

Corticosteroid Resistant Idiopathic Thrombocytopenic purpura: Case report and literature review

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Abstract

Idiopathic thrombocytopenia purpura (ITP), also known as immune thrombocytopenic purpura, is defined as isolated thrombocytopenia with normal bone marrow aspirate and the absence of other causes of thrombocytopenia. The first line of treatment of ITP is corticosteroids. We present a case of a patient who was diagnosed with ITP but his ITP was resistant to corticosteroids.

INTRODUCTION

The differential diagnoses of a patient with decreased number of platelets:

- Disorder of platelet production
- Viral Infections (Rubella, Mumps, varicella, Hep C, EBV, HIV)
- Bone marrow disorder (Hypoplasia, megakaryocytic aplasia, Alcohol induced marrow suppression)

Disorders of Platelet destruction:

- Idiopathic thrombocytopenic purpura (ITP)
- Thrombotic thrombocytopenic purpura (TTP)
- Disseminated intravascular coagulation (DIC)
- Pseudo thrombocytopenia
- Hypersplenism

Here is illustrated a case of decreased platelets fitting with diagnosis of steroid resistant Idiopathic thrombocytopenic purpura (ITP).

HISTORY

A sixty year old Hispanic male presented to us with the following complaints:

- Flu like symptoms and sore throat from last 2 days.

- Fever and chills from last 2 days.
- Pin Point red spots on different parts of body from last 1 day.
- One episode of epistaxis, one day before presentation.

There is no history of chest pain and shortness of breath, hemoptysis, and hematuria, black stools, bleeding per rectum or bleeding from any part of the body, previous history of blood transfusion, drug abuse and recent vaccinations.

He was diagnosed with hypertension 10 years back but he never used any anti-hypertensive medicines.

He used to take 20 bottles of bear per day from last 20 years and 1 pack of cigarettes from last 39 years.

He has no history of any hematological problem in his family.

ON EXAMINATION

A 60 year old Hispanic male, of average build with no obvious distress. His blood pressure at time of presentation was 200/120. He had diffuse petechial hemorrhage scattered over the whole body and bruises on both left and right lower legs. Petechial hemorrhages were also noted on the palate. There was no hepato-splenomegaly.

Figure 1

Fig 1. Petechie on legs

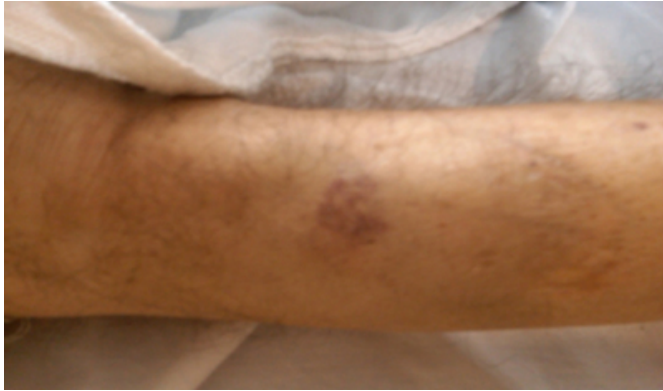


Figure 2

Fig 2: Bruises and Petechie on leg



Figure 3

Fig 3: Petechial hemorrhages on the palate



Investigations

Routine investigations show:

Figure 4

| | | |
|--|--|--|
| <ul style="list-style-type: none"> • Wbc: 5.3 • P = 59 • L = 22 • M= 60 • Hb: 14.9 • Hct:44.3 • Plt: 3 • MCV:93.2 • RDW:13.8 • PT: 13.8 • INR: 1.02 • PTT: 30.9 | <ul style="list-style-type: none"> • Na: 140 • K: 4.4 • Cl: 106 • Hco:-29 • BUN: 9 • Cr: 1.13 • Gluc: 160 • Ca: 9.5 • Mg : 1.6 • Phos : 1.9 | <ul style="list-style-type: none"> • ALT : 57 • AST :56 • ALK phos: 48 • Total Protein :18.1 • Albumin : 4.1 • Total Bil : 1.2 • Direct Bil : 0.6 |
|--|--|--|

HOSPITAL COURSE

In the emergency department, CT scan of the brain was taken to rule out any intracranial bleed because of the very low platelet count at presentation, which showed no significant findings. The patient was started in IV steroids and globulins with the diagnosis of ITP. Anti hypertensive therapy was also started because of the high presenting blood pressure. With this treatment, patient’s platelet counts came in normal range. IV globulins were stopped and steroids were tapered off and patient was discharged home with a stable platelet count on oral steroids.

But the patient again presented after 8 days with platelet counts of 9,000 and multiple petechie and bruises. Patient was again started on IV steroids and globulins and his platelets count began to increase. At this stage the patient was labeled as “steroid resistant ITP”. But patient refused for splenectomy. So he was discharged with stable platelet count on oral steroids.

Just in 6 days, he again presented with platelet count of 4,000. He was again started on IV steroids and globulins to get a stable platelet count to plan for elective splenectomy.

DISCUSSION

Definition:

In 1997, American Society of Hematology (ASH) described two criteria’s for the diagnosis of ITP;

Isolated thrombocytopenia with otherwise normal CBC and peripheral smear.

No other condition or factors that may cause thrombocytopenia.

Types of ITP:

- Acute ITP

- Chronic ITP

Figure 5

| ACUTE ITP | Chronic ITP |
|--|---|
| <ul style="list-style-type: none"> • More Prevalent in Late Spring to Winter • Prevalent among children <10 y • Peak incidence age 2-5 years • Equal male: female | <ul style="list-style-type: none"> • Thrombocytopenia for > 6 months • No seasonal predilection • More prevalent in adolescents and adults • 3:1 Female to Male • More likely to have underlying autoimmune disease |

Clinical presentation:

ITP is often diagnosed on the basis of routine labs, if thrombocytopenia is mild.

Most commonly, patients of ITP usually present with mucocutaneous bleeding (oral ulcers, epistaxis), menorrhagia, pupura; which is non-palpable, painless and localized to dependent areas.

Figure 6

Fig 4: Muco-cutaneous bleeding



Less commonly, ITP patients may present as GI bleeding, hematuria, intracranial hemorrhage and hemarthrosis.

Splenomegaly, if present, always suggests an alternate diagnosis.

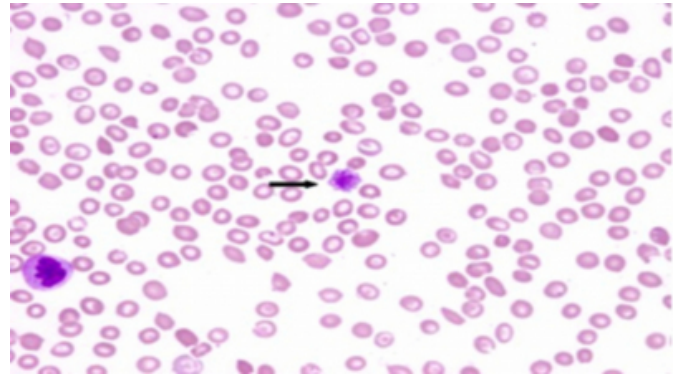
LABORATORY DIAGNOSIS

ITP is basically diagnosis of exclusion. On complete blood count, the hall mark of ITP is the isolated thrombocytopenia. On peripheral blood smear, Red blood cells and leukocytes are normal. The morphology of platelets is typically normal,

with varying numbers of large platelets. Some patients with acute ITP may have megathrombocytes or stress platelets, reflecting the early release of megakaryocytic fragments in to circulation.

Figure 7

Fig 5: Peripheral smear showing megathrombocytes



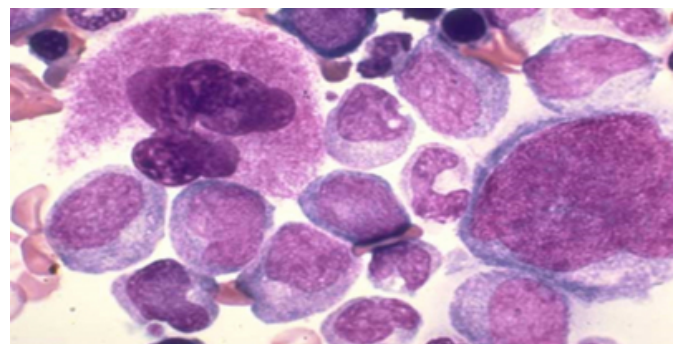
Assays for platelet antigen-specific antibodies, platelet-associated immunoglobulin, or other platelet antibodies are available in some medical centers. These tests are usually not recommended by American society of hematology because of poor positive/negative predictive values. Testing of anti-platelet antibodies is not required to diagnose ITP (1).

Computed tomography (CT) scanning and magnetic resonance imaging (MRI) are relatively benign and useful non-invasive imaging studies that can be used to rule out other causes of thrombocytopenia.

The primary diagnostic evaluation is bone marrow aspiration and biopsy. Patients with ITP have normal-to-increased number of megakaryocytes in the absence of other significant abnormalities. The cellularity of the aspirate and the morphology of erythroid and myeloid precursors should be normal (2).

Figure 8

Fig 6: Bone marrow Aspirate showing Megakaryocytes in the absence of any other abnormality.



MANAGEMENT

Major Bleedings are rare if the platelet counts are more than 10,000. Treatment goal for ITP is to get safe platelet levels and prevent bleeding.

American Society for hematology gives the following guidelines for the treatment of ITP,

Don't treat if,

Platelet count > 50,000 and patient is asymptomatic.

Consider treatment if;

Platelet count > 50,000 and there is mucous membrane bleeding.

Definitely treat if;

Platelet count < 50,000

Hospitalize if;

There is severe bleeding regardless of platelet count or platelet count < 20,000 and mucous membrane are bleeding.

Corticosteroids i.e. oral prednisone, IV methylprednisolone or high-dose dexamethasone is the drug of choice for the initial management of ITP. It's important to get the bone marrow biopsy to confirm the clinical presentation, because corticosteroids may change marrow morphology (3, 4, and 5).

IV immunoglobulin (IVIG) has been the drug of second choice. For Rh(D)-positive patients with ITP and intact spleens, IV Rho immunoglobulin (RHIG) offers comparable efficacy, less toxicity, greater ease of administration and a lower cost (6, 7).

In patients with acute ITP, splenectomy usually results in rapid, complete and life-long clinical remission. In patients

with chronic ITP, the results of splenectomy are less predictable.

REFRACTORY ITP

Refractory ITP is defined as platelet count < 50,000 for 3 months despite gluco-corticoids and splenectomy. There is no census on when and how to treat this condition. American society of Hematology makes no recommendations regarding treatment because of poor data quality.

In case of refractory ITP, withhold the treatment if platelet count is 10,000 to 30,000 and there is no significant bleeding. Chronic low-dose corticosteroids, IVIG, Anti-Rho and accessory splenectomy, Danazol and immunosuppressive/chemotherapy agents are the other available options for the refractory ITP.

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