PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**Primary Immune Thrombocytopenia (ITP) – CPS Podcast"** These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Primary Immune Thrombocytopenia (ITP) – CPS Podcast

Developed by Stephanie Zachary, Sarah Weicker, Dr. Jeremy Friedman, Dr. Carolyn Beck, and Dr. Lauren Kitney for PedsCases.com.
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Introduction:

[Stephanie]: Hello everyone, welcome to this episode of PedsCases. My name is Stephanie Zachary

[Sarah]: And my name is Sarah Weicker

[Stephanie]: We are fourth year medical students at the University of British Columbia. In this podcast, we will be discussing the newly published 2018 Canadian Pediatric Society (CPS) statement on the **Diagnosis and Management of typical, newly diagnosed primary immune thrombocytopenia of childhood.** This podcast was created under the guidance of Dr. Jeremy Friedman, a general and complex care pediatrician at the University of Toronto, and Dr. Carolyn Beck, a general pediatrician at the University of Toronto. They are the lead authors of this CPS statement. We would also like to thank Dr. Lauren Kitney, a general pediatrician, at the University of British Columbia in Victoria for her contributions to this podcast.

[Sarah]:
Today, our learning objectives are to

1. Define Immune thrombocytopenia, which we will abbreviate as ITP
2. Review the diagnostic criteria for typical ITP
3. Discuss red flag features, suggestive of other diagnoses
4. Review the management of ITP
5. Apply the CPS management recommendations to a clinical case

[Stephanie]:
Now, let's get started with a clinical case. You are working in a community pediatrics office, and your preceptor asks you to see a 5-year-old girl, Victoria, who is accompanied by her mother. She was referred to your clinic due to a history of bruising and petechiae.

As you walk to the exam room, you think back to your pre-clinical classroom sessions and remind yourself of the differential diagnosis of petechiae and bruising in a child. Your

differential diagnosis includes but is not limited to isolated thrombocytopenias such as ITP, coagulopathies such as von Willebrands disease, vasculitides such as HSP, trauma including non-accidental injury, malignancies such as leukemia, and infectious causes such as meningococcus.

When you walk into the room, you see a playful, well-appearing child with a diffuse petechial rash on her limbs. Her family doctor has already ordered some bloodwork, which shows an isolated thrombocytopenia with normal hemoglobin and white cell count. Her peripheral smear is normal. You wonder if Victoria may have ITP. You go to the CPS website and pull up the new 2018 statement on ITP.

[Sarah]: Let's take a pause from the case and review the key points from the CPS statement.

Primary immune thrombocytopenia or ITP, is a condition characterized by immune-mediated destruction of platelets. The condition most commonly affects children ages 2 to 5; however, this CPS statement can be applied to children aged 90 days old to 17 years of age. ITP typically presents as mild petechiae and bruising; although, some cases present with more severe bleeding episodes.

Usually, the cause of ITP is not known; however, in some cases, preceding viral illnesses or other immune mediated phenomena are triggers. The incidence of ITP is 5 in 100,000 children per year. ITP is typically a self-limited illness, lasting less than 6 months in 75-80% of cases and approximately 90% of cases resolved by one year.

Stephanie, now that we suspect Victoria may have ITP, how can we diagnose it?
[Stephanie]: Typical ITP can be diagnosed with a thorough history, physical examination and review of laboratory investigations. Clinical features often include a sudden onset petechial rash, bruising, and/or new onset bleeding in an otherwise well and healthy child. The majority of children present with mild symptoms but up to 3% may have more serious bleeding such as prolonged epistaxis, mucosal bleeding or melena. Intracranial hemorrhage is rare, occurring in less than 1% of cases. The presence of any systemic symptoms point away from a diagnosis of primary ITP. We will discuss these "red flag" features in a later portion of this podcast.

Lab investigations should reveal an isolated thrombocytopenia with a platelet count of below 100 x 10^9/L, but this is often below 20 x 10^9/L. There should be no abnormalities of hemoglobin, reticulocyte or WBC count, including differential. Peripheral blood smear should be normal without evidence of hemolysis or blasts. Presence of these should prompt further investigations and an alternative diagnosis.

Bone marrow aspirations are not performed in children with suspected ITP unless clinical and laboratory findings raise suspicion for an alternative diagnosis. Hematology consultation should be considered in the presence of any red flags.

[Sarah]: Ok, so in summary, the key features that suggest a diagnosis of ITP are

1. New onset petechiae, bruising, and/or bleeding in an otherwise healthy child

2. Isolated thrombocytopenia with an otherwise normal CBC and a normal peripheral smear
3. Absence of systemic symptoms or red flags to raise concerns for other diagnoses

[Stephanie]:
Sarah, could we discuss some of these red flags features that would suggest alternate diagnosis?

[Sarah]:
Definitely. As you mentioned earlier, the diagnosis of typical ITP can be made with a good history, physical exam and review of laboratory investigations. A good approach is to break down red flag features in to each of these categories.

Red flags on history include:
1. Constitutional symptoms, such as fevers, weight loss, and night sweats
2. Bone pain
3. Poor response to treatment
4. Recurrent thrombocytopenia

Red flags on physical exam include:
1. Lymphadenopathy
2. Hepatomegaly
3. Splenomegaly
4. Signs of chronic illness
5. Unwell appearing child

Red flags in investigations include:
1. Unexplained abnormalities in hemoglobin, WBC or neutrophil count
2. Abnormalities in the peripheral smear

Presence of any of these red flags should prompt you to consider alternative diagnoses, such as coagulopathies, vasculitides, trauma, malignancies, and infectious causes, and to involve a pediatric hematologist.

[Stephanie]: Great, now let's get back to our clinical case.

You assess Victoria and perform a history and physical exam. The patient's mother reports that she first noticed a red rash on her daughter's legs about a week ago. She has experienced several mild nose bleeds since then, lasting only a few minutes each time. There has been no oral mucosal bleeding or GI bleeding. She has not had any headache. Upon further questioning, Victoria is generally healthy and does not take any medications. There is no history of a preceding viral illnesses, weight loss, anorexia, or bony pain.

On exam, Victoria is well-appearing and afebrile with normal vital signs. You find that she has a diffuse non-blanchable, petechial rash on her limbs and torso. There is no palpable lymphadenopathy and abdominal exam is unremarkable with no hepatosplenomegaly. Her neurological exam is normal.

On her laboratory investigations, Victoria has an isolated thrombocytopenia. Her most recent platelet count is 5 x 10^9/L. The rest of her CBC is unremarkable and she has a normal peripheral smear, with no abnormal cellular morphology.

After reviewing with your preceptor, you make the diagnosis of ITP.

[Sarah]: Now that we've made a diagnosis, let's go back to the CPS statement and explore the management recommendations.

Management options for ITP depend on the severity of bleeding, and include observation with or without pharmacologic therapies - such as corticosteroids and IVIG. ITP is often a self limiting condition in 75-80% of cases, regardless of treatment. For patients with mild or no bleeding, treatment does not statistically impact the overall rates of bleeding or developing of chronic ITP. The decision making process should include a family centered approach to discuss what the best management plan is according to each individual patient's needs. This is known as shared decision making.

Mild bleeding is characterized by no bleeding or mild bleeding such as petechiae, bruising and occasional mild epistaxis, which is brief and stops with routine measures. This should have minimal interference with daily living. First line management for these patients includes observation, with restrictions placed on certain activities such as contact sports. Following a shared decision making approach, medication may be indicated in particular cases, for example in an extremely active child, or in a family for whom close follow-up is difficult.

Moderate bleeding constitutes symptoms such as menorrhagia, epistaxis, or other skin or mucosal bleeding. First line therapy includes pharmacotherapy, such as corticosteroids or IVIG. Anti-D immune globulin can be considered in Rh positive children but is not considered first line because of rare but potentially serious adverse effects. Pharmacotherapy aims to increase the platelet count to a point at which the child has adequate hemostasis (i.e. no active bleeding, menorrhagia, or bloody stools).

Severe bleeding includes any of the above that warrants hospital admission. The most severe complication is intracranial hemorrhage. For non-life-threatening severe bleeding, corticosteroids or IVIG can be used. For life-threatening disease, treatment includes a combination of IV corticosteroids, IVIG and platelet transfusion. Tranexamic acid may be added as an adjunct therapy.

[Stephanie]:
There are risks and benefits to consider when choosing a course of treatment. Observation is associated with a longer period of activity restriction and is associated with the slowest rise in platelets, which for some patients and families causes significant anxiety. However, observation does not require a hospital admission, avoids any medication side effects, and is the most cost effective. Importantly, if used for children with no or mild bleeding, this route has not been shown to increase the risk of bleeding or of the development of chronic ITP.

Among pharmacologic options, corticosteroids tend to be the least costly option and can be given as an outpatient. The possible side effects of corticosteroid therapy should be

reviewed with families, including weight gain, elevated blood pressures, increased appetite, gastritis, and changes in mood. A rise in platelets can often be seen within 48h.

IVIG, by contrast, must be given in a day hospital or inpatient setting and is more costly. Potential adverse effects should be reviewed with patients, including headache (from aseptic meningitis), rashes, nausea/vomiting, and fever or chills. Serious side effects are rare but include anaphylaxis and severe hemolysis. IVIG typically increases platelets within 24 hours, while peaking between 2 and 7 days. IVIG is the option of choice when a faster increase in platelet count is desired. It is effective greater than 80% of the time.

After pharmacotherapy has been given, it is important to have frequent follow up with these patients and re-check platelet levels. Approximately 30% of children will relapse 2 to 6 weeks after treatment, with platelet counts falling below 20 $x10^9$/L. A similar approach to management should be applied to retreatment as described above, while also factoring in what side effects the child experienced and how well they responded to the medication.

Some children do not respond to initial therapy. Pharmacologic therapies should be monitored to assess for responsiveness. If platelet levels are not increasing as expected or the patient is not clinically improving, further treatment may be warranted and often involves switching modalities to a different one than was initially trialed. In these situations, a hematology consultation should be placed to confirm the diagnosis.

[Sarah]: Now let's go back to our case.

You suspect that Victoria has typical ITP with mild bleeding, as she has no red flags and her only symptoms include petechiae and mild self-resolving epistaxis. You recall that 1st line management for mild bleeding is observation, with second line treatment options including corticosteroids and IVIG.

You explore the patient and family's thoughts and social context, which may impact their choice of management. Victoria lives within 30 minutes driving of the tertiary care hospital. She does not participate in any high risk activities at school or during play. You explore the risks and benefits of observation vs. pharmacological therapy.

After a shared discussion between the health care team, Victoria, and her family, the decision is made to observe Victoria with frequent follow up. She is counselled to return sooner if there are any changes in her clinical status. You counsel Victoria and her family to avoid medications that have anti-platelet activity such as NSAIDs, as well as high risk activities such as contact sports that may result in serious bleeding. You remind her and her family to share their child's diagnosis with future care providers.

Victoria and her family feel reassured by this management plan and thank you for your team's compassionate care.

[Stephanie]: I'm glad that Victoria and her family were able to decide on a management plan that reflected their unique needs!

Now, let's review some of the key points discussed in this Podcast:

- Typical ITP can be diagnosed with a thorough history, physical exam, and review of lab investigations
- Diagnosis can be made in a well appearing child with isolated thrombocytopenia on CBC and normal peripheral smear.
- Any 'red flags' on history, exam, or investigations warrant consideration of alterative diagnoses, further evaluation, and referral to hematology.
- Management recommendations should be based on severity of symptoms and patient/family factors, and range from observation when bleeding is mild, to corticosteroids or IVIG in cases with moderate or severe bleeding
- Shared decision making with families should take place to create an individualized approach that tailors management to the individual's specific needs.

[Sarah]:
Thank you for listening to this PedsCases podcast based on the new CPS statement on the diagnosis and management of typical, newly diagnosed primary immune thrombocytopenia of childhood. Stay tuned for more podcasts to come!

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