Consultant360 Multidisciplinary Medical Information Network

CASE IN POINT

PEER REVIEWED

Idiopathic Thrombocytopenic Purpura

Authors:
Frederick Hernaez, MD
Graduate, American University of the Caribbean, Sint Maarten

Anne Margaret Hernaez, MS-IV
St. Matthew's University, Grand Cayman, Cayman Islands

Nida Blankas-Hernaez, MD
Attending Physician, Advocate Lutheran General Hospital, Park Ridge, Illinois;
Hospitalist/Consultant, Ann & Robert H. Lurie Children's Hospital of Chicago, Illinois

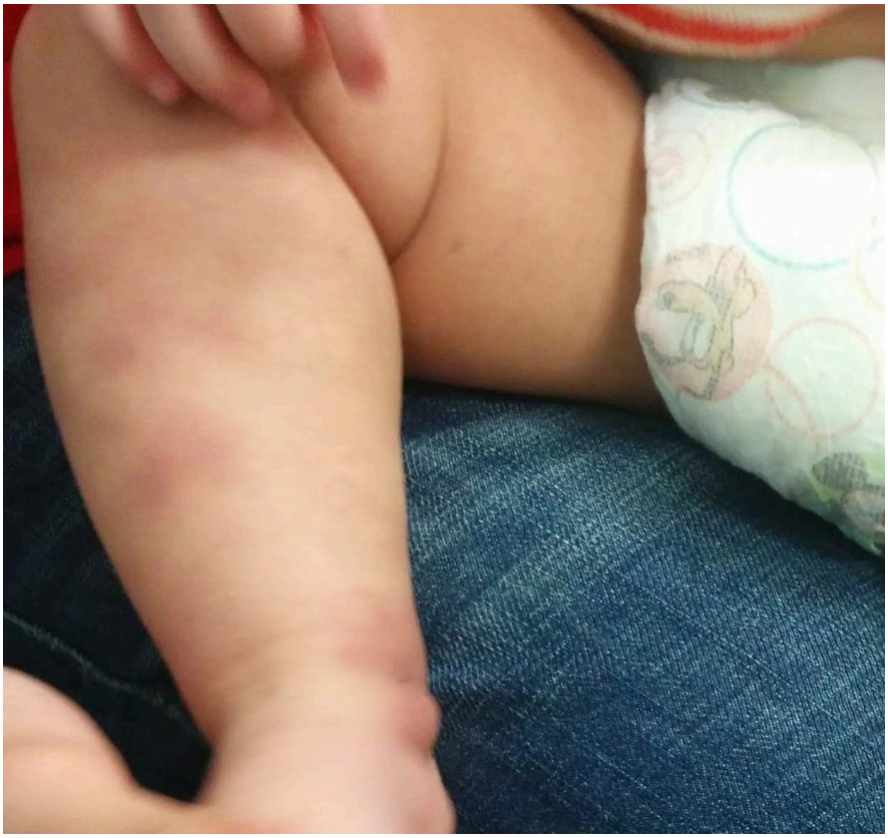
Citation: Hernaez F, Hernaez AM, Blankas-Hernaez N. Idiopathic thrombocytopenic purpura [published online December 19, 2018]. Consultant360.

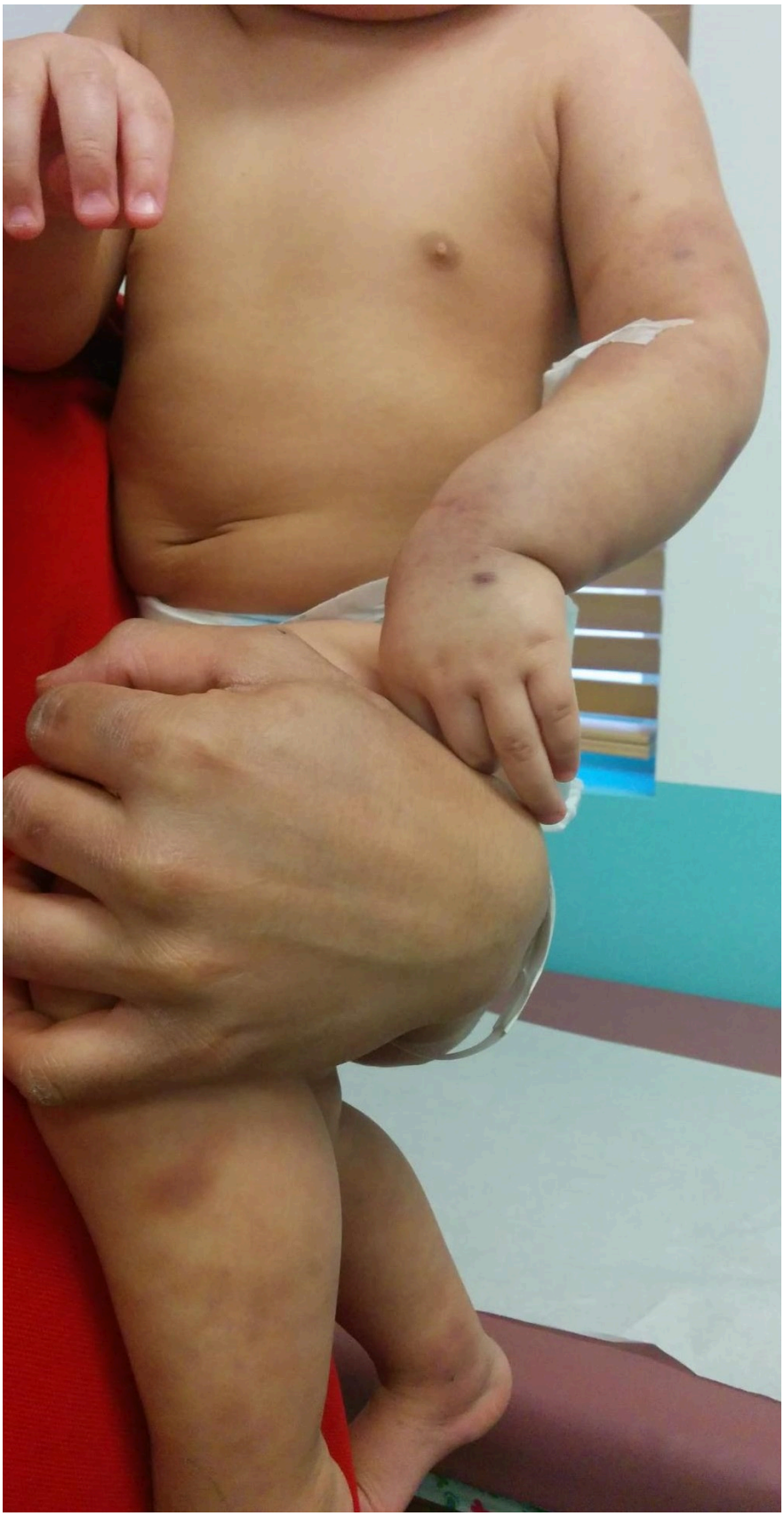
A 10-month-old boy presented to the emergency department (ED) with epistaxis and new-onset bruising.

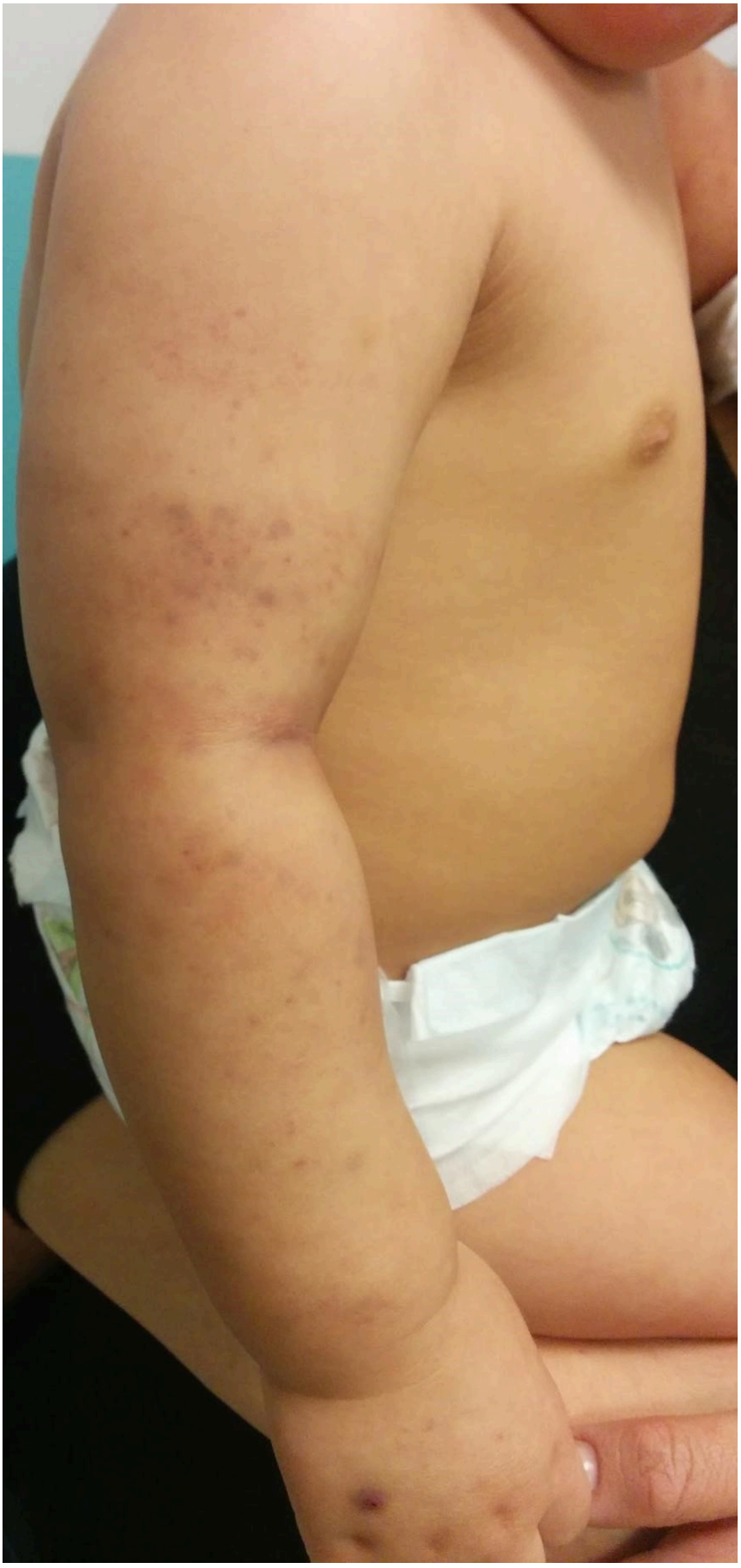
History. The boy's medical history is significant for a urinary tract infection with vesicoureteral reflux at 2 months of age. His immunizations were up to date; the measles, mumps, and rubella (MMR) vaccine for international travel had been administered 7 days prior to the onset of illness. There was no family history of autoimmune or bleeding disorders.

The bruising had started on his upper and lower extremities, trunk, and face 3 days prior to presentation. He had had a single, self-limited episode of epistaxis and an episode of blood-streaked hard stool 2 days prior to presentation. A dark red spot had developed on his tongue, but there had been no overt bleeding and no further episodes of gum bleeding, epistaxis, hematochezia, or hematuria. He had had no changes in behavior, appetite, or bowel pattern. His urine output had been appropriate. There had been no fever, vomiting, diarrhea, or symptoms of upper respiratory tract infection. He had been brought to his primary care provider, who referred him to the ED.

Physical examination. In the ED, physical examination findings were significant for dried blood in the right naris, multiple scattered ecchymoses bilaterally on the shins and arms, and multiple petechiae over the arms, lips, and face (**Figures**). Neurological examination findings were normal.







Diagnostic tests. A complete blood cell count, a comprehensive metabolic panel, and a disseminated intravascular coagulation panel were done. The platelet count was significantly depressed at 4000/μl. All other results were within normal limits.

depressed at 4000/μL. All other results were within normal limits.

Peripheral smear results showed a mix of large and giant platelets and an absence of blasts consistent with idiopathic thrombocytopenic purpura (ITP). Based on these findings, together with the symptoms and history, he received a diagnosis of ITP. A consultant hematologist recommended administration intravenous immunoglobulin (IVIG).

Upon admission, the patient had significant purpura and petechiae but otherwise appeared well. After unsuccessful attempts at placement of an intravenous line, oral prednisolone was started but was not tolerated.

The next morning, the platelet count was 1000/μL, an external jugular line was inserted, and 1 dose of IVIG (1 mg/kg) and dexamethasone (0.6 mg/kg) were administered. No further bruising, petechiae, hematochezia, or hematuria developed.

Posttreatment, the boy's platelet count rebounded to 57,000/μL, and he was discharged with 2 days of oral prednisone. After 2 weeks, the platelet count had normalized. After 10 months, an MMR vaccine was administered without complication for nonimmune rubella titer.

Discussion. Thrombocytopenia in the pediatric population can have multiple etiologies. Thrombocytopenia is classified as a platelet count less than 150,000/μL, and in order to differentiate between the different types, one must take into account platelet size, acquisition, and the mechanism. Large platelets suggest a giant platelet disorder or an immune-mediated disorder. Small platelets may suggest Wiskott-Aldrich syndrome or X-linked thrombocytopenia. Further workup can help differentiate between thrombocytopenia from platelet destruction vs decreased platelet production.[1]

The cause-effect relationship between the MMR vaccine and ITP has long been demonstrated. In a 2003 nested case-control analysis of ITP and the MMR vaccine among infants aged 13 to 24 months, the incidence of developing ITP within 6 weeks of the vaccine was found to be approximately 4 in 100,000 doses.[2] In a 2012 self-controlled case series study of vaccine-associated ITP among children aged 6 weeks to 17 years, the incidence of developing ITP within 6 weeks of the vaccine was found to be approximately 1.9 in 100,000 doses.[3] Including the median incidence of MMR vaccine-associated ITP—2.6 in 100,000 doses, from a 2010 meta-analysis[4]—the incidence is low relative to that of the ITP incidence associated with natural measles or rubella, which ranges from 6 to 1200/100,000 doses.[4]

The most common symptoms of ITP are petechiae and bruising. Patients may present with minor epistaxis or minor gastrointestinal (GI) tract bleeds, but scarcely do the bleeds progress to hemodynamic compromise. Of 8 children who developed ITP after the MMR vaccine in one study, 2 were revaccinated without recurrence.[3] In a 2010 MMR vaccine-associated ITP meta-analysis, revaccination of patients with prior ITP did not lead to a recurrence.[4] The same meta-analysis showed a 7% incidence of chronic ITP after the initial diagnosis of MMR vaccine-

related ITP, which was comparable to the 10% incidence of non-MMR–related ITP among infants aged 12 to 18 months.[4]

Approximately 60% to 75% of pediatric patients with ITP fully recover within 6 months, and 20% to 30% develop chronic ITP. Patients who develop chronic ITP (ie, ITP for more than 1 year) are usually older, have an insidious onset of symptoms, lack preceding vaccination or infection, or lack mucosal bleeding at diagnosis. However, these risk factors have not been studied reliably and cannot be used to predict whether a patient will develop chronic ITP.[5]

Clinicians often opt for conservative treatment in mild cases of ITP. Many of these cases are managed in the outpatient clinic with careful observation. According to 2003 British guidelines,[6] treatment for ITP should not be initiated if the patient only has skin findings and thrombocytopenia. The 2006 guidelines from the Indian Academy of Pediatrics recommend starting specific treatment if the patient has less than 20,000 platelets or a severe mucosal bleed.[7] Examples of severe mucosal bleeds include GI tract bleeding, prolonged epistaxis, pulmonary hemorrhage, or muscle or joint hemorrhage.

Treatment options include IVIG or IV anti-D given with methylprednisolone. If severe hemorrhaging or an intracranial bleed develop, a platelet transfusion can be done. A study by Warrier and Chauhan concluded that 80% of such cases can be managed with weekly clinic visits for observation.[7] In the outpatient setting, treatment is recommended only if the patient is at high risk of severe bleeding complications. These include head trauma; a planned surgical procedure that induces blood loss; severe unexplained headache; and grade 3 bleeding symptoms (brief epistaxis, intermittent gum bleeding, menorrhagia). Pharmacologic treatment also can be started in the outpatient setting if the platelet count is less than 30,000/μL and the patient is using antiplatelet/anticoagulant medications (eg, nonsteroidal anti-inflammatory drugs, heparin), has a concomitant bleeding disorder, has a lifestyle prone to frequent trauma, or if close follow-up, supervision, and/or access to medical care is limited.[5]

In 2012, a study assessed the risk of ITP with other vaccines in children aged 6 weeks to 17 years. This study gathered data on 1.8 million children from several organizations from 2000 to 2009. Results of the study showed an association between ITP and other vaccines among children aged 7 to 17 years, especially with the hepatitis A, varicella, and Tdap (tetanus, diphtheria, and pertussis) vaccines. However, there was little evidence to support that ITP occurs with other vaccines in the 12- to 19-month age group.[3]

Newer studies have looked at the human papillomavirus (HPV) vaccine and its association with ITP. A 2017 study in France assessed the incidence of autoimmune diseases (central demyelination/multiple sclerosis, connective tissue disease, Guillain-Barré syndrome, type 1 diabetes, autoimmune thyroiditis, and idiopathic thrombocytopenic purpura) after HPV vaccine administration in a population of women aged 11 to 25 years, with autoimmune disorders

administration in a population of women aged 11 to 25 years, with autoimmune disorders, between 2008 and 2014. With an adjusted odds ratio of 0.58, autoimmune disorders were negatively associated with the HPV vaccine. It is important to note that autoimmune thyroiditis and ITP did not reach statistical significance in this study, so further surveillance must be done to confirm this association.[8]

Summary. Clinicians must be aware of and educate their patients on the positive correlation between ITP and the MMR vaccine. Infants and adolescents with symptoms of ITP, therefore, need a thorough check of their immunization history. However, the MMR vaccine is safe, and developing MMR vaccine-associated ITP should not affect the immunization schedule. Incidence rates of rubella- and measles-related ITP is double that of MMR vaccine–associated ITP. MMR vaccine–associated ITP has a lower incidence rate of long-term sequelae and recurrence. Even after revaccination, there have been no documented cases of ITP recurrence.

Although skin findings and thrombocytopenia in pediatric patients are alarming, most ITP cases can be treated in an outpatient setting, with admission only warranted with severe symptoms. These patients respond well to treatment, but need to be closely followed for development of chronic ITP after discharge.

Further research is ongoing to clarify which vaccines are associated with ITP, with the latest being the HPV vaccine. These studies have shown a negative association, but more studies need to be done to attain statistical significance.

References

1. Despotovic JM. Causes of thrombocytopenia in children. UpToDate. https://www.uptodate.com/contents/causes-of-thrombocytopenia-in-children. Updated September 18, 2018. Accessed December 19, 2018.
2. Black C, Kaye JA, Jick H. MMR vaccine and idiopathic thrombocytopaenic purpura. *Br J Clin Pharmacol.* 2003;55(1):107-111.
3. O'Leary ST, Glanz JM, McClure DL, et al. The risk of immune thrombocytopenic purpura after vaccination in children and adolescents. *Pediatrics.* 2012;129(2)248-255.
4. Mantadakis E, Farmaki E, Buchanan GR. Thrombocytopenic purpura after measles-mumps-rubella vaccination: a systematic review of the literature and guidance for management. *J Pediatr.* 2010;156(4):623-628.
5. Bussel JB. Immune thrombocytopenia (ITP) in children: initial management. UpToDate. https://www.uptodate.com/contents/immune-thrombocytopenia-itp-in-children-initial-management. Updated September 10, 2018. Accessed December 19, 2018.
6. British Committee for Standards in Haematology General Haematology Task Force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. *Br J Haematol.* 2003;120(4):574-59
7. Warrier R, Chauhan A. Management of immune thrombocytopenic purpura: an update. *Ochsner J.* 2012;12(3):221-22
8. Grimaldi-Bensouda L, Rossignol M, Koné-Paut I, et al; PGRx-AD Study Group. Risk of

autoimmune diseases and human papilloma virus (HPV) vaccines: six years of case-referent surveillance. *J Autoimmun.* 2017;79:84-90.