CLINICAL VIGNETTE

Monocytopenia and Thrombocytopenia in a Patient with a New Rash

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Case

A 40-year-old man with no significant past medical history presented to hematology for evaluation of new leukopenia and thrombocytopenia seen on a routine complete blood count (CBC). He used no medications except topical clotrimazole, which had been prescribed 2 weeks earlier for a pruritic, non-tender, demarcated, and erythematous left axillary rash. He was otherwise in good health without systemic symptoms, specifically denying fevers, night sweats, weight loss, and family history of cancer or blood disorders.

His physical exam was negative for palpable lymphadenopathy or splenomegaly. The only pertinent finding was his rash, he reported improved since starting clotrimazole. Repeat CBC with differential was significant for a white blood count of 3.6 x 10^3 cells/µL, platelet count of 81 x 10^3 cells/µL (N=150-450), and an absolute monocyte count of 0.11 x 10^3 cells/µL. Rheumatoid factor was elevated at 34 IU/mL (N<14IU/mL). His antinuclear antibody (< 1:40 titer), hemoglobin (14.5 g/dL), vitamin B12 (374 pg/mL), methylmalonic acid (0.12 µmol/L), folate (8.1 ng/mL), and ceruloplasmin (23 mg/dL) were all within normal limits.

What is your diagnosis?

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A. Levamisole-induced vasculitis
B. Lymphoma infiltrating the bone marrow
C. Hairy cell leukemia
D. Human immunodeficiency virus

Correct answer: C

Discussion

A bone marrow (BM) biopsy with subsequent flow cytometry and sequencing revealed lambda-restricted CD11c+/CD25+/CD103+/CD5-/CD10- B-cells harboring a BRAF V600E mutation, consistent with hairy cell leukemia (HCL). Abdominal ultrasound demonstrated moderate splenomegaly measuring 15.2 cm in length. He was treated with a single course of cladribine and 6 months of prophylactic antibiotics. Shortly after completing purine nucleoside analog (PNA) therapy, he experienced an episode of febrile neutropenia which was treated with levofloxacin and pegfilgrastim. He remains asymptomatic in remission 31 months after his diagnosis.

HCL[1,2] is a rare indolent malignancy of mature B-cells caused by the constitutive activation of RAF-MEK-ERK signaling. There is a strong male preponderance, with a 4:1 male-to-female ratio[3]. Patients often present with fatigue, infections, and pancytopenia. Routine complete blood count (CBC) testing may identify pancytopenia before patients develop symptoms. Palpable splenomegaly, while common, is noted less frequently now than in the past. Diagnosis is established with a bone marrow biopsy and flow cytometry to detect monotypic CD11c+/CD25+/CD103+/CD123+/CD5-/CD10- B-cells. Further confirmation is provided by identification of the canonical BRAF V600E mutation and observing hair-like projections on a peripheral smear (Figure 1). Patients who report symptoms or develop declining hematological parameters require treatment with a PNA. As cladribine and pentostatin are both very immunosuppressive, they are given with antiviral prophylaxis. Active infections should be treated prior to initiating therapy. However, patients with uncontrollable infections who need immediate therapy have been safely given either reduced-dose pentostatin,[4] vemurafenib,[5,6] or interferon-alpha.[7] For those with relapsed or refractory disease, a variety[2] of treatment options exist including the alternative PNA followed by rituximab, BRAF inhibitors, and antibody-drug conjugates. All patients should be offered enrollment in a clinical trial.

This patient was unusual, with diagnosis before developing symptoms or pancytopenia. Key to early detection was the presence of monocytopenia, a near-ubiquitous feature of classical HCL. While BM-infiltrating lymphoma can also cause monocytopenia and thrombocytopenia, it usually presents with lymphadenopathy, which is notably absent in most cases of HCL. Similar to our patient's presentation, levamisole-induced vasculitis (LIV) is characterized[7] by a rash, thrombocytopenia, and leukopenia. In LIV, however, the drop in white blood cells is driven by neutropenia and agranulocytosis rather than monocytopenia. Moreover, our patient's rash was demarcated and erythematous, varying substantially from the retiform and black/purple purpura more typical of LIV. Early HIV infection can manifest as asymptomatic thrombocytopenia[8] and monocytopenia.[9,10] However monocytopenia occurs infrequently and, when present, is of a lesser magnitude than that seen in HCL.

Although rare, HCL represents[3] up to 4.5% of all leukemias and may be encountered by oncologists at some point in their careers. Our case highlights an atypical presentation of HCL

that underscores the importance of including it in the differential diagnosis for patients with unexplained monocytopenia.

REFERENCES

1. **Troussard X, Maître E, Cornet E**. Hairy cell leukemia 2022: Update on diagnosis, risk-stratification, and treatment. *Am J Hematol*. 2022 Feb 1;97(2):226-236. doi: 10.1002/ajh.26390. Epub 2021 Nov 8. PMID: 34710243.
2. **Grever MR, Abdel-Wahab O, Andritsos LA, Banerji V, Barrientos J, Blachly JS, Call TG, Catovsky D, Dearden C, Demeter J, Else M, Forconi F, Gozzetti A, Ho AD, Johnston JB, Jones J, Juliusson G, Kraut E, Kreitman RJ, Larratt L, Lauria F, Lozanski G, Montserrat E, Parikh SA, Park JH, Polliack A, Quest GR, Rai KR, Ravandi F, Robak T, Saven A, Seymour JF, Tadmor T, Tallman MS, Tam C, Tiacci E, Troussard X, Zent CS, Zenz T, Zinzani PL, Falini B**. Consensus guidelines for the diagnosis and management of patients with classic hairy cell leukemia. *Blood*. 2017 Feb 2;129(5):553-560. doi: 10.1182/blood-2016-01-689422. Epub 2016 Nov 30. PMID: 27903528; PMCID: PMC5290982.
3. **Wiber M, Maitre E, Poncet JM, Duchenet V, Damaj G, Cornet E, Troussard X**. A population-based study of hairy cell leukemia over a period of 20 years. *Cancer Treat Res Commun*. 2020;25:100236. doi: 10.1016/j.ctarc.2020.100236. Epub 2020 Nov 9. PMID: 33227559.
4. **Andritsos LA, Dunavin N, Lozanski G, Jones JA, Blachly JS, Lucas DM, Byrd JC, Kraut E, Grever MR**. Reduced dose pentostatin for initial management of hairy cell leukemia patients who have active infection or risk of hemorrhage is safe and effective. *Haematologica*. 2015 Jan;100(1):e18-20. doi: 10.3324/haematol.2014.113290. Epub 2014 Oct 31. PMID: 25361945; PMCID: PMC4281329.
5. **Bohn JP, Pircher A, Wanner D, Vill D, Foeger B, Wolf D, Steurer M**. Low-dose vemurafenib in hairy cell leukemia patients with active infection. *Am J Hematol*. 2019 Jun;94(6):E180-E182. doi: 10.1002/ajh.25474. Epub 2019 Apr 4. PMID: 30916799; PMCID: PMC6593695.
6. **Shenoi DP, Andritsos LA, Blachly JS, Rogers KA, Moran ME, Anghelina M, Jones JA, Grever MR**. Classic hairy cell leukemia complicated by pancytopenia and severe infection: a report of 3 cases treated with vemurafenib. *Blood Adv*. 2019 Jan 22;3(2):116-118. doi: 10.1182/bloodadvances.2018027466. PMID: 30630817; PMCID: PMC6341189.
7. **Brunt TM, van den Berg J, Pennings E, Venhuis B**. Adverse effects of levamisole in cocaine users: a review and risk assessment. *Arch Toxicol*. 2017 Jun;91(6):2303-2313. doi: 10.1007/s00204-017-1947-4. Epub 2017 Mar 17. PMID: 28314885.
8. **Vishnu P, Aboulafia DM**. Haematological manifestations of human immune deficiency virus infection. *Br J Haematol*. 2015 Dec;171(5):695-709. doi: 10.1111/bjh.13783. Epub 2015 Oct 9. PMID: 26452169.
9. **Mir N, Costello C, Luckit J, Lindley R**. HIV-disease and bone marrow changes: a study of 60 cases. *Eur J Haematol*. 1989 Apr;42(4):339-43. doi: 10.1111/j.1600-0609.1989.tb01222.x. PMID: 2721658.
10. **Knudsen AD, Bouazzi R, Afzal S, Gelpi M, Benfield T, Høgh J, Thomsen MT, Trøseid M, Nordestgaard BG, Nielsen SD**. Monocyte count and soluble markers of monocyte activation in people living with HIV and uninfected controls. *BMC Infect Dis*. 2022 May 11;22(1):451. doi: 10.1186/s12879-022-07450-y. PMID: 35546661; PMCID: PMC9097376.