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Recurrent Fractures

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Introduction:

Hi, my name is Liyana Kukkadi and I am a final year medical student from Chatham, Ontario in the 6 year accelerated medicine program at the Royal College of Surgeons in Dublin, Ireland. This podcast was developed under the guidance and supervision of Dr. Gina Catena, a pediatrician and clinical fellow in child maltreatment, and Dr. Erin Boschee, a pediatric hospitalist and child maltreatment pediatrician at the Stollery Children's Hospital in Edmonton, Alberta. Today, we will discuss an approach to recurrent fractures in the pediatric population. As we go through a clinical case, we will develop an approach to assessing a child with recurrent fractures by exploring common pathologic etiologies and touching on management options for recurrent fractures.

Learning Objectives

We hope that by the end of this podcast, listeners will be able to:

1. Identify red flags in a pediatric patient presenting with recurrent fractures which may prompt consideration of an underlying medical condition or inflicted injury.
2. Formulate a broad differential diagnosis for a child with recurrent fractures and list key investigations to consider.
3. Briefly discuss management options to consider for a child with recurrent fractures.

Fractures are a commonly seen occurrence in childhood, most often due to accidental trauma.[1] Fractures that occur in radiologically abnormal bone, in an atypical location (such as the humerus and femur in a non-mobile child or the vertebral body) or due to low impact trauma may require further investigation for medical conditions such as a primary bone fragility disorder or osteoporosis secondary to a chronic medical condition.[2]

This podcast covers an important topic. It is a crucial skill to be able to identify red flags and recognize the possibility of underlying medical conditions contributing to bone fragility. Early identification of an underlying medical disorder which may predispose a child to fractures may help to reduce further morbidity. Furthermore, the ability to recognize a pathological fracture will help you determine whether to view the fracture as an isolated entity or as a sequela of a potential underlying medical condition.[3] All fractures should be evaluated to assess whether they are in keeping with the mechanism of injury available, as well as whether there are red flags that should prompt further investigation for an underlying medical cause or inflicted trauma. While inflicted injury may be an important consideration if the fracture is atypical or is not in keeping with the biomechanics of the injury or developmental ability of the child, this podcast is focusing on medical conditions that may result in bone fragility.

Acute complications that can result from a fracture include neurovascular injury, hemorrhage, fat embolism and/or compartment syndrome.[4] Chronic complications may include limb length discrepancy as a result of premature fusion of the growth plate, non-union (where the bone does not heal), malunion (where the bone does not align correctly), post-traumatic osteolysis or avascular necrosis.[4]

Introduction to bone health

We'll start with a brief introduction to bone physiology and discuss some of the broad categories that may impact bone health and cause fractures.

Bone mass, development and strength are influenced by a combination of factors including genetics, muscle mass, nutrition and hormones.[5] You have around 300 bones when you are

born and end up with 206 as an adult.[6] Some bones are made up partially or entirely of cartilage, which is slowly replaced by bone with the help of calcium.[7] Once all of the cartilage has been replaced by bone, growth is considered to be complete.[7] Children have more flexible bones than adults, as they contain a higher proportion of cartilage. This means that, while an adult's bone is more likely to break than bend, a child's bone is actually more likely to bend than break.[6] Another difference between the bones of children and adults is the growth plate. In adults, the growth plate has fused, so a fracture will not have significant clinical ramifications on growth. In children, a fracture of the growth plate can actually impair growth and prevent the bones from reaching their maximal length, as well as possibly causing significant deformity.[6]

Examples of medical conditions that may impact bone health include nutritional deficiencies such as rickets, hormonal imbalance or genetic disorders such as osteogenesis imperfecta.

Nutrients such as calcium, vitamin D and magnesium are important for bone health. A lack of dietary calcium means that the body will reabsorb the required calcium from bones, which can negatively impact bone strength. Vitamin D is necessary for calcium to be absorbed in the intestine and magnesium regulates both vitamin D and calcium. Hormones such as parathyroid hormone, calcitriol and calcitonin are important for bone health because they promote bone resorption/formation, promote the intestinal absorption of calcium and inhibit bone breakdown, respectively.

Case presentation

Now that we've covered a basic introduction to bone health and the implications of fractures, let's start our clinical case. Imagine that you are a pediatric resident working in the ER when an 8-year-old boy named Harry presents with a suspected fracture of his forearm. When reviewing his medical chart, you note that Harry had 2 fractures last year as well. His mom says that Harry gets injured really easily, with multiple bruises regularly present on his skin. She recalls a recent fracture resulting after a playdate with friends and another one occurring during a relatively minor-seeming household accident.

Definition of recurrent fractures

A significant fracture history is defined as when a child has ≥2 fractures before the age of 10, ≥3 fractures before the age of 19 or a vertebral compression fracture at any point.[8] A fracture that occurs more than twice in the same segment of bone is defined as recurrent, and should raise suspicion for an underlying pathology.[3] The mechanism of injury for any fracture should be considered to determine if it is an appropriate explanation and whether red flags that prompt further investigation for a possible underlying medical cause are present. A history of multiple fractures may indicate a pathologic fracture, defined as a fracture in bone weakened by an underlying bone abnormality. [9] Certain types of fractures are more concerning for possible pathologic fracture, including fractures located in an atypical location (such as the humerus, femur or vertebral body), fractures in radiologically abnormal bone and injury context inconsistent with the observed fracture.[3]

Differential diagnosis for recurrent fractures

Fractures as a result of trauma, including accidental and inflicted, are more common than fractures related to an underlying medical condition.[1,10] It is important to be able to recognize red flags and features that might suggest that an underlying medical cause is responsible for the recurrent fractures.The possibility of inflicted (non-accidental) injury should always be considered, and it is important to remember that children with an underlying medical condition affecting bones can also experience abuse. Further discussion of the medical assessment of fractures due to suspected child maltreatment is available in a separate podcast.

The differential for an underlying pathology can be subdivided into primary disorders of bone (e.g. genetic disorders) or medical disorders with secondary effects on bone. Medical disorders with secondary effects on bone can be further subdivided into endocrine disorders, nutritional deficiency, chronic renal disease, medication or invasive neoplastic bone fragility. These secondary pathologies weaken the bone, leading to osteoporosis and therefore make it easier for fractures to occur. Children with reduced mobility due to significant neurologic or musculoskeletal disorders are also at risk of osteoporosis, due to decreased osteoblast activity as a result of decreased regular mechanical stress on the bone. Risk factors for secondary bone fragility include inflammatory diseases, chronic immobilization, nutritional/intestinal/malabsorption disorders, hematologic disorders, prematurity, endocrine

disturbances, chronic kidney disease, cholestatic liver disease and therapies such as chemotherapy, chronic steroid use or solid organ transplant.[11] Many of these disorders may predispose a child to fractures with lesser trauma, but are unlikely to result in fractures in the complete absence of trauma.

Nutritional deficiencies that can result in fracture include vitamin D deficiency (rickets), anorexia nervosa and celiac disease.[12,13] Endocrine disorders that can result in fracture include Cushing syndrome, growth hormone deficiency, hypogonadism, and hyperthyroidism.[12,13] A few of the genetic disorders that can result in fracture include osteogenesis imperfecta, homocystinuria and McCune-Albright syndrome.[12,13] Some medications that can predispose a patient to recurrent fractures include corticosteroids, methotrexate and anticonvulsants such as phenytoin and carbamazepine.[12,13]

Key questions to be asked during history[3]

A thorough history is essential when investigating recurrent fractures. After asking initial questions about trauma and the events surrounding the fracture, it is important to ask questions pertaining to as far back as the birth history.

Examples of questions to ask regarding the birth history to help elicit any neonatal risk factors for bone fragility include gestational age, NICU history and the need for steroids, diuretic medications or total parenteral nutrition (TPN).

In addition to general past medical history, key questions must be posed regarding any possible chronic disease processes, such as celiac disease, chronic kidney disease or malignancy in any location. Examples of these specific questions include: “Does your child experience foul smelling stool or flatulence? Has there been any recent weight loss?” Further history and investigation may be indicated if the history and review of systems is concerning for an underlying medical condition that may affect bones.

When inquiring about medications, it is helpful to ask if there is a history of steroid or anti-epileptic medication use. It is also important to ask if the child is taking any supplements, such as calcium or vitamin D.

Dietary history is another component that is important to investigate. Questions like “Does your child avoid dairy?” or “Would you say they are eating a balanced diet?” can help you assess whether nutritional status has played a role in their presentation.

Family history should be assessed for osteoporosis, bone dysplasia, metabolic disorders and malignancies in childhood (especially of the bone).[3] Asking whether there is a known family history of an inherited bone disorder like osteogenesis imperfecta, or of recurrent or unexplained fractures is also important.

Social history can help uncover if the child is experiencing any restrictions of mobility or activity, whether there are financial barriers to accessing adequate nutrition and if there are any significant hindrances to their quality of life.

Asking about overall growth pattern can also be insightful, as chronic disease processes tend to result in stunted growth.[14] It is important to have a high degree of suspicion and ask questions pertaining to causes of primary and secondary bone fragility to ensure these risk factors are ruled out.

Physical examination

On physical examination, the pubertal status and growth parameters of the child must be assessed, along with the overall nutritional status.

On general inspection, observe for any bruising or bowing of the limbs. Head shape can be assessed for frontal bossing, open fontanelles and abnormal shape. Assessment for skeletal abnormalities of the rib cage, spine, pelvis or widening of the wrists may also be conducted. Blue sclera on examination of the eyes or discoloured teeth may point towards a diagnosis of osteogenesis imperfecta. General dentition and tooth eruption should be noted as well.

Palpation may reveal lymphadenopathy or hepatosplenomegaly and bony tenderness may raise suspicion for malignancy. Muscle weakness may be evident on manipulation of limbs and joint laxity can also be assessed. Additionally, dysmorphic features and developmental abilities can be assessed.

Back to the case

Harry's history, as recounted by his mother, is significant for recurrent fractures since the age of 5. She said that his height dropped to the 75th centile from the 90th 2 years back, according to his pediatrician, but he has been tracking well since. Harry does not currently take any medications and enjoys a variety of dairy in his diet, including milk and cheese. Harry's mom noted that a relative on her husband's side of the family had "a problem to do with bones and blue eyes" and wondered if this might have anything to do with that. There are no signs or symptoms concerning for an underlying chronic disease or history of malignancy in the family.

On physical examination, Harry is reluctant for you to examine his arm but you can appreciate erythema and slight swelling on visual inspection. There is no evidence of dysmorphic features, bowed limbs, bony tenderness, lymphadenopathy, hepatosplenomegaly or muscle weakness on examination. Harry's dentition is normal and he doesn't show any signs of abnormal tooth eruption. You check Harry's eyes for blue sclera, which you think you can appreciate. You start to suspect a diagnosis of osteogenesis imperfecta type I, based on the history of fractures, family history of a descriptively similar nature and the absence of severe symptoms (such as poor muscle development, significant scoliosis). You decide to examine the eyes under a slit-lamp, after which you can clearly distinguish the bluish-grey nature of the sclera. Ideally, you would perform a hearing test to assess whether bone remodelling has impacted his hearing.

Investigations to consider

Important investigations to conduct include both laboratory studies and imaging, usually tailored by the differential diagnosis based on history and physical examination.

First line laboratory investigations include a complete blood count, renal and liver function tests, mineral metabolism screen (including serum calcium, phosphate and alkaline phosphatase) and urinalysis.[15,16] Bone turnover markers, such as alkaline phosphatase, must be interpreted while remembering that pediatric levels vary from adults.[15] Other laboratory tests, such as parathyroid hormone, 25-hydroxy-vitamin D, serum copper, ceruloplasmin, sex hormone/growth hormone levels, inflammatory markers or celiac screening, may be ordered based on clinical suspicion.[16]

A plain radiograph is first line for imaging, used to compare the injured with the unaffected side, as well as to evaluate for radiographic signs of osteopenia or other bony abnormalities.[17] To confirm low bone density, a dual energy X-Ray absorptiometry (DXA) scan is the gold standard.[17] There are challenges and limitations to interpreting bone mineral density in the pediatric population, especially in infants and young children, where standard reference ranges haven't been determined. A DXA scan may be indicated in children on systemic long-term steroids, children who have chronic inflammatory conditions, hypogonadism, prolonged immobilization, osteogenesis imperfecta, idiopathic juvenile osteoporosis, recurrent low trauma fractures, or apparent osteopenia on radiographs.[18] However, it is important to remember that DXA scan results must be interpreted in the context of a clinical picture, as a diagnosis of osteoporosis cannot be made on the results of the scan alone; the child must have a history of being prone to fractures.[11,19] If a diagnosis of osteogenesis imperfecta is considered, a skull x-ray can assess for the presence of wormian bones.[4] Genetic testing can be ordered if there is clinical suspicion and a genetics consult may be considered. It is important to note that not all types of OI have a known molecular basis. Therefore, a negative molecular workup does not effectively exclude the condition and the diagnosis is made clinically, based on the history and clinical manifestations.

Back to the case

Starting with laboratory investigations, you order a mineral metabolism screen, inflammatory markers, complete blood count and bone turnover markers. The results demonstrate normal levels of calcium, phosphate, parathyroid hormone, vitamin D and normal renal and liver function. The complete blood count is normal as well, but his ALP is high, indicating increased bone turnover.

You decide to order a plain radiograph of his forearm, to confirm the diagnosis of a fracture, and his skull, to look for Wormian bones. The forearm radiograph confirms the fracture and displays thinning of the radius with thin cortices. The skull radiograph confirms the presence of multiple Wormian bones. At this point, you are more concerned about the diagnosis of type 1 osteogenesis imperfecta. You decide to order a DXA scan to confirm osteoporosis. You also

make a referral to genetics for assessment and genetic testing to potentially confirm the diagnosis of osteogenesis imperfecta.

Potential management options for bone fragility

The following management options may be applicable to children in general with underlying bone fragility, not just for this specific case. The child should be supported by a multidisciplinary team, monitoring bone health, pubertal status and nutrition. It is also important to manage any underlying medical disorders that are contributing to bone fragility. Recommended initial management options include optimizing dietary intake of calcium and vitamin D, as well as an increase in weight bearing exercise (e.g. dance). Calcium supplementation outside of adequate dietary intake can also be considered. Risk reduction strategies, such as avoidance of contact sports and wearing protective gear where required, are also recommended. More specific treatment varies with the underlying pathology causing the recurrent fractures. Bisphosphonates may be considered in some circumstances. Collaboration with a bone health specialist if available is often beneficial.

Back to the case

You decide to recommend supplementing vitamin D and ensuring adequate calcium intake, as well as weight-bearing activity to strengthen Harry's bones. You also refer him to a pediatric endocrinologist or bone health specialist to assist with optimizing his management, consideration of further therapies like bisphosphonates and for ongoing follow-up. Other management would include treatment for future fractures and regular follow-ups to assess Harry's quality of life and the efficacy of his bone-strengthening regimen.

Review of Key Learning Points

We hope that you now know the following key points about recurrent fractures in the pediatric population:

1. Red flags for a pathologic fracture due to an underlying medical condition in a pediatric patient presenting with recurrent fractures include fractures located in an atypical location, fractures in radiologically abnormal bone and injury context inconsistent with the observed fracture.
2. A broad differential diagnosis for a child with recurrent fractures includes trauma (both accidental and inflicted), genetic disorders, endocrine disorders, nutritional deficiency, chronic renal disease, medication or invasive neoplastic bone fragility; Key investigations include laboratory investigations assessing mineral metabolism, plain radiographs of fractures and DXA scans in certain situations.
3. A brief overview of management options for a child with recurrent fractures may include conservative management through maintaining sufficient levels of calcium and vitamin D, as well as regular exercise. Bisphosphonates may be used as pharmacological treatment in some circumstances.

Thank you for listening to this PedsCases podcast discussing the approach to recurrent fractures! Check out the website for the CPS inflicted fracture statement (by Chauvin-Kimoff et al.), the podcast on fractures (by Vogels and Dulai), podcasts on other topics, cases and more!

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