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An Approach to Bleeding and Bruising, Part 1

Developed by Gabriel Blank and Dr. Thomas McLaughlin for PedsCases.com.
Published Jan 14, 2021

Introduction:

Hello and welcome to our PedsCases episode on an approach to bleeding and bruising, part 1 of our exciting two-part series! I am Gabriel Blank, a fourth-year medical student at the University of British Columbia. This podcast was created in collaboration with Dr. Tom McLaughlin, a general pediatrician at BC Children's Hospital. Let's begin as all good detective stories start, with a case.

The Case:

You are a third-year medical student doing your clinical rotation at a general pediatrics outpatient clinic. You enter the room to see a vibrant 16-month-old boy by the name of Jacob. Young Jacob was brought in by his Grandma who is concerned about Jacob's bruising and limp with walking. She has noticed bruises on Jacob's knees, shins, and arms, as well as a big bump on his forehead. There is no specific known trauma to explain these bruises and she also notes that Jacob seems to be favouring his right leg and his gait is altered. There is no history of constitutional symptoms, like fever or weight loss. His grandma is from the paternal side, and is unaware of any family history of bleeding or easy bruising. She is uncertain if there was a cephalohematoma at birth, bleeding after circumcision or umbilical cord separation, or any historical signs of bleeding problems.

You perform a brief physical exam and note what looks like a forehead hematoma. There are also bruises of various colours over the bony prominences on the anterior and lateral surfaces of Jacob's extremities, with none on the trunk, buttocks, or face. There are no other rashes or

petechiae. Looking at Jacob's right leg, you note swelling around the ankle. It feels warm, appears painful to the touch and has a decreased range of motion. Otherwise, the cardiac, respiratory, and abdominal exams are unremarkable with no cervical, clavicular, or axillary lymphadenopathy noted and no splenomegaly.

Uncertain what to do next, you leave to review with the supervisor, frantically scrolling through UpToDate as you wait.

Learning Objectives:

The learning objectives we will cover in this podcast are:
1. Demonstrate a basic approach to bleeding and bruising.
2. Differentiate causes of bleeding & bruising into non-hematologic and hematologic.
3. Discuss the key history questions and physical exam findings when a child presents with bruising and bleeding.
4. Delineate aspects of the history and physical exam that are concerning for inflicted trauma (i.e. child abuse).

How Bleeding Happens:

Let's first go through a crash course on hemostasis. There are two main processes that stop bleeding, formation of a platelet plug – primary hemostasis – and stabilization of this plug through the coagulation cascade, or secondary hemostasis. Primary hemostasis starts when platelets contact damaged blood vessels, releasing granules that promote platelet aggregation. In secondary hemostasis, the coagulation cascade turns fibrin monomers into a blood stopping fibrin polymer. Along with vessel constriction, the aggregated platelets and fibrin polymers work in unison to stop bleeding.[1]

Non-Hematologic Causes of Bleeding and Bruising:

Now onto the approach. The conditions that cause apparent bruising or bleeding can be broadly categorized as nonhematologic and hematologic. Non hematologic causes include dermatologic, vascular, accidental trauma and inflicted trauma (also known as child abuse).

Dermatologic findings can sometimes be mistaken for bruises or bleeding under the skin. Causes include hemangiomas, eczema, and congenital dermal melanocytosis. Congenital dermal melanocytosis is more colloquially referred to as Mongolian spots and is characterized by blue-gray patches commonly on the lower back and buttocks.[2]

Vascular type bleeding leads to cutaneous bleeds, or bleeding in the skin, and may progress to hemorrhaging into organ parenchyma. Causes include vasculitides, inherited connective tissue disorders, chronic steroid use and vitamin C deficiency.[3] Vasculitis is a fancy way of saying blood vessel inflammation. The most common vasculitis in children is IgA vasculitis, also known as Henoch Schonlein Purpura (HSP). It is characterized by colicky abdominal pain, arthritis, and a raised reddish-purple rash, known as palpable purpura, typically over the buttocks and lower extremities.[4] Ehlers-Danlos is the archetypal inherited connective tissue disorder. It presents with a history of poor wound healing, sprains, and joint dislocations with hypermobile joints and paper-thin scars on exam.[3,5]

Alright we covered dermatologic mimics of cutaneous bleeding, such as hemangiomas, eczema and congenital dermal melanocytosis, and four causes of vascular type bleeding: vasculitis, inherited connective tissue disorders, chronic steroid use, and vitamin C deficiency. Accidental trauma encapsulates the non-pathologic, unintentional causes of bruises. Bruises are, in fact, very common in mobile children and increase with mobility. A systematic review showed bruising happens in seventeen per cent of infants starting to mobilise, 53% of walkers, and most schoolchildren.[6] Bruises commonly occur on the front of the body over body prominences.[6] Bruising over the anterior tibias is very common in toddlers. It is crucial to differentiate this from inflicted trauma (child abuse). It is a tragic reality for many kids and a diagnosis you do not want to miss.

While bruising is very common in all kids, it is also the most common sign of inflicted trauma (or physical child abuse). Inflicted injuries should be suspected when the severity or distribution of the injury does not align with the history, the history keeps changing, or the injury is inconsistent with the developmental age of the child.[2] As we've said before on PedsCases, if you're not cruising, you're not bruising. In fact, less than 1% of non-independently mobile babies show any signs of bruising.[6]

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Bruises that are away from bony prominences should also be a flag for potential inflicted trauma. The most common sites are the head and neck followed by the buttocks, trunk, and arms. Bruises are commonly large in inflicted trauma, and typically occur in clusters. They are often associated with other injuries that may be older. Some bruises carry the imprint of the implement used, such as a hand outline or parallel lines of a belt.[6,7] Patterned bruises or symmetrical bruising (i.e. appearing on both upper arms) always requires a clear explanation to rule out inflicted trauma.

Since hematologic conditions are not commonly associated with bony trauma, skeletal injury with bony trauma should raise child abuse alarm bells. Multiorgan dysfunction can be a clue to another diagnosis, though organ dysfunction can also be secondary to direct trauma. For example, an injury to a child's right upper abdomen could cause transaminitis.[8]

If you suspect child abuse, Child Protective Services must be notified! Even us medical students have a duty to tell someone if we suspect it. In every province and territory, there is legislation that this must be done. It cannot be delegated to someone else and it must be done in a timely fashion. It is also important to do a diligent work-up for hematologic conditions when child abuse is suspected. This is partly because many hematologic problems can be confused with inflicted trauma. Additionally, if the case is brought to court, a thorough work up provides crucial medico-legal evidence that other medical causes were considered and ruled out.

Alright, that was heavy. Before we dive into hematologic conditions, lets review the nonhematologic causes. They include derm mimics like hemangiomas, vascular problems like IgA Vasculitis, accidental injuries, and inflicted injuries. Some child abuse red flags are an unexplained injury, bruising in a non-mobile child, associated skeletal trauma, and multiple, large bruises away from bony prominences, like on the ears or neck.

Hematologic Causes of Bruising and Bleeding:

Next up, hematologic causes of bruising and bleeding. Broadly, the two heme ingredients responsible for stopping bleeding are platelets and coagulation factors.[1] The location of the bleeding can be a clue to where the problem is. If platelets are the issue you classically see

cutaneous bleeding, immediate surgical bleeding, and bleeding from mucous membranes such as epistaxis, gum bleeding, and menorrhagia. Cutaneous bleeding is usually characterized by petechiae, which are, non-blanchable discrete lesions that are less than 2-3 mm long. These petechiae can coalesce into larger lesions known as purpura, and even larger areas called ecchymoses.[9,10] In contrast, coagulation cascade can cause deep, often palpable ecchymosis, soft tissue hematomas, and hemarthroses, which is bleeding into the joint space.[9,10]

This episode focuses on coagulation cascade abnormalities. We will talk about platelet problems in the next podcast.

Coagulation Defects:

Let's start with a rapid review of the coagulation cascade, with some quick mnemonics to hopefully make it less painful. There are three pathways: intrinsic, extrinsic, and common. The intrinsic and extrinsic pathways both converge on the common pathway. For the common pathway, think of Canadian currency denominations. It starts at factor ten then goes factors five, two, and one. Extrinsic pathway involves factor VII, a lucky number, and what is luck but an extrinsic benefit. Factor VII, extrinsic pathway. The intrinsic pathway is the other factors, starting at 12—factors 12, 11, 9, and 8.[1]

Now three main clotting tests are PT, aPTT, and mixing studies.[1] PT is used to calculate INR, which is used to monitor the effect of the anticoagulant warfarin. PT measures the common and extrinsic pathways. You can think PT for play tennis, an outdoor sport. Outside for extrinsic pathway. aPTT measures the common and intrinsic pathways. Think PTT for play table tennis, something you do inside or intrinsically. If either PT or aPTT are abnormal, you can do a mixing study, where you combine normal plasma with the patient's plasma. If the clotting time corrects think factor deficiency. If it does not correct then a factor inhibitor, typically an autoantibody, is present.[1] There you have it, PT for extrinsic pathway, aPTT for intrinsic pathway, and mixing studies for factor inhibitors.

Now onto coagulation defects. These can again be conceptually broken down into inherited and

acquired causes. The three most common inherited causes in order are von Willebrand Disease, Hemophilia A, and Hemophilia B. Based on lab data, von Willebrand has a prevalence of 1%, though the percent of people who require specialist care is closer to 0.01%.[11] Its marked by a deficiency or abnormal function in von Willebrand factor, a molecule responsible for binding platelets to damaged vessel walls and stabilizing factor VIII. The disordered platelet function causes mucocutaneous bleeding, though because von Willebrand factor stabilizes factor VIII, severe cases may also have joint bleeding.[11] For more talk on von Willebrand Disease, see the PedsCases episode dedicated to it.

Hemophilia A is caused by Factor VIII deficiency. I remember this as A sounds like 8, for factor VIII deficiency. Hemophilia A occurs in 1 in 5000 live male births. Hemophilia B is caused by a deficiency in factor IX and is present in 1:20000 male births[2,12,13] Notice, I am emphasizing male births. This is because both Hemophilias are X-linked recessive, making them more common in males. And since they affect factors VIII and IX the intrinsic pathway, not extrinsic, is impaired. This classically gives a prolonged aPTT with a normal PT.[8] Obvious signs of coagulation problems, such as easy bruising, intramuscular hematomas, and hemarthroses, usually do not begin until the child starts to cruise.[9] Before children start to cruise, diagnostic clues can be bleeding with circumcision, excessive bleeding with bloodwork, bleeding with forceps or vacuum delivery, or serious spontaneous bleeding into the head or joints. There is a family history of hemophilia in about 2/3 of cases. The cornerstone of effective hemophilia treatment is quick administration of factors. Factor VIII in hemophilia A, and factor IX in hemophilia B. Low resource settings unable to afford factors commonly give FFP and cryoprecipitate.[12, 13]

Next up to bat, the acquired causes of coagulation problems. These can be from consumption of coagulation factors, or decreased production of factors. Consumption of coagulation factors could be due to the systemic inflammation in DIC or factor inhibitors.[8] Factor inhibitors include anticoagulants like warfarin and autoantibodies.[9] Antibodies against specific factors are much less common in children than in the elderly, though about one third of hemophilia patients receiving factor infusions can develop specific factor autoantibodies.[9,14] Regarding decreased factor production, two main causes are liver disease and vitamin K deficiency. [8,15] We have another episode dedicated to Vitamin K deficiency in newborns that you can listen to for a more thorough and well-structured explanation. In short, it can occur as soon as the first 24 hours after birth for the early onset variant, and up to 6 months for late onset. A big cause is

low intake of vitamin K, with chronic malabsorption also being a major culprit behind late onset bleeding. We prophylax against “hemorrhagic disease of the newborn” with vitamin K IM at birth.[16]

Alright, we discussed some inherited and acquired causes of coagulation cascade defects. Inherited causes include the hemophilias and von Willebrand disease. Acquired coagulation problems of note include DIC, factor inhibitors, liver disease and vitamin K deficiency.

History and Physical Rapid Review:

With this information under our belt, let’s review the key components of the history and physical exam.

First and foremost, you should ask about a history of previous bleeding problems, such as cephalohematoma at birth, petechiae at clothing line pressure sites, and post-circumcision, post-venipuncture, and umbilical stump bleeding.[2] Make sure to elucidate the type of bleeding. Remember, this classically means deep bleeding for coagulation problems and mucocutaneous bleeding for platelet issues. Of course, you can ask questions for specific disorders. This includes constitutional symptoms for malignancy, family history for inherited causes, and drug history for pharmacologic causes. The timeline of onset can also help differentiate more rapid onset bleeding causes from potentially more chronic pathology, like Hemophilia and other inherited causes.

Next is our physical exam. As with really all clinical encounters**,** you should start with ABCs, vitals, and general appearance. Ask yourself, does this patient look sick. If they look acutely ill, grab help! Otherwise, physical exam consists of carefully assessing the skin, oropharynx, and joints for signs of bleeding. Look for any enlarged structures, like lymphadenopathy, splenomegaly, and hepatomegaly. Assess for skeletal abnormalities or fractures.[17] And finally, always have the child abuse alarm triggers at the back of your head. This includes injuries inconsistent with the history provided, bruises in a baby who is non-mobile, and injuries that are away from bony prominences or not on the front of the body.

Cases Revisiting:

Remember 16-month-old Jacob? I know we talked about a lot since then. He had bruises along his extremities with that peculiar swelling around the right ankle. The vague history with seemingly unexplained bruises may have made you think of inflicted trauma, an important consideration, and a diagnosis you do not want to miss. You and the preceptor decide to call the mom for more information. She mentions Jacob has always seemed like an easy bruiser, and she is happy that her mother in law was able to bring him in. The mom notes Jacob did have prolonged bleeding after his circumcision and had what sounds like a cephalohematoma at birth. When asked, the mom mentions her Dad, Jacob's granddad, had a bleeding disorder, though the mom is uncertain what specific condition it was.

History of bleeding, bruising, and now an apparent joint bleed in a male, with a potential positive family history for a bleeding disorder on the maternal side. This makes you suspicious of a certain diagnosis. After discussion with the family, you decide to admit the patient for further workup. You order the following hematologic labs: CBC, blood smear, aPTT, PT, mixing study, and Factor VIII and IX levels. The CBC, blood smear and PT are normal, though the aPTT is prolonged with correction on mixing study. A radiograph of the right ankle is performed to rule out fracture, which shows a joint space effusion consistent with hemarthrosis and no fracture. Given the hemarthroses, history, and high aPTT, the team forgoes a skeletal survey and CPS consult for child abuse given the high suspicion for another diagnosis. The factor levels return, and factor VIII is reported as 0.01 IU/mL, right on the upper boundary for severe hemophilia A. You have your diagnosis. The family is told about the diagnosis, are informed that factor replacement is a vital part of management and will be following up with the hematology service for further care.

Conclusion and Review:

Let's finish things off by reviewing what we learned. Causes of bleeding and bruising can be differentiated into non-hematologic and hematologic aetiologies. Non-hematologic causes include vascular pathology like IgA-Vasculitis, dermatologic mimickers like hemangiomas, and both accidental and inflicted trauma. Think of inflicted trauma when you have large

unexplained bruises away from bony prominences in a non-mobile child. Coagulation cascade pathology can be categorized as inherited or acquired. Inherited causes of coagulation abnormalities include the Hemophilias and von Willebrand disease. Two categories of acquired coagulation problems are factor destruction, think DIC or factor inhibitors, and decreased production, think liver disease or vitamin K deficiency. On history you should ask questions that point toward a bleeding disorder, such as cephalohematoma at birth, umbilical stump bleeding, petechiae at clothing pressure sites, and post-circumcision or post-venipuncture bleeding. Then, ask about the type of bleeding. Classically, mucocutaneous suggests platelets pathology, deep bleeds point to coagulation problems, and bleeding in the skin and organ parenchyma suggests vascular pathology. On physical exam, carefully examine the skin, while also assessing for lymphadenopathy, hepatosplenomegaly, and skeletal malformations or injuries.

That's all for now! Join us in our next episode as we discuss the platelet pathologies that cause bleeding and bruising.

Thanks for listening!

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