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Case Presentation

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Chronic Pruritis: Can it be more than Just a Skin Disease?

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Abstract

Classical Hodgkin Lymphoma (CHL) is the most common lymphoma in adolescents and young adults. The typical clinical presentation of Hodgkin lymphoma is painless palpable lymphadenopathy. Patients with advanced stage Hodgkin's lymphoma can also experience unintentional profound weight loss, night sweats, and fevers. When CHL is suspected, an initial diagnosis is typically made by biopsy of involved tissue and analysis of morphology and flow cytometry. Peripheral blood flow cytometry has not been a useful tool in the diagnosis of Hodgkin lymphoma classically. We present a case of a 36-year-old woman who presented with cutaneous symptoms and loss of CD26 on peripheral blood flow cytometry and was ultimately diagnosed with CHL. The patient initially presented with generalized pruritus that progressively worsened over 2 years and was refractory to multiple lines of therapy. Physical exam findings were notable for xerosis of the extremities, knuckles, and knees. Abnormal laboratory findings included low absolute lymphocyte count. Peripheral blood flow cytometry revealed T cells with partial loss of CD26, an abnormality typically observed in Sézary syndrome. Multiple involved skin biopsies were negative for malignancy. She ultimately had a PET/CT scan which showed an anterior mediastinal mass. Biopsy of this mass led to the diagnosis of Classic Hodgkin Lymphoma, nodular sclerosis subtype. Pruritis responded to lymphoma treatment. This case demonstrates a unique clinical presentation of CHL and alludes to overlap in symptoms and laboratory findings between different lymphomas.

Introduction

Chronic pruritis is defined as pruritis lasting for more than 6 weeks. It affects 8-16% of the general population [1,2]. Chronic pruritis can be a presenting sign of cutaneous and extra cutaneous disorders. However, the etiology of chronic generalized pruritis remains unknown in up to 44.5% of patients [3]. Of note, chronic pruritis has been associated with certain malignancies, particularly lymphomas, as a paraneoplastic phenomenon [4]. The current practice of diagnosis and management of chronic pruritis however, under recognizes the significance of malignancy workup. Classical Hodgkin Lymphoma (CHL) is the most common lymphoma in adolescents and young adults (age 15-34 years), comprising 10-15% of all lymphomas [5,6]. The typical presentation of Hodgkin lymphoma is painless lymphadenopathy above or below the diaphragm. Extranodal sites may become involved by hematogenous dissemination of disease. Patients with advanced stage Hodgkin's lymphoma can also experience "B" symptoms, which include unintentional profound weight loss, night sweats, and fevers [7]. Paraneoplastic phenomena (symptoms not explained by direct dissemination of lymphoma to an organ) are rarely associated with Hodgkin's disease. When CHL is suspected, an initial diagnosis is typically made by tissue biopsy and analysis of morphology and flow cytometry of the biopsied tissue [5]. The typical immunophenotype of biopsied tissue in CHL reveals expression of CD30, CD15, CD40, CD71, CD86, CD95, CD64 and HLA-DR and Pax-5 and lack of expression of CD3, CD20, and CD45 [8]. Peripheral blood evaluation e.g., by flow cytometry is not thought to be helpful in diagnosis of CHL [8].

On the other hand, peripheral blood flow cytometry is an established diagnostic tool for some other lymphomas e.g., cutaneous lymphomas like Sézary syndrome [9]. Peripheral blood flow cytometry in patients with Sézary syndrome typically shows clonal T lymphocytes that are CD4+ with loss of CD7 and CD26 [9]. Loss of CD26 is nearly 80% sensitive and up to 100% specific for this diagnosis. Official diagnosis of Sezary syndrome requires a combination of molecular, immunophenotyping, and histopathological studies [9]. Clinically, Sézary syndrome typically presents with diffuse erythroderma, lymphadenopathy, and other cutaneous symptoms [10].

We present the case of a 36-year-old woman who presented with chronic pruritis and T cells with loss of CD26 on peripheral blood flow cytometry and ended up getting diagnosed with CHL with no cutaneous dissemination.

Case Presentation

History: In December 2017, a 32-year-old woman with history of depression, anxiety, and gastroesophageal reflux disease was started on sertraline by her primary care provider for management of anxiety. A month later, she started experiencing generalized pruritus; pruritus was worse at night and interfered with sleep. Nothing seemed to relieve or exacerbate the symptoms. She opted to discontinue Zoloft in August 2018, however, pruritus worsened after discontinuation of the drug. She was seen by an allergist who prescribed fexofenadine twice daily, cetirizine nightly, diphenhydramine nightly, and hydroxyzine nightly, which she used in succession for 9 months without significant relief. She was then referred to Dermatology and went through trials of topical steroids (triamcinolone ointment), gabapentin, amitriptyline, aprepitant, UV light therapy, and Dupixent, with no notable benefit. After two and half years of onset of pruritis (May 2021), she started experiencing night sweats, fatigue, and loss of appetite.

Physical exam: Skin exam at symptom onset in 2017 was unremarkable. Over the time, she noted scattered brown macules, intermittent diffuse erythema, and excoriations from scratching. By 2021, she had developed significant xerosis of extremities, knuckles, and knees.

Investigation: Labs and imaging during the first year after onset of symptoms included a complete blood count (CBC), comprehensive metabolic panel, thyroid stimulating hormone level, erythrocyte sedimentation rate, zinc level, antinuclear antibody test, strongyloides IgG, toxacara IgG, allergy skin test, and chest x-ray. All these test results were within normal limits. CBC however on multiple occasions showed lymphopenia (an absolute lymphocyte count of 792). Oncological investigation conducted through Allergy and Immunology department included serum protein electrophoresis and T-cell gene rearrangement studies (looking for clonal/cancerous T lymphocytes in peripheral blood). These tests were within normal limits. Skin biopsies (x 2) were performed in November 2021 due to concern for cutaneous T-cell lymphoma i.e., Sezary syndrome, but they showed no evidence of lymphoma infiltration in the skin.

The patient was ultimately referred to hematology clinic in January 2022 for the constitutional symptoms she had developed. At that time, serum immunoglobulin levels were normal and repeat evaluation for T-cell receptor gene rearrangements was normal (polyclonal). Peripheral blood flow cytometry, however, revealed lymphopenia and T-cells with partial loss of CD26, a finding typically seen in cutaneous lymphomas. Since skin biopsies from involved areas had been unsuccessful in diagnosing cutaneous lymphoma, a PET/CT scan was ordered to look for the best site to biopsy. PET/CT scan was repeatedly denied by the patient's insurance as prior skin biopsies had shown no evidence of cutaneous lymphoma. Eventually, the study was approved, and it surprisingly showed a 10.5 x 7 cm mass/nodal conglomerate in the anterior mediastinum, as well as additional mediastinal, left paratracheal, and supraclavicular lymph node enlargement. No FDG-avid skin infiltration as suspected based on peripheral blood flow cytometry was seen. This prompted a core needle biopsy of the mass by Interventional Radiology in February 2022, leading to the diagnosis of "classic Hodgkin lymphoma, nodular sclerosis subtype."She was stage IIIB at diagnosis. She established care with an oncologist and underwent CHL treatment with chemotherapy including Adriamycin, Bleomycin, Vinblastine, and Dacarbazine. She started experiencing improvement in pruritus during the first cycle of treatment with near resolution three months later.

Discussion/Conclusion

This young female patient struggled with chronic pruritis for 3-4 years and went through 3 different specialists to be ultimately diagnosed with CHL. She had developed "constitutional/B symptoms" when she got diagnosed with CHL upstaging her cancer to stage IIIB. It is important to consider malignancies particularly lymphoma for patients presenting with chronic pruritis refractory to first-line treatments. While peripheral blood flow cytometry showing T cells with loss of CD26 is typically seen in cutaneous lymphoma i.e., Sézary syndrome, this can be seen in other lymphomas too. Hence, the workup of this abnormal peripheral blood flow cytometry finding should not be limited to involved skin biopsies. A comprehensive imaging evaluation e.g., a PET/CT should be considered for undiagnosed cases. This case demonstrates an under recognized paraneoplastic presentation of CHL and alludes to importance of understanding the overlap in laboratory findings between different lymphomas. A lot remains unknown about the utility of peripheral blood flow cytometry in the diagnosis of CHL, and more research is needed in this area to guide diagnostic approach to CHL.

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