"One Platelet Left"

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Dawn's Case

Dawn is a previously healthy 45-year-old female who presents with a two day history of "rash" and "unexplained bruising." She describes developing bruising on her arms (Figure 1) and petechiae on her legs (Figure 2), which have both now spread to her abdomen. She has several bruises on her arms and a blister on the lateral aspect of her tongue (Figure 3). Before coming to the emergency department, she had a brief episode of epistaxis.

She has no history of fever, headache, weight loss, or arthralgias. She takes no medications other than levothyroxine.

Upon examination, her vital signs are within normal limits. The petechiae and bruising are as described, and she has no hepatosplenomegaly or lymphadenopathy. The exam is otherwise unremarkable. There is no family history of bleeding disorders.

CBC reveals thrombocytopenia with a platelet count of 1.6 x 10^3/microliter, but other cell lines are within normal limits. The peripheral smear shows thrombocytopenia but no other abnormalities. Coagulation studies are normal.

Read on for more on Dawn.

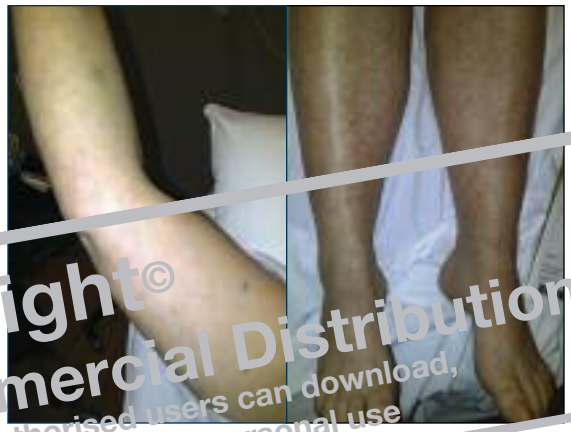

Figure 1 and Figure 2 (Left to Right): Bruising on arms; petechiae on legs

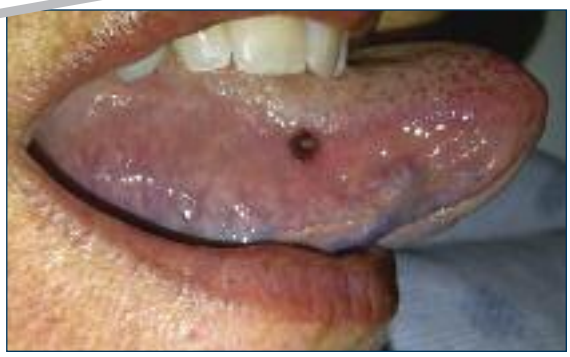

Figure 3: Blister on the lateral aspect of the tongue

Questions and Answers

1. What are the possible causes?

In this case the most likely etiology is primary immune thrombocytopenia (ITP), formerly idiopathic thrombocytopenic purpura. It is a disorder characterized by isolated thrombocytopenia (platelet count < 100 x 10^3/microliter). However, this is a diagnosis of exclusion, and it is critical to rule out other causes through history, physical examination, and testing.

The differential diagnosis includes (but is not limited to) thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), sepsis, Heparin (HIT) and other drug-induced

Table 1

Typical Signs and Symptoms of Various Causes of Thrombocytopenia*

Etiology	Associated Signs and Symptoms
ITP	A rapid onset of isolated bleeding, bruising, or petechiae, sometimes postviral or postvaccination
TTP	May have neurological changes (confusion, visual changes) or fever as well as signs of anemia and thrombocytopenia
DIC	Usually very unwell with significant bleeding due to coagulation defects. Fever, cough, dyspnea, confusion, possible signs of sepsis, obstetric complications, such as abruptio placentae, malignancy, or tissue trauma *(e.g.,* surgery)
Malignancy and other marrow infiltration	Associated symptoms may include fatigue/malaise, anorexia, bone pain, weakness, and other constitutional symptoms. Possible left upper quadrant discomfort associated with splenomegaly
Sepsis	Hypotension, fever, and other signs of sepsis
HIT	History of use of heparin or low-molecular-weight heparin
Drug-induced	Medications including quinidine, quinine, rifampin, and bactrim. Herbal remedies, such as tonic water have also been found to be causative agents
Cirrhosis / ETOH	History of alcohol abuse. Signs of liver disease, including hepatosplenomegaly, ascites, palmar erythema, spider telangiectasias, and jaundice

* Modified from Lichtin A: Evaluation of Thrombocytopenia. BMJ Point of Care 2011[2] and Rodeghiero F, Ruggero M: Idiopathic Thrombocytopenic Purpura. BMJ Point of Care, 2011[1]

thrombocytopenia, malignancy, viral infections (*e.g.*, HIV/CMV/mononucleosis), rheumatologic and hepatic disorders.

2. *How do we exclude other causes?*

History, physical examination, and initial laboratory investigations are used to differentiate ITP from other potential causes in the ED setting.

2a. History/Physical examination

Patients with ITP present with isolated bruising, bleeding, and/or petechiae (see Table 1). Reduced platelet count may also be an incidental finding. These patients usually feel otherwise well. There may be a history of recent viral illness, and it is important to ask about recent medication additions or modifications. It is also important to inquire about a personal and/or family history of bleeding disorders and malignancy. There are no specific groups at risk for ITP other than females of child bearing age and persons of either sex less than 10 years of age and greater than 65. Pregnancy is an important risk factor for TTP as are hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.

Table 2

Investigation Results for Various Causes of Thrombocytopenia*

Etiology	Investigation
ITP	• CBC with differential: *low platelet count* • Peripheral smear: *isolated low platelets; otherwise normal* • Serum PT and activated PTT: *normal*
TTP	• CBC with differential: *pancytopenia* • Peripheral blood smear: *schistocytes* • LDH: *elevated* • Reticulocyte count: *elevated* • Indirect bilirubin: *elevated* • PT and activated PTT: *normal* • Creatinine: *normal or elevated*
DIC	• CBC with differential: *pancytopenia* • Peripheral blood smear: *schistocytes* • PT and activated PTT: *elevated* • D-dimer: *elevated*
Malignancy and other marrow infiltration	• CBC with diff, peripheral: *disease specific* • *Disease specific testing (i.e., Imaging and bone marrow aspirate)*
Sepsis	• CBC with differential: *low platelet count, elevated WBC count* • Peripheral blood smear: *may be schistocytes* • Blood cultures: *may be positive* • PT and activated PTT: *elevated*
HIT	• Heparin aggregation study: *positive*
All Cases of Low Platelets	• CT scan brain: *if intracranial bleed suspected* • Pregnancy test: *in women of childbearing potential*

* Modified from Lichtin A: Evaluation of Thrombocytopenia. BMJ Point of Care 2011[2] and Rodeghiero F, Ruggero M: Idiopathic Thrombocytopenic Purpura. BMJ Point of Care, 2011[1]

2b. Investigations

Central to the diagnosis of ITP and differential is the CBC and peripheral smear. CBC shows isolated thrombocytopenia with no other abnormalities (see Table 2). In ITP, the peripheral smear shows no evidence of myelodysplasia or other abnormalities other than low platelets. Abnormal smears differentiate various other conditions, including schistocytes and nucleated RBCs with TTP or DIC, blasts in acute leukemia, and rouleaux formation in multiple myeloma.

Bone marrow biopsy/aspirate is indicated in patients older than 60-years-of-age or with atypical features for evaluation of myelodysplasia and other conditions.

3. *What is an approach to the treatment of ITP?*

The treatment approach to ITP in the Emergency Department setting is based on the platelet count and the presence and severity of bleeding.

The mainstay of treatment of patients with severe active bleeding (regardless of platelet count) is corticosteroids, intravenous immunoglobulin (IVIG) +/- platelet transfusion. For example:

- IVIG 1g/kg per day for 2 to 3 days
- Methylprednisolone 30 mg/kg per day p.o. for 7 days or
- Prednisone 1 to 2 mg/kg per day for 3 weeks then taper

Possible adjuvant therapy with aminocaproic acid and tranexamic acid is a consideration to stabilize clots, but it is notably contraindicated in patients with hematuria and high risk of thrombosis from other etiologies.

Patients with a platelet count < 30 x 10^3/microliter require corticosteroids (*i.e.*, Prednisone as described above or dexamethasone 40 mg/day for 4 days with 3 cycles every 2 weeks)

Patients with a platelet count > 30 x 10^3/microliter and bleeding symptoms require corticosteroids (*i.e.*, Prednisone as above).

Asymptomatic patients with a platelet count > 30 x 10^3/microliter are able to be observed with close clinical follow-up and repeated platelet counts with the occurrence of bleeding symptoms or surgery.

Back to Dawn

Dawn has a platelet count of 1.6 x 10^3/microliter! Additional investigations, such as LDH, bilirubin, and reticulocyte count are within normal limits. She is promptly given prednisone 75 mg p.o. and consented for IVIG 73 mg IV. She is transferred to the care of hematology for further investigations to determine secondary causes of ITP and to consider further treatment. Three days after admission, she has responded well to initial treatments with a slowly increasing platelet count and no further bleeding symptoms.

Splenectomy is reserved for patients who fail medical therapy. Consultation with a hematologist may be appropriate regarding diagnosis, treatment, disposition, and follow-up. Dx

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Resources

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