon contributed significantly for manuscript editing and expertise.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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