**Title**: A case of scurvy with rapidly enlarging palatal masses initially concerning for Acute Myeloid Leukemia

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**Running title**: Scurvy initially concerning for AML

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| **Abbreviation** | **Full term or phrase** |
| AML | Acute Myeloid Leukemia |

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**Introduction**

Scurvy is a nutritional deficiency caused by a lack of ascorbic acid, or vitamin C. Vitamin C is an essential cofactor in collagen cross-linking and iron utilization, which results in a wide constellation of symptoms such as anemia, bone pain, gingival swelling, easy bruising, and petechiae[[1]](#endnote-1). Though scurvy is well-known, it is traditionally considered a disease of the past given our broad understanding of nutrition and a greater accessibility to food. Despite this, scurvy is still prevalent in developed countries, specifically in pediatric patients with developmental disorders and/or restrictive eating habits[[2]](#endnote-2). Scurvy’s nonspecific symptoms, its ability to mimic several autoimmune, infectious, or hematologic conditions, and it’s perceived rarity, can lead to a delayed diagnosis[[3]](#endnote-3). Here, we describe a patient with autism spectrum disorder, who presented with symptoms closely mimicking acute myeloid leukemia (AML), and **following extensive work-up and prolonged hospitalization** was given a final diagnosis of scurvy.

**Case Description**

*Initial Presentation*

An 8-year-old girl with autism and a history of a desmoplastic infantile ganglioma resected at 12 months of age presented to the emergency department with rapidly enlarging bilateral maxillary masses causing displacement and loss of teeth over the prior month. Over the same period, the patient developed gingival bleeding, fatigue, weight loss, bruising, petechiae, and bilateral lower extremity pain. Physical exam revealed large bilateral oral lesions to the hard palate (***Figure 1***) in addition to tachycardia, flow murmur, pallor, prolonged capillary refill, petechiae, ecchymosis, and refusal of manipulation of the bilateral lower extremities. Sinus computed tomography showed lobulated and heterogeneously enhancing soft tissue lesions along the roof of the oral cavity bilaterally. Initial labs demonstrated a severe normocytic anemia (Hemoglobin 4.9 g/dL) with appropriate reticulocytosis.

*Hospital Admission*

The patient was admitted for blood transfusion due to symptomatic anemia and for further work-up of her oral cavity lesions. She responded to transfusion but required repeat transfusions to maintain hemoglobin >7 g/dL. CBC was otherwise unremarkable, with normal platelet count, white blood cell count and differential. Blood smear showed normocytic anemia with hypersegmented neutrophils. Other significant labs included elevated INR, elevated soluble transferrin receptor, elevated ferritin, elevated haptoglobin, normal fibrinogen, elevated D-dimer, elevated ESR, and elevated CRP. Vitamin B12 was normal but folate levels resulted in error twice. EBV, parvovirus, and HIV were negative. No clear source of bleeding was identified in sputum, urine, stool, or joint spaces. Due to concerns that the maxillary growths could represent chloromas, a biopsy of the oral cavity masses was performed, with pathology revealing benign fibroblastic and myofibroblastic proliferation, without suggestion of a malignant process.

Throughout hospitalization, the patient experienced bilateral lower extremity pain and swelling of the knees and ankles, causing refusal to ambulate or to work with physical therapy. Lower extremity radiographs revealed mild osteopenia with soft tissue swelling to the bilateral knees and ankles (***Figure 2***).

On the eighth day of hospitalization, a dietary history of avoidant restricted food intake was obtained. This raised concern for scurvy given her constellation of anemia, oral lesions, extremity pain and swelling, and petechiae. Ascorbic acid levels were sent and empiric therapy with 250 mg ascorbic acid daily was initiated. Levels returned 1 week later with ascorbic acid <0.1 mg/dL. Vitamin D and folate levels also returned low at this time. All other vitamins levels returned normal, including copper, vitamin A, vitamin B12, zinc, homocysteine, and methylmalonic acid. Following supplementation with ascorbic acid, multivitamin, and iron, symptoms slowly resolved, hemoglobin stabilized, and the patient did not require additional blood transfusions. Patient was discharged with appropriate supplementation.

*Outpatient follow up*

The patient was seen by hematology 12 days following hospital discharge with improvements in energy, oral lesions, petechiae, and gingival bleeding. Labs at that time showed hemoglobin 11.9 g/dL. Patient followed with rheumatology, orthopedics, and physical therapy with complete resolution of symptoms. She continues vitamin supplementation while she works with occupational therapy on oral sensory challenges and with a dietician for proper nutritional intake.

**Discussion**

The classic presentation of AML includes anemia, easy bruising, easy bleeding and bone pain, all of which were noted in our patient. Inflammatory markers are often elevated in scurvy, which can also be misleading[[4]](#endnote-4). Although gingival lesions are well-known manifestations of scurvy, the size, location, extent and rapid development of these lesions was atypical (***Figure 1***). Her anemia, which appeared to reflect a combination of red cell aplasia and peripheral destruction, further clouded her clinical picture[[5]](#endnote-5).

Vitamin C plays a critical role in collagen stabilization. Humans are unable to synthesize vitamin C and are therefore dependent on dietary sources. Defects in collagen synthesis result in most scurvy symptoms, such as fragile blood vessels, gingival hyperplasia, and poor formation of bone osteoid. Vitamin C also plays a role in iron utilization and folic acid stabilization, which may contribute to the anemia seen in scurvy.

Scurvy is a preventable condition that should be included in the differential diagnosis for pediatric patients with anemia, refusal to walk, oral lesions, and/or gingival bleeding. The index of suspicion should be higher in patients with neurodevelopmental disorders and/or restrictive diets. Symptoms are nonspecific and mimic many conditions, therefore prompt clinical diagnosis followed by empiric treatment is critical to avoid invasive testing and prevent disease morbidity.

**Conflict of interest statement**: We do not have any conflicts of interest to disclose

**Ethics Statement**: Informed consent was obtained from patient’s mother regarding this case report.

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FIGURE 1: Oral Lesions

A person's mouth with a sore

Description automatically generatedA close-up of a person's mouth

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FIGURE 2: Radiograph of Knees with Soft tissue Swelling, Mild Osteopenia

X-ray of a knee joint

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1. Kinlin LM, Weinstein M. Scurvy: old disease, new lessons. *Paediatr Int Child Health*. 2023;43(4):83-94. doi:10.1080/20469047.2023.2262787 [↑](#endnote-ref-1)
2. Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the doctor away: scurvy in the year 2000. *Pediatrics*. 2001;108(3):E55. doi:10.1542/peds.108.3.e55 [↑](#endnote-ref-2)
3. Agarwal A, Shaharyar A, Kumar A, Bhat MS, Mishra M. Scurvy in pediatric age group - A disease often forgotten?. *J Clin Orthop Trauma*. 2015;6(2):101-107. doi:10.1016/j.jcot.2014.12.003 [↑](#endnote-ref-3)
4. Kinlin LM, Weinstein M. Scurvy: old disease, new lessons. *Paediatr Int Child Health*. 2023;43(4):83-94. doi:10.1080/20469047.2023.2262787 [↑](#endnote-ref-4)
5. Cox EV. The anemia of scurvy. *Vitam Horm*. 1968;26:635-652. doi:10.1016/s0083-6729(08)60779-7 [↑](#endnote-ref-5)