The Oklahoma ITP Registry Newsletter

November 2012

Hello!

We would like to welcome you to our ninth Oklahoma ITP Registry newsletter.

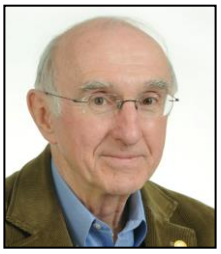
The ITP Registry

The Oklahoma ITP Registry began in November 2001. Since that time we have enrolled 108 people. With your participation we hope to document the clinical course and long-term outcomes of patients with ITP.

Follow-Up Reminder

Thank you to all of you who have returned your follow-up surveys! We send out surveys once a year so that we can document your general health. We just wanted to remind those who have not returned their follow-up surveys to please do so. If you need a new survey or would like to do your survey over the phone, please contact us (contact information on page 7).

Dr. George's Perspective



Dr. George writes a column entitled "An American Perspective" for the ITP Support Association that is based in the United Kingdom. Below is an article he wrote on ITP in the Elderly. For more information please visit their website at www.itpsupport.org.uk/american.htm

Some have suggested that ITP is more dangerous in the elderly than in younger patients. There are reasons that this may be true, but there are also reasons that this is not true. Perhaps because older people have more routine blood counts, ITP is diagnosed more often in older people. Typically, we think of ITP in adults as principally affecting young women, and many reports describe ITP as twice as common in women as in men. This is different from ITP in children, which occurs nearly equally in boys and girls. However, more recent surveys have suggested that ITP may be just as common in older people as it is in younger persons, and may be just as common among older men as in women.

Therefore, doctors have recently focused on specific issues related to ITP in the elderly. The risk for bleeding may be greater in older patients, because they frequently have other health problems that contribute to bleeding, such as high blood pressure, stomach ulcers, and risk for stroke. Therefore, a very low platelet count, such as less than 10,000, may cause minimal problems in a healthy young person but may be a risk for serious bleeding in an older person with high blood pressure. Some doctors have therefore suggested that older patients with ITP should be treated to maintain a higher platelet count. But the problem with this approach is that older patients are also at greater risk for complications from treatment. Steroids are particularly risky. Steroids can cause thinning of the bones (osteoporosis), already a common problem in older people, particularly women, even without any steroid treatment. Steroids can also increase the risk for cataracts, already common in older people. The elderly may also not tolerate chemotherapy medicines as well as younger patients.

Accordingly it seems to us that that the management of ITP should be the same for all adults, regardless of age. Of course, when other health problems are present, they need to be recognized and treated effectively. A good example of how an older woman can do very well with no treatment in spite of severe thrombocytopenia is told in "Crystal's Story" on our website, http://www.ouhsc.edu/platelets. Crystal was 75 years old when I first met her, and her platelet count was only 9,000. She was taking daily prednisone. She had already had a splenectomy and she had also been treated with IVIG and anti-D. However, she was very healthy, her blood pressure was normal, and she was taking no other medications. This, of course, is unusual because most people her age have health problems that require medications. Crystal was very insistent that the prednisone be stopped. She hated its side effects, the puffiness of her face, the bruising on her arms and trouble sleeping. She also insisted that she wanted no

further treatment. Her husband supported her in this decision. Her son, who had come for California for this visit, also provided support. I was nervous about discontinuing prednisone treatment and just observing her but I thought this was the right thing to do and the right way to do it. She had never had any bleeding problems except for minor purpura. When there is no firm evidence to guide medical decisions, the responsibility for what is to be done medically needs to be shared by the doctor, patient, and family.

Over the next 5 weeks we gradually tapered and then discontinued her prednisone. During this time her platelet count remained between 4,000 and 9,000, but she had no bleeding symptoms. Then she had platelet counts done every two weeks. Two months after we stopped the prednisone, when her platelet count was once as low as 1,000, her primary doctor thought that some treatment was necessary, even though she continued to have minimal symptoms. She was treated with 4 weekly injections of vincristine (we believe this was not a good decision.) Although her platelet count temporarily went up to 38,000, she felt bad with the expected side effects of vincristine, constipation and numbness and tingling in her fingers. So then our plan was to stop doing platelet counts so often! Over the next year, her platelet count gradually increased to 53,000, and now, 3 years after I first saw her, her platelet count is normal, 213,000.

I think of Crystal (the pseudonym we gave for this patient when she told her story for our website) as an example for how ITP can be successfully managed without steroids or other treatment, in spite of the patient's age. Her recovery without treatment may not be common, and therefore her story may not be the best one to tell. But I learned valuable lessons from Crystal. We doctors always learn a lot from our patients.

Platelets and English Walnuts

This is the story of a very rare occurrence. However rare occurrences may teach important lessons as well as make a good story. The story of platelets and English walnuts teaches us that not all thrombocytopenia is ITP. There can be other causes.

This is the story of a 70 year old man who was discovered to have a platelet count of 32,000/μL when he had a blood count done because of nausea, vomiting, and fever. He was taking no medicines and he was taking no quinine-containing beverages. Four days later the platelet count was normal with no treatment. Several months later he again had nausea, vomiting, and fever, and again his platelet count was low (37,000/μL); as before, his

platelet count returned to normal in several days. After the second episode, he remembered that he had eaten English walnuts each time before he became sick. Then he did the test that explained what happened with 100% certainty. He was admitted to the hospital; his platelet count was normal at 233,000/μL; he ate 3.5 oz. of English walnuts; 4 hours later he had nausea and fever and his platelet count was 4,000/μL! There were no abnormalities of his other blood cells. He had hematomas at the sites of needle sticks for blood counts, but no other bleeding. His platelet count was normal again in 4 days.

The next tests, performed at the Blood Center of Wisconsin in Milwaukee, explained how this happened. English walnuts were ground up and then stirred with saline (salt and water). When this saline extract was mixed with serum from the patient and platelets from a normal subject, there was a strong positive reaction of antibodies from the man's serum with platelets. When saline extracts from other nuts were used, there was no reaction with platelets. When the saline extract of English walnuts was mixed with serum from a normal subject, there was also no reaction with platelets. These tests documented that the patient's serum contained an antibody that destroyed platelets only in the presence of English walnuts. The complete story of this man has been published by Dr. Roos Achterbergh and his colleagues from The Netherlands and Dr. Brian Curtis and his colleague at the Blood Center of Wisconsin (*Lancet* 2012; 379:776).

This is an allergy to English walnuts that causes platelet destruction, as well as the nausea, vomiting, and fever. This, of course, is very rare. Much more common are allergic reactions that cause a skin rash or asthma. This type of sudden, severe thrombocytopenia can occur with quinine, either as a medicine or in beverages, such as tonic water and Schweppes bitter lemon. Thrombocytopenia caused by allergies to foods and herbal remedies are rare. These drugs, beverages, foods and herbal remedies are listed on our website (www.ouhsc.edu/platelets). The importance of this story is that not all episodes of thrombocytopenia are ITP. It is particularly important to learn that repeated episodes of sudden and severe thrombocytopenia are almost always related to an allergic reaction to a medicine, food, beverage, or herbal remedy.

(Note from Dr. George: I don't think anyone should avoid walnuts because of this story. This allergy must be very, very, very rare.)

Haely's Project

My name is Haely and I am a recent college graduate. I was diagnosed with ITP a few years ago, experiencing short-lived responses to steroid treatments and finally a successful response to rituxan. Since then I have been maintaining high platelet counts with no treatment. My journey with ITP wasn't an easy one though. During the course of my treatments I experienced the typical highs and lows that most patients encounter, from initially learning about the world of ITP to dealing with side effects from treatments. I'd like to share my story with you on how learning more about ITP changed my outlook on my own blood disorder and how it brought me to where I am today.

I was first diagnosed with ITP during my early college years. I was at that "in-between age", where my hematologists couldn't quite decide whether to treat me as an adult or as a pediatric case. The first hematologist I saw set me on high doses of prednisone before recommending that I undergo a course of WinRho followed by a splenectomy. Being a newer (and younger) ITP patient, I was reluctant to jump into any type of surgery, so I decided to seek a second opinion. The second hematologist I visited prescribed a high dose of prednisone, followed by intermittent doses of the pulse steroid-dexamethasone. The hope was to drive me into a "steroid-induced remission", but after a year of this regimen, the side effects had left me miserable, uncomfortable and with counts that were as low as when I began treatment.

My counts stayed low, but I was experiencing no immediate bleeding symptoms. The side effects from my previous stints with prednisone and dexamethasone seemed to be everlasting, so I personally decided that I'd rather risk walking around with low counts than be on high doses of steroids. I moved away from home for a year for an out of state internship and took a break from the medication and stressful side effects. I was lucky to maintain a platelet count that was still low but high enough to avoid any anxiety from my hematologists (and parents!). But after returning to Oklahoma my counts began to drop even more, this time to a dangerously low number of 3,000. This pushed me into a severe case of menorrhagia, sending me to the hospital for an emergency platelet and blood transfusion. Apparently my "self-prescribed" methods of dodging treatments were beginning to fail and I was forced to finally make a decision about the future of my ITP.

A visit to a third hematologist yielded something new; a recommended course of the infusion therapy- rituxan. At this point I was back on a maintenance dose of steroids and was up for anything. After 4 rounds of infusion my platelets hiked up and I am happy to say, have stayed high ever since then. After graduating college, I become increasingly interested in blood disorders and physician-patient dynamics. After being given so many options from different physicians, I was curious as to what led each of my hematologists to their treatment decisions. Was it correlated to their years in practice? Or was it based on their past experiences of ITP patients with similar cases?

That search led me to Drs. George and Terrell, both wonderful experts in the field of hematology and related autoimmune issues within the state and internationally. We developed a project to survey the hematologists in Oklahoma to determine the selection and sequence of treatments of different ITP patient scenarios. We received 83% of responses from pediatric and adult hematologists from across Oklahoma and compared survey results to two recent practice guidelines for ITP, an International Consensus report (ICR) and an American Society of Hematology (ASH) guideline.

As an ITP patient, I can personally attest to the confusion that accompanies the diversity of available ITP treatment options. The goal of this project was to gain a better understanding of how guideline recommendations are incorporated into current clinical practice. We believe it is important for patients to have a solid understanding of the judgment and practice decisions of their hematologists and hope that in the end, treatment choices are a direct result of a partnership between patients and their physicians.

MANAGEMENT OF PRIMARY IMMUNE THROMBOCYTOPENIA, 2012:
A SURVEY OF OKLAHOMA HEMATOLOGISTS-ONCOLOGISTS

Introduction: The treatment of ITP has been addressed in two recently published practice guidelines: an International Consensus report (ICR) and the American Society of Hematology (ASH). Practice guidelines are usually developed by experts in the field to help guide other clinicians on 'best practices' of treatment of the disease of interest. To understand how or if the recommendations of ASH and ICR have become incorporated into current clinical practice, we surveyed hematologists-oncologists in Oklahoma.

Methods and Results: Surveys specific for children and adults were developed. Both the adult and pediatric surveys contained three clinical situations. The adult survey described a 28 year old otherwise healthy woman with varying degrees of a low platelet count and bleeding symptoms. We asked the hematologist-oncologist which treatment they would prescribe given the information described. A shortened version of the adult patient scenarios, treatment choices, and results are below:

Adult Scenario 1: An active healthy, 28 year-old woman is discovered to have a platelet count of 40,000/µl. She has no bruising or other bleeding problems. Everything else on her blood work is normal she just has the low platelet count. **Physicians were told to please choose one treatment choice: Win-Rho; daily oral prednisone; intermittent high-dose dexamethasone; IVIg; observation only (watch the platelet count and not give any drug treatment); Rituxan; Nplate or Promacta ; and other (please describe the other treatment that was not listed).**

> **Results:** 78/83 (94%) adult hematologists-oncologists selected observation only without drug treatment. Given this scenario, both expert panels (ASH and ICR) would also recommend observation only without giving any drug treatment. The other 5 (6%) adult hematologists-oncologists all chose to treat with daily oral steroids.

Adult Scenario 2:
The same 28 year old woman but now her platelet count is 9,000/µl and she has scattered petechiae and several small bruises on her arms and legs. She's also been having slightly heavy menstrual periods for the last 2 months. **Physicians were told to please choose one treatment choice: Win-Rho; daily oral prednisone; intermittent high-dose dexamethasone; IVIg; observation only (watch the platelet count and not give any drug treatment); Rituxan; Nplate or Promacta; and other (please describe the other treatment that was not listed).**

> **Results:** 63/83 (76%) adult hematologists-oncologists would treat this patient with daily oral prednisone. Given this scenario, neither expert panel had a strong recommendation on the best way to treat this patient. Seventeen (20%) adult hematologists-oncologists would give this patient short doses of high dose dexamethasone, and 3/83 (4%) physicians would give this patient IVIg.

Adult Scenario 3:
The same 28 year old woman was given steroids and her platelet count went from 9,000 /µl up to 170,000/µl. When the steroids were stopped her platelet count went back down to 9,000 /µl and she had a nose bleed and blood blisters in her mouth. Her doctor gave her steroids and IVIg, but she doesn't like the side effects of the steroids and doesn't want to take them anymore but the IVIg by itself isn't keeping her platelet count high enough to stop the bleeding symptoms. **Physicians were told to please choose one treatment choice: Win-Rho; daily oral prednisone; intermittent high-dose dexamethasone; IVIg; observations only (watch the platelet count and not give any drug treatment); Rituxan; splenectomy; Nplate or Promacta; and other (please describe the other treatment that was not listed).**

> **Results**: Thirty-two of 83 (39%) adult hematologists-oncologists selected splenectomy which was the treatment recommendation by one of the expert panels. Thirty-one of 83 (37%) adult hematologists-oncologists selected Rituxan, and 13/83 (16%) selected either Nplate or Promacta. Treatment with either Rituxan or Nplate or Promacta was recommended by the other expert panel. The remaining 8% treated with Win-Rho, offered both splenectomy and Nplate or Promacta, or let the patient decide.

The pediatric survey described a 3 year old boy and 6 year old girl with varying degrees of a low platelet count and bleeding symptoms. We asked the pediatric hematologist-oncologist which treatment they would prescribe given the information described. A shortened version of the pediatric patient scenarios, treatment choices, and results are below:

Child Scenario 1:
A 3 year-old boy has been bruising and has petechiae with a platelet count is 8,000/µl. **Physicians were told to please choose one treatment choice: Win-Rho; steroids; IVIg; observation only (watch the platelet count and not give any drug treatment); Nplate or Promacta; and other (please describe the other treatment that was not listed).**

> **Results**: 5/13 (39%) pediatric hematologists-oncologists selected observation without drug treatment (recommended by both expert panels). Physicians who chose to treat would use Win-Rho (15%), steroids (23%), or IVIg (23%).

Child Scenario 2:
The same 3 year-old boy develops a nose bleed in your office that lasts about 15 minutes. His platelet count is still 8,000/µl. **Physicians were told to please choose one treatment choice: Win-Rho; steroids; IVIg; observation only (watch the platelet count and not give any drug treatment); Nplate or Promacta; and other (please describe the other treatment that was not listed).**

> **Results:** Seven of 13 (54%) pediatric hematologists-oncologists treated with either steroids or IVIg which was consistent with recommendations of both expert panels. Other treatment included Win-Rho (38%), and 1 physician would observe without drug treatment.

Child Scenario 3:
A 6 year-old girl was diagnosed with ITP 12 months ago and continues to have a platelet count of 8,000/µl. She's been treated with IVIg, Win-Rho, and recently steroids have stopped working for her. She often has nose bleeds that require her to be sent home from school. **Physicians were told to please choose one treatment choice: Win-Rho; daily steroids; high dose dexamethasone; IVIg; observation only (watch the platelet count and not give any drug treatment); Rituxan; splenectomy; Nplate or Promacta; and other (please describe the other treatment that was not listed).**

> **Results:** Rituxan was the choice of 7/13 (54%) of the pediatric hematologists-oncologists; splenectomy was the choice of only one. This is consistent with recommendations by one of the expert panels but not the other. Four (31%) of the physicians would treat this child with either Nplate or Promacta, and 1 physician would treat with a combination of therapy including steroids and either IVIg or WinRho.

Conclusion: Understanding current clinical practice is important for improving the care of patients with ITP. The translation of practice guideline recommendations into actual clinical practice is often limited and always uncertain. Management of children and adults with ITP has changed during the past 16 years related to the introduction of new agents that have become available for the management of both children and adults. Two practice guidelines published in 2010 and 2011 address these changes.

Our survey of Oklahoma hematologists-oncologists documents the frequent use of the new agents, Rituxan, Nplate and Promacta. In the end it is important for physicians to discuss with the patient all potential treatment options and side effects so the patient can be a partner in their care.

Send Your Suggestions

Is there anything you'd like to see in the next newsletter? We'd like to hear from you! Please contact us if you have any suggestions as to what you would like to see in this newsletter in the future either by emailing Dee Terrell at **Dee-Terrell@ouhsc.edu**, Jessica Reese at **Jessica-Reese@ouhsc.edu, or** Kaelyn Lu at **Kaelyn-Lu@ouhsc.edu** or calling at **(405) 271-8001** extension **48386**.

Resources for ITP Patients

Visit our website, Platelets on the Web, at http://www.ouhsc.edu/platelets.

There is also an informative website from the United Kingdom you can visit at www.itpsupport.org.uk. This site includes a support group with newsletters, publications, and information on ITP. Dr. George contributes "An American Perspective" found on this page, where you can find additional topics about ITP.
www.itpsupport.org.uk/american.htm

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