Idiopathic Thrombocytopenic Purpura: Advances in Management

Cindy Neunert, MD, MSCS
Assistant Professor
Department of Pediatrics
University of Texas Southwestern Medical Center at Dallas
Dallas, Texas

**H&O** What is idiopathic thrombocytopenic purpura (ITP) and how does it present?

**CN** ITP is an autoimmune condition, caused by an unknown stimulus, that results in destruction of platelets. The decreased number of circulating platelets and impaired platelet production leads to thrombocytopenia and bleeding symptoms. Many patients will experience only minor bleeding, such as bruising or petechiae. Some patients, however, will have more significant hemorrhage, such as bleeding from the gastrointestinal tract or severe epistaxis. The most concerning type of bleeding, intracranial hemorrhage, is believed to be a rare event. Most patients with ITP are otherwise well because this condition does not cause additional systemic or constitutional symptoms, such as fever or weight loss.

**H&O** How is ITP diagnosed?

**CN** Unfortunately, there is no gold standard diagnostic test for ITP, and it is usually a diagnosis of exclusion. It is based on the finding of isolated thrombocytopenia—platelet count of less than 100,000 mm$^3$—in an otherwise healthy patient with no additional hematologic abnormalities. The diagnosis requires a careful examination of the complete blood count, with attention to changes in white or red blood cell count and consideration of red blood cell indices. The peripheral blood smear should be examined for any additional changes or white blood cell abnormalities. Lastly, the patient should undergo a careful physical examination that includes evaluation for signs of organomegaly, lymphadenopathy, or any other findings that could suggest a condition other than ITP. After this careful evaluation, the presence of isolated thrombocytopenia with no additional findings is considered sufficient for the diagnosis of ITP.

**H&O** When does ITP require treatment?

**CN** The decision of when to administer treatment is difficult and differs somewhat for children and adults. ITP
in most children is usually self-limited, and significant bleeding is rare, so treatment is not usually required. In this case, the decision to treat is based less on a platelet count number and more on the patient’s bleeding symptoms and/or impaired quality of life. For example, treatment should be considered for a child who desires to get back to sports or activities but is limited by persistent thrombocytopenia.

In adults, treatment is suggested when the platelet count is less than 30,000 mm3. This approach in adults is followed probably because they have other conditions that increase their risk of bleeding, such as hypertension and use of ongoing medications, including warfarin. In addition, bleeding risks have been demonstrated to increase with age, so therefore there is some thought that in adults, use of a platelet threshold is more necessary than in children.

H&O What are the most common treatments?

CN The most common first-line treatments used at the time of diagnosis include corticosteroids, intravenous immunoglobulin, and anti-D immunoglobulin. In children who require treatment, all 3 agents are generally considered very good first-line options. Short courses of oral corticosteroids will work slightly slower than intravenous immunoglobulin or anti-D immunoglobulin; therefore, if the patient requires a rapid increase in platelet count, those agents might be preferred over corticosteroids.

In adults, longer courses of corticosteroids are usually considered standard first-line therapy. Intravenous immunoglobulin or anti-D immunoglobulin are used either in conjunction with steroids or as a substitute for steroids in patients who have a contraindication.

H&O What is the role of splenectomy?

CN Splenectomy remains the only curative therapy for ITP, with very good success rates. In adults, splenectomy is currently recommended for patients who fail corticosteroid treatment. In children, splenectomy should be considered in patients with persistent or chronic disease, significant bleeding, lack of response to first-line therapies, or impaired quality of life. The biggest concern with splenectomy is the risk of sepsis, however, this risk has been reduced with the use of prophylactic antibiotics and improved vaccinations. There is no evidence to guide the optimal timing of splenectomy in the era of newer drug therapy, but it still remains the only true curative therapy.

H&O What are the novel treatments in ITP?

CN The newest agents in ITP are the thrombopoietin receptor agonists. These agents work by stimulating the bone marrow to make more platelets and therefore increase the number of circulating platelets. There are 2 agents currently available: romiplostim (Nplate, Amgen), a subcutaneous agent given once weekly, and eltrombopag (Promacta, GlaxoSmithKline), an oral agent taken daily. Both agents have been shown to effectively increase the platelet count, improve quality of life, and reduce bleeding symptoms. The only drawback to these treatments is that they do not address the underlying antibody formation, and therefore once the patient stops taking them, the platelet count declines again. We are still trying to learn more about how to best utilize these agents.

H&O What is new in the management of ITP?

CN There is new literature to help guide ITP management, specifically some consensus documents and guidelines from the American Society of Hematology. In 2009, an international working group led by Dr. Francesco Rodeghiero recommended that the platelet count threshold for diagnosis be lowered from 150,000 mm3 to 100,000 mm3. The working group also made recommendations regarding nomenclature, suggesting that newly diagnosed ITP refer to the phase between diagnosis to 3 months, persistent ITP refer to the phase between 3 months to 12 months, and chronic ITP refer to ITP lasting longer than 12 months. Disease severity was also redefined: severe ITP was reserved for patients who have clinically relevant bleeding, and refractory ITP was defined as the presence of severe ITP after splenectomy. Non-splenectomized patients were defined as responders or nonresponders to individual drug therapies. This nomenclature will help the research community to standardize the classification of patients, and it will help physicians to appropriately categorize their patients when trying to select the best option for treatment.

H&O What are some areas of ITP research?

CN There is a lot of effort to try to address the underlying changes and modifiers of the immune system that lead to ITP and to help understand what alters the course of the disease in patients. This research could determine why some patients develop chronic disease and others do not, and it may also identify potential targets for therapy within the immune system.

More data are needed to help practitioners better select second-line therapies. We currently have splenectomy, novel thrombopoietic agents, and rituximab (Rituxan, Genentech/Biogen Idec), which is an anti-CD20 antibody that destroys antibody-producing B cells. However, we do not have much evidence to guide the use of these different therapies, or to match individual patients with the best personal therapeutic approach.
Lastly, researchers are investigating how to modify the disease course. For example, there is some thought that different combinations of treatment at diagnosis might reduce the chance the patient will develop refractory or chronic disease.

References