Scurvy in a pediatric patient with trisomy 21: A case study

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The case

A 2-year-old girl with a past medical history of trisomy 21, complete atrioventricular canal defect status post repair, West Syndrome, and developmental delay presented to her primary care provider with inability to bear weight on her legs and decreased oral

intake for 3 days. Her mother also described intermittent ear tugging, fussiness, and poor sleep. She denied any convulsions, rashes, bleeding, bruising, fevers, cough, congestion, trouble breathing, diarrhea, lethargy, or history of trauma.

On physical exam, her vital signs were normal. Her weight was at the 65th percentile and her height was at the 99th percentile. Examination of the ears, eyes, mouth, throat, heart, lungs, and abdomen were benign. She had notable weakness in both her upper and lower extremities, with inability to bear weight on her legs or push herself up from prone with her arms. She was also noted to have pain with bilateral knee extension and hip rotation. The tone in her bilateral upper and lower extremities was normal and there were no obvious deformities, signs of trauma, edema or erythema on her extremities. Her joints had full range of motion and no warmth, tenderness, or swelling.

Our patient's birth history was remarkable only for a prenatal diagnosis of trisomy 21 and cardiac defects. She was born at term and had an unremarkable nursery course. Our patient's social history was generally unremarkable. Our patient's family was from Ghana though she was born in the United States. She lived with her mother, father, and 4 older siblings. She was a selective eater and her diet was limited to cornmeal porridge, fufu (made with steamed or boiled cassava dough), banku (made with steamed corn and cassava dough), mashed beans, mashed yams, and oatmeal, though at presentation her mother reported she was refusing even her preferred foods. Her developmental history was remarkable for global developmental delay. At baseline she had fewer than 20 words, primarily crawled on her hands and knees but could take 2-3 steps on her own and would walk more if holding her mother's hands. She could eat finger foods but could not use utensils.

Background:

Vitamin C deficiency, also known as scurvy, is one of humanity's earliest described diseases. Vitamin C is a key micronutrient essential for both immune function and protein synthesis, and its deficiency results in an array of pathologies. In modern times, scurvy is easily preventable with adequate dietary diversity and easily treatable with vitamin C supplementation. At the same time, it remains a clinical challenge because its relative rarity and wide-ranging presentation can often delay diagnosis.

Importantly, case reports of vitamin C deficiency in pediatrics frequently focus on children with autism spectrum disorder (ASD), whose restrictive diets put them at higher risk. Relatively little attention has been paid to vitamin C deficiency in children with trisomy 21. The diagnosis of scurvy in this population can be particularly challenging given the overlap of symptoms with leukemia, for which patients with trisomy 21 are at a

10-to-20-fold increased risk.[1] This case report describes a patient with trisomy 21 and scurvy and discusses the unique diagnostic challenges in this special population.

Diagnosis

She was sent for bilateral hip and femur x-rays which showed bilateral distal femur metaphyseal lucencies that according to the radiologist's report were most concerning for hematological malignancy or metabolic bone disease. Initial blood work showed elevated c-reactive protein (27, ref: 0-5.0 mg/L), normal LDH (276, ref: 170-450 U/L), and a complete blood count (CBC) was significant for normocytic anemia (Hgb 9.7, ref: 10.3 - 13.2 g/dL; MCV 72.7, ref: 69.5 - 81.2 FL) and leukopenia (WBC 3.6, ref: 6.2 - 15.5 x10E3/uL). Her respiratory viral panel was also positive for rhinovirus/enterovirus.

The differential diagnosis at her initial presentation included infectious, metabolic, and hematologic causes, the most concerning of which was leukemia. She was immediately referred to hematology-oncology, where a flow cytometry and peripheral blood smear were performed. Both were normal.

One week later she was seen in the emergency department, still with decreased oral intake and refusal to bear weight. She was evaluated by a dentist who noted an eruption cyst on the lower gums and mild gingival swelling which may have contributed to decreased oral intake. She was discharged and her work-up continued outpatient. The patient had repeated CBCs over the following week that showed the resolution of the leukopenia (WBC 6.3) but persistent anemia (Hgb 9.7). Iron studies confirmed iron deficiency anemia (Transferrin saturation 6%, ref: 15-50%; Serum iron 19, ref: 50-200 mcg/dl).

To further elucidate a possible metabolic cause of her x-ray findings, she was seen by endocrinology. Her lab results showed a low vitamin D 25-OH level (16.7, ref: 30.0 - 100.0 NG/ML), normal iPTH (27, ref: 10 - 65 PG/ML), elevated B12 (1772, ref: 211 - 911 pg/mL), and normal methylmalonic acid (155, ref: 0 - 378 nmol/L).

Three weeks after her initial presentation, she was again seen by her primary care provider. Her refusal to bear weight was unchanged and her oral intake had further decreased. Her weight was now at the 44th percentile. The decision was made to admit the patient for further workup and nutrition optimization.

When admitted, our patient underwent an extensive work up, including endocrine studies that were significant for elevated TSH (6.836, ref: 0.400 - 4.200 uIU/mL) with normal free T4 (0.93, ref: 0.80 - 1.50 NG/DL). During her admission, she had worsening anemia (lowest Hgb 7.7), uptrending LDH (highest LDH 324), and worsening leukopenia (lowest WBC 3.9). Given her increased risk of leukemia due to trisomy 21, a decision was made to pursue bone marrow biopsy, which was normal. Several micronutrient studies were sent, with normal results except for her vitamin C level, which resulted as <0.1 (ref: 0.4-2 mg/dL).

Management

A vitamin C level was sent for our patient on admission and resulted a week later. During the interim, a presumptive diagnosis of vitamin C deficiency was made and our patient was started on nasogastric tube feeding with nutrient supplementation. Once the diagnosis of scurvy was confirmed, she was continued on her nasogastric tube feeding for a week prior to discharge to allow for optimization of her regimen and extensive teaching with her family. She was evaluated by speech and language pathologists who diagnosed our patient with developmental feeding disorder and recommended intensive feeding therapy outpatient with a goal of increased dietary diversity.

Since discharge, our patient has had steady improvements. She is again bearing weight on her legs and her weight has improved to the 76th percentile. Her management has been complicated however by continued poor oral intake and limited dietary diversity, necessitating prolonged nasogastric tube feeding with supplementation. A multidisciplinary approach, working with nutritionists, occupational therapists, and pediatricians, will be essential for improving her nutritional status.

Discussion

Although vitamin C deficiency is relatively rare, it is a potentially important cause of pathologies in children with chronic conditions, especially in the hospital setting. A recent study at a large children's hospital found 32 cases of vitamin C deficiency over a 5 year span.[2] Although the majority of patients in that study had vitamin C deficiency secondary to iron overload, 4 of these children had vitamin C deficiency stemming from a lack of dietary diversity. Relevant to our case, 3 had ASD and 1 had an undescribed developmental delay. These trends emphasize the importance of including vitamin C deficiency in the differential for any child presenting with weakness and developmental delay, as the lack of dietary diversity may be particularly extreme in this population. Though no cases of trisomy 21 were described by Golriz et al, a brief review of the

literature reveals a handful of cases of scurvy in patients with trisomy 21 stemming from a lack of dietary diversity.[3,4,5] Although trisomy 21 is more classically associated with excess caloric intake and obesity, the potential for restrictive eating and subsequent micronutrient deficiencies should not be overlooked.

As in our case, however, a co-morbid trisomy 21 diagnosis can complicate an already challenging work up. Patients with trisomy 21 are at a 10-to-20-fold increased risk of developing acute leukemia, with the highest incidence in children aged younger than 5 years.[1] Leukemia and scurvy share many common signs and symptoms, including: anemia, which is common in Vitamin C deficiency given vitamin C's role in iron absorption; weight loss; limp pain; petechiae; mucosal bleeding; and radiographic abnormalities like metaphyseal lucencies. In cases like ours where the unique characteristics of scurvy, such as follicular hyperkeratosis, are absent, the 2 diagnoses may be even harder to distinguish clinically. Given this overlap, children with trisomy 21 presenting with this constellation of symptoms may warrant presumptive treatment for micronutrient deficiencies when pursuing a simultaneous evaluation for both hematological and nutritional pathologies. Our case highlights both the importance of considering scurvy as a potential diagnosis in patients with trisomy 21 presenting with weakness and the challenges of making this diagnosis.

References

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