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Gingival Enlargement and Facial Petechiae: Early Indicators of Pediatric Leukemia

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Abstract
In 2020, there were 311,594 deaths due to leukemia. It is reported that leukemia accounts for only 4% of new cancer cases in males and 3% in females. Nevertheless, leukemia is the most common malignancy in children and adolescents. Childhood leukemia is typically diagnosed by pediatricians or family doctors. This report presents a case of leukemia in a 14-year-old male, initially suspected by a dentist at a dental hospital, with the diagnosis confirmed by a complete blood count laboratory test. Gingival enlargement and petechiae throughout the body—especially on the face and arms—were key signs leading to suspicion and diagnosis, which had previously been overlooked by the family doctor and an otorhinolaryngology (ENT) consultant.
Keywords: Gingival Enlargement, Leukemia, Oral Diagnosis, Petechiae

Introduction

Leukemia represents a diverse range of hematologic malignancies characterized by dysfunctional proliferation of developing leukocytes. From both clinical and pathological perspectives, it is classified as either acute or chronic based on the speed of proliferation and further categorized as myelocytic or lymphocytic depending on the cell of origin; it is worth noting that despite being rare, other blood cells can initiate leukemias. (1,2).

Subtypes emerging from the lymphoid progeny include acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL), while primary subtypes such as acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) are associated with the myeloid lineage. Other less frequent variants, including mature B-cell and T-cell leukemias, as well as NK cell-related leukemias, arise from mature white blood cells (3).

In acute leukemias, either ALL or AML, the atypical blood cells, known as blasts, often remain immature, failing to fulfill their expected functions. These leukemias are characterized by rapid onset, often requiring immediate attention. In chronic leukemias, either CLL or CML, although some blast cells are still present, they are not the exclusive cell type. However, unlike in acute leukemias, these blast cells are comparatively more mature and may still function normally. As a result, chronic leukemias may not necessitate immediate treatment because they progress much more gradually (4).

In lymphoblastic leukemia, malignant changes occur in marrow cells that typically develop into lymphocytes later. In myeloid leukemia, malignant changes occur in marrow cells that typically develop into red blood cells, various types of white cells, and platelets later (5).

Understanding and recognizing the differences between subtypes is essential for healthcare professionals as it enables

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them to tailor treatment strategies to individual patients and improve outcomes in this heterogeneous group of diseases, the following table outlines key differences between common leukemia subtypes. Table I shows subtypes of leukemia (6)

Case Report

A 14-year-old male patient presented to the hospital of the Faculty of Dentistry, Minia University, complaining of gingival swelling and slight bleeding that had persisted for more than two months. Despite prior visits to multiple dental clinics and consultations with an ear, nose, and throat (ENT) specialist, antibiotic treatment failed to improve the status of his gingiva, and the underlying cause remained elusive. The case was subsequently referred from an oral diagnosis resident to an assistant teaching staff member of oral medicine, oral diagnosis, and periodontology for further evaluation. Upon examination, significant gingival hyperplasia was observed, which easily bled upon provocation and was accompanied by purulent discharge (Figure 1). Systemic manifestations of weakness and facial pallor were also noted. Additionally, small petechial spots were observed on the face and palms (Figure 2), prompting suspicion of an underlying hematologic disorder. Other findings included cervical lymphadenopathy, and the patient reported experiencing nightmares as a subjective symptom. Given the concerning clinical presentation, including the presence of unusual petechial lesions, a complete blood count with differential was ordered. Laboratory results revealed marked leukocytosis, severe anemia, and thrombocytopenia, consistent with the diagnosis of leukemia. The complete blood count further showed marked normocytic normochromic anemia and significant thrombocytopenia. There was also pronounced leukocytosis with a left shift extending to blasts, with 88% of the cells identified as abnormal promyelocytes. These promyelocytes were moderate to large, exhibited butterfly-shaped nuclei, and contained Auer rods. Additionally, there was marked absolute neutropenia (Table II).

Diagnostic Approach and Referral Protocol

As a dental hospital, the main role centers on early recognition of symptoms requiring urgent referral rather than providing advanced oncology diagnostics. Upon identifying signs suggestive of hematologic malignancy, such as gingival hyperplasia and petechiae, the patient was promptly referred to a specialized oncology center for further evaluation, including advanced tests like bone marrow biopsy and flow cytometry.

Follow-up and Patient Outcome

After referral to the specialized oncology center, the patient was diagnosed with acute myeloid leukemia (AML-M3). Treatment was initiated with intensive chemotherapy as per the center’s protocol for managing high-risk pediatric leukemia cases. Unfortunately, despite the early intervention, the patient’s condition deteriorated, and he passed away approximately 10 days after the referral.

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Table I: subtypes of leukemia (6)

Types	Cell affected	Main Symptoms	Cytology	Most affected age group	Prevalence*
AML	Immature white blood cells	1. Anemia 2. Spontaneous bleeding	1. Oncogene mutations 2. Single myeloblast mutation 3. Cytogenic abnormalities	✓ Adults ✓ children	24.11%
CML	Myeloid stem cells	1. Anemia 2. Splenomegaly 3. thrombocytopenia	1. Chromosomal translocation 2. granulocytes	Rare in children	9.53%
ALL	Immature B or T cell and macrophages	1. Disturb marrow function	1. Chromosomal aberration	Common in Children	63.36%
CLL	Lymphoid B or T cell	1. Swelling of lymph nodes 2. splenomegaly	1. Chromosomal abnormalities	Common in older +55	2.43%

AML: Acute Myeloid Leukemia, **CML**: Chronic Myeloid Leukemia, **ALL**: Acute Lymphoblastic Leukemia, **CLL**: Chronic Lymphocytic Leukemia

*Percentage of each leukemia subtype (e.g., AML, CML, ALL, CLL) cases among the total sample population over the entire period (2008–2018).

Table II: Complete blood count analysis

Test	Result	Unit	Reference Range
Hemoglobin	4.40	g/dL	13-17
Hematocrit	12.2	%	40-50
Red cell count	1.36	$x10^6$/uL	4.5-6.2
MCV	89.7	fL	78-96
MCH	32.0	pg	26-32
MCHC	36.0	g/dL	31-36
RDW	14.5	%	11.5-14.5
Platelet Count	9	$x10^3$/uL	150-410
T.L.C	84.9	$x10^3$/uL	4-11
Basophils	Percentage: 0%	%	0-1
	Absolute: 0.0	$x10^3$/uL	0 – 0.11
Eosinophils	Percentage: 0%	%	0-6
	Absolute: 0.0	$x10^3$/uL	0 - 0.6
Stab (band neutrophils)	Percentage: 0%	%	0-7
	Absolute: 0.0	$x10^3$/uL	-
Segmented	Percentage: 0%	%	40-75
	Absolute: 0.0	$x10^3$/uL	2 - 7
Lymphocytes	Percentage: 3%	%	20-45
	Absolute: 2.5	$x10^3$/uL	1.5 - 4
Monocytes	Percentage: 0%	%	1-10
	Absolute: 0.0	$x10^3$/uL	0.2 - 1
Blasts	9%	%	
Promyelocytes	88%	%	

Hb: Hemoglobin, **Hct**: Hematocrit, **RBC**: Red Blood Cell Count, **MCV**: Mean Corpuscular Volume, **MCH**: Mean Corpuscular Hemoglobin, **MCHC**: Mean Corpuscular Hemoglobin Concentration, **RDW**: Red Cell Distribution Width, **TLC**: Total Leukocyte Count, **Stab**: Band Neutrophils, **Blasts**: Immature Blood Cells.

This Complete blood counts show:

•Marked normocytic normochromic anemia.

•Marked thrombocytopenia.

•Marked leukocytosis with a shift to the left up to blasts with a presence of 88% abnormal promyelocytes that are moderate to large in size, butterfly-shaped nuclei, and with Auer rods.

•Marked absolute neutropenia.

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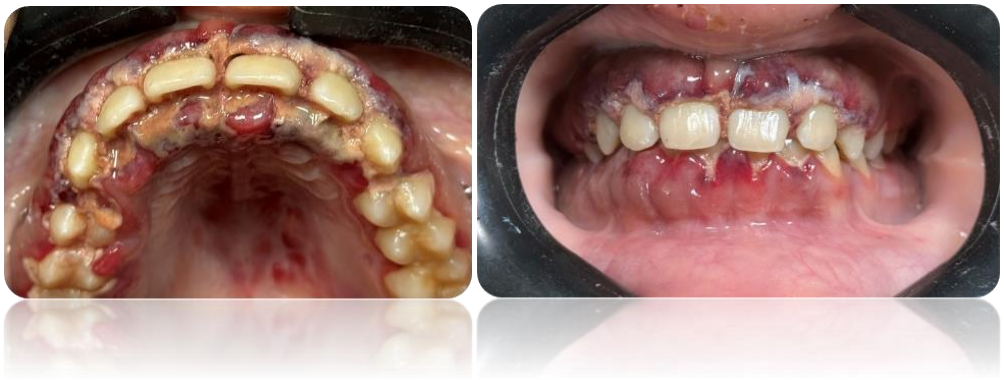

Figure 1. Gingival hyperplasia, bleeding and purulent exudate

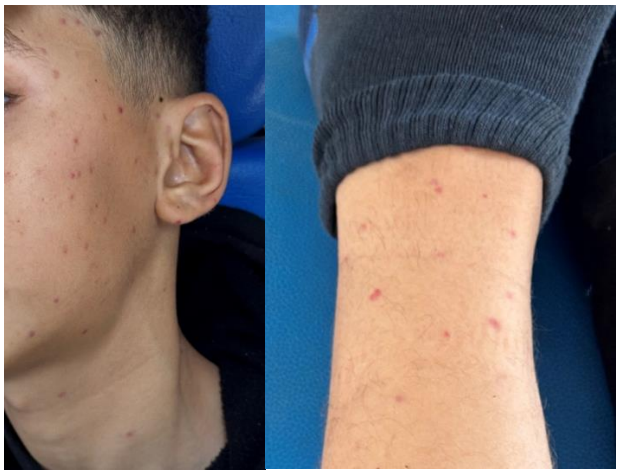

Figure 2. Petechiae in the hand of the patient

Discussion

Gingival swelling is a common chief complaint and even when accompanied by bleeding it still can indicate a diverse range of diseases, differential diagnosis of such clinical presentation must be systematically oriented, first of all, clinicians must observe whether the gingival swelling is isolated or generalized, examples of isolated gingival swelling includes as examples peripheral fibroma, Angiogranuloma, Peripheral giant cell granuloma and many others lesions which must be excluded in case of generalized gingival swelling (7).

Upon observation of generalized gingival swelling, the clinician should first exclude three main groups of common causes of generalized gingival hyperplasia namely: Genetic causes (syndromes), drug-induced gingival enlargement, hormonal gingival enlargement so as to make it easier to diagnose the case (8).

According to Rosa et al. (2018), gingival enlargement stands out as one of the predominant initial oral signs of leukemia. Their study revealed that petechiae or bleeding were the most frequently observed initial diagnostic indications of leukemia, noted in 56% of cases, followed by

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ulceration at 53%, and gingival enlargement at 36% (9).

Leukemic gingival enlargement primarily stems from AML, although occasional instances of ALL have been documented. This enlargement results from extensive infiltration of leukemic cells into the gingival connective tissue. Diagnosis is aided by symptoms such as pallor, lethargy, petechiae, and a history of recurrent infections (10).

The interconnection between oral and overall health underscores the oral cavity and its soft tissues as reflective of broader health concerns. This highlights the importance of collaborative efforts among healthcare professionals, particularly the referral of cases with atypical oral manifestations from physicians or General dental practitioners to specialized dentists in oral medicine and diagnosis. Such collaboration facilitates prompt identification of underlying causes of oral manifestations, leading to swift and accurate management (11).

Acute myeloid leukemia subtype M3 (AML-M3), also known as acute promyelocytic leukemia (APL), has distinct treatment protocols due to its characteristic sensitivity to targeted therapies. Standard treatment includes all-trans retinoic acid (ATRA) combined with anthracycline-based chemotherapy, which promotes the differentiation of leukemic promyelocytes. More recently, arsenic trioxide (ATO) has emerged as a key agent, either in combination with ATRA or as a standalone therapy in low-risk cases. Supportive care, including transfusions and management of coagulopathy, is critical during treatment to mitigate complications like disseminated intravascular coagulation (DIC), commonly associated with APL (12).

The outcomes in AML-M3 have significantly improved due to advances in targeted therapies, with remission rates exceeding 90% in early diagnosed and properly managed cases. However, outcomes vary based on factors such as the timing of diagnosis, the presence of complications like DIC, and response to therapy. While early referral and treatment are critical, aggressive disease progression or treatment-related complications can result in poor outcomes, as seen in this case where the patient passed away 10 days after diagnosis despite timely chemotherapy initiation. This highlights the importance of early detection, prompt intervention, and vigilant supportive care to maximize survival in aggressive leukemia subtypes (13). So, this case underscores the importance of a thorough diagnostic workup in patients presenting with atypical symptoms or exaggerated forms of common symptoms, even in the dental setting. The initial symptoms of gingival swelling, while commonly attributed to dental pathology, but when mixed with other manifestations such as petechia and lethargy further investigation and higher level of suspicion must be considered.

Importance of Early Detection in Dentistry

This case underscores the crucial role of dental professionals in recognizing systemic health issues and the potential consequences of delays in diagnosis. Dentists can play a pivotal role in early cancer detection, particularly in cases initially presenting with atypical oral signs. In this case, a delay in reaching a definitive diagnosis may have contributed to the patient's unfortunate passing, highlighting the need for heightened vigilance and timely referrals to specialized care. Early recognition and expedited management are critical in improving outcomes for patients with life-threatening conditions like leukemia.

Conclusion

Physicians and general dental practitioners should consider referring patients when the underlying cause of their symptoms cannot be identified, to specialists in oral medicine

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and oral diagnosis. Additionally, oral medicine and oral diagnosis specialists must remain vigilant for clinical presentations with mixed symptoms and consider the potential for underlying systemic diseases, especially in pediatric patients who present with chronic gingival swelling alongside symptoms such as pallor, bleeding, lethargy, or ulceration. This approach allows for early exclusion or confirmation of diagnoses such as leukemia.

Ethical Considerations

The case report was conducted in accordance with the institutional code of ethics, and informed consent was obtained from the patient's legal guardian prior to the study.

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Author's Contributions

Hussein Fathy Abo-elkheir: Performed the diagnosis of the case, drafted the manuscript, and handled correspondence with the journal.
Ahmed Ashraf El-sayed: Captured clinical photographs and coordinated case documentation.
Ahmed Abdallah Khalil: Provided supervision and critical revisions to refine the manuscript.

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Conflict of Interest

The authors declare no conflict of interests regarding this manuscript.

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