CLINICAL VIGNETTE

Petechial Rash in a Six-Month-Old Girl

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An otherwise healthy 6-month-old female infant presented to her primary care physician for her 6-month well-child check. During the visit, the parents indicated a viral infection 2-3 weeks prior. Since that time, they had noticed “red dots" on different parts of her body. These “red dots” had become even more prominent in the past 2 days, and the patient also seemed more fatigued than usual.

The patient was recently evaluated one month prior for 2-3 episodes of blood in stool. She had a normal appetite for the past 2 weeks and no episodes of fevers, headaches, joint pain, vomiting, hematuria, or rashes. The parents reported nasal congestion, without cough. They reported a small amount of blood-tinged mucus from her nares prior to presentation. They believed this was related to the use of a nasal aspirator to help clear her mucus. Her parents recalled other incidents that might have indicated a potential bleeding diathesis. At age 4 months, the patient experienced prolonged bruising after having her ears pierced. Two weeks before her well-child check, a forehead bruise secondary to a fall took a week to resolve.

Past medical and family history is significant for paternal grandmother with vitiligo, hyperthyroidism, and Type I Diabetes Mellitus, as well as a maternal great aunt with Type I Diabetes Mellitus. The patient was a full-term infant and received an infant multivitamin with iron, with no other medications or herbal supplements.

On exam, the patient was well-appearing, and without signs of acute distress. Skin exam noted diffuse petechiae on her chest, abdomen, back and her extremities. HEENT was clear of hemotympanum, conjunctival or retinal hemorrhages, and nares blood. Petechiae were noted on the hard palate, without signs of gingival bleeding. The rest of the physical exam was within normal limits including no hepatosplenomegaly, and no additional ecchymosis or bleeding. The patient was transferred to the emergency room for further evaluation.

CBC showed a white blood cell count of 12.4 x10E3/µl, hemoglobin 11.6 g/dL, hematocrit 33.7%, and platelets of 7000 (normal 214-459 k/µl). The manual differential and smear showed giant platelets, 17% neutrophils, 76% lymphocytes, 4% monocytes, 2% eosinophils and 1% basophils. The chemistry panel included: NA 130 mmol/L, K 4.5 mmol/L, Cl 108 mmol/L, BUN 10 mg/dL, Creatinine 0.22 mg/ldL CO2 24 mmol/L, glucose 89 mg/dL, Ca 10.6 mg/dL, Albumin 41 g/dL, total protein 6.8 g/dL, ALT 37 U/L, AST 44 U/L, Alk Phos 187 U/L, total bilirubin 0.4 mg/dL.

Bleeding studies included prothrombin time of 13.5 sec, APTT 32.3 sec, INR 1.02, Coombs was negative. Head CT showed no evidence of acute intracranial hemorrhage. The patient was admitted to the hospital and transfused platelets.

She was diagnosed with Idiopathic Thrombocytopenia. After IVIG, her platelets improved to 41,000 prior to discharge. Over the following months, the patient continued to have persistent thrombocytopenia less than 10,000, which was refractory to steroid therapy. Her evaluation included a bone marrow biopsy, which revealed normal trilineage hematopoiesis. Her CMV antigen was positive during the hospitalization. Rheumatology testing was positive for double-stranded DNA, and ABP+, low C3 transiently. UW showed an atypical stem cell-like myeloid blast population, with normal cytogenetics and flow cytometry.

Discussion

Immune Thrombocytopenia (ITP) is an immune-mediated hematological disorder in which impaired thrombopoiesis and autoantibody-induced platelet destruction combine to reduce total blood platelet count. ITP was previously known as *idiopathic thrombocytic purpura*, as researchers speculated about possible causes, including bacterial and viral infections, vaccinations, immune disorders, and exposure to some common medications such as ibuprofen and acetaminophen. This designation changed to *immune thrombocytopenia* to better reflect improved understanding of pathogenesis in the majority of patients, who do not present with apparent bleeding.[1] Provan, et al. reported that “77% of children have no or mild bleeding, 20% have moderate bleeding, and 3% have severe bleeding. Bleeding signs decreased during the follow-up period. Severe, life-threatening bleeding (i.e., intracranial hemorrhage) is rare, affecting less than 1% of patients.”[2]

Before ordering labs it is worth weighing the benefits of a readily available–if incomplete– explanation versus unnecessary testing with potentially misleading results. The majority of pediatric primary ITP diagnoses end in remission within 6 months of diagnosis.[1] Bleeding assessment tools, including the *Pediatric Bleeding Questionnaire* and *Self BAT and International Society on Thrombosis and Haemostasis* (ISTH) BAT are validated research tools used to assist in diagnosis in increasing number of clinical applications.[3] If the provider

decides to order lab evaluation, basic initial ITP testing should include:

CBC with WBC differential and RBC indices
Peripheral blood smear
Prothrombin Time (PT)
Activated partial thromboplastin time (aPTT)

For a more extensive testing, consider the pre-referral panel suggested by *Children's Hospital of Orange County's Children's Specialists in Hematology Program*. This includes:

Reticulocytes
Direct antiglobulin, if anemia is also noted
Panel 18, LDH, Uric Acid, UA, IgG, lgM, IgA
ABO typing
EBV serology
CMV serology
Parvo Virus serology
(ANA, HIV, HBV, HCV, fibrinogen, Von Willebrand plasma profile)[4]

Overtreatment and Spontaneous Remission

Aside from a low platelet count (<100 k/μL)[5] and an obligation to exclude other known causes of thrombocytopenia, there are no further specific diagnostic criteria or laboratory testing to establish ITP's pathogenic signature, account for the heterogeneity of clinical presentations or the variable responses to treatment. ITP, therefore, largely remains a diagnosis of exclusion. This exclusion process may mean patients can face a daunting roster of referrals, testing, and treatment. Therefore, newly diagnosed ITP patients should be carefully assessed to determine whether it is possible to prefer observation to (over)treatment. Many authors believe it is appropriate to defer the more extensive testing including, bone marrow biopsy, genetic testing, rheumatology, infectious disease labs until after the 6-month mark for the 20% of children who continue to present with bleeding symptoms and low platelets.[1]

Support

For patients, who continue to exhibit platelet dysfunction after 6 months, physicians associated with larger health systems may elect to refer to multidisciplinary resources like case management to help patients coordinate appointments, treatment, and results. The copious information already in the patient's medical record can be cumbersome to access, especially across different health systems. Motivated parents may be asked to collate an abridged timeline of significant lab and imaging results to bring to each specialist to encourage continuity of care and avoid duplicate testing. In-clinic patient education should include: when and where to seek care, acceptable forms of exercise and the exclusion of NSAIDS. This can help patients and families feel more empowered and prepared. Finally, early connection of patients and their families with support services through organizations such as *National Organization for Rare Disorders* or *the Platelet Disorder Support Association* (PDSA) can enhance care by providing financial assistance, age-appropriate education, as well as reliable caregiver information.[6] These resources can deepen patients' and caregivers' engagement with their treatment team and provide a community to rely on for support.

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