Title

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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?

What is your diagnosis?

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.

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