When Hyperpigmentation Signals Malignancy: A Paraneoplastic Presentation of CML

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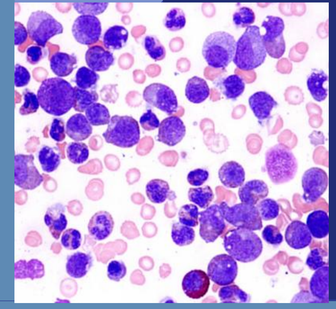
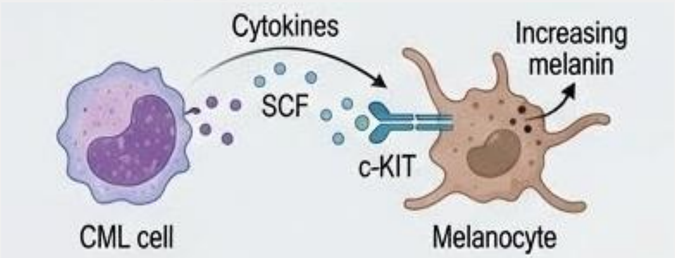


Introduction

Cutaneous manifestations of CML are rare and unusual. However, cases have been reported and may arise as either direct leukemic cell infiltration of the skin (leukemia cutis) or cytokine-mediated pathways. Stem cell factor and its receptor c-KIT play a role in melanocyte proliferation and melanin synthesis. Evidence indicates that tyrosine kinase inhibitors used in CML treatment can cause hypopigmentation of skin due to inhibition of c-



Objectives

- To describe a rare cutaneous paraneoplastic manifestation of chronic myeloid leukemia (CML).
- To emphasize hyperpigmentation as a potential early clinical indicator of underlying hematologic malignancy.
- Highlight the importance of basic lab exams.
- To distinguish cytokine-mediated melanocyte activation from leukemia cutis and inflammatory dermatoses such as eczema.

Methods

40-year-old Hispanic female who presented to the family medicine clinic. She is a Spanish speaker. The patient has not seen a physician since moving to the United States of America due to the lack of healthcare insurance.
Patient noted development of dark hyperpigmented patches over upper back and calves for 8 months with intermittent burning.

Results

Component	Result	Units	Flag	Reference Range
BCR-ABL1 p190 (Minor), Quantitative	Cancelled	%		<0.003
BCR-ABL1 p210 (Major), Quantitative	27.448	% (IS)	High	<0.003
p210 Result Reviewed & Interpreted	See Comment			
p210 Final Result	Detected			

Figure 1: BCRL-ABL1 Quantitative PCR Results. Molecular testing demonstrating detection of the BCR-ABL1 p210 (major) fusion transcript with a markedly elevated level of 27.448%, confirming the presence of the Philadelphia chromosome–associated tyrosine kinase activity characteristic of chronic myelogenous leukemia (CML). The p190 (minor) transcript was not detected.

Component	Result
Hematocrit	30.2
Hemoglobin	8.5
MCH	29.7
MCHC	28.1
MCV	105.6
MPV	10.8
Platelet Count	516
RBC	2.86
RDW (CV)	19.0
RDW (SD)	72.8
WBC	194.2

Figure 2:CBC demonstrates marked leukocytosis (WBC 194.2 ×10³/µL), thrombocytosis (platelets 516 ×10³/µL), macrocytic anemia (hemoglobin 8.5 g/dL, hematocrit 30.2%, MCV 105.6 fL), and elevated red cell distribution width, consistent with significant myeloproliferative activity.

Component	Value
Absolute Basophil	19.4
Absolute Eosinophil	29.1
Absolute Lymphocyte	19.4
Absolute Metamyelocytes	25.2
Absolute Monocyte	7.8
Absolute Myelocytes	31.1
Absolute Neutrophil	52.4
Absolute Other	9.7

Figure 3:Differential reveals marked myeloid predominance with elevated absolute neutrophils, myelocytes, metamyelocytes, basophils, and eosinophils, demonstrating a left-shifted granulocytic proliferation typical of chronic myelogenous leukemia.

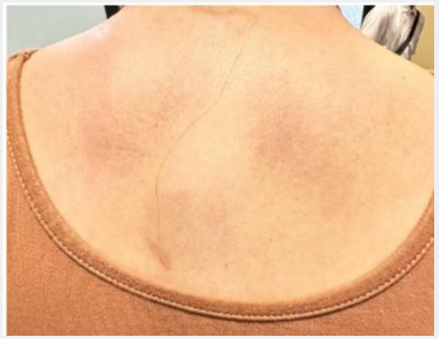


Figure 4: Hyperpigmentation of the upper scapular region. Flat, symmetric, erythematous-brown plaques with subtle hyperpigmentation. No scaling, nodularity, ulceration, warmth, or drainage.

Discussion

This case highlights a rare cutaneous manifestation of untreated chronic myeloid leukemia (CML) presenting as reversible hyperpigmented plaques that resolved after tyrosine kinase inhibitor (TKI) therapy. The rash was initially misdiagnosed as eczema, but lack of steroid response and clinical course argued against this. Leukemia cutis was unlikely given the absence of indurated papules or nodules and resolution without biopsy-confirmed infiltration.

A cytokine-mediated mechanism is most plausible. CML-associated inflammatory signaling can activate melanocytes through the stem cell factor (SCF)–c-KIT pathway, increasing melanin production. This pathway is well established in hyperpigmentation disorders and aligns with CML biology.

Resolution after TKI initiation further supports this mechanism, as TKIs such as asciminib and imatinib inhibit c-KIT signaling and are known to suppress melanocyte activity.

Conclusion

This case highlights the rare dermal presentation of CML. The patient's reversible hyperpigmentation is supportive of a cytokine-mediated paraneoplastic process rather than eczema or leukemia cutis. This case highlights the importance of performing a thorough review of systems in all patients, as well as obtaining basic labs in all new patients, especially those who have not been seen by a physician in years. It is also important to maintain a broad differential. Clinicians should consider atypical CML presentations and recognize that hyperpigmentation can occasionally serve as a visible marker of underlying malignancy.

References