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Case Report

Idiopathic Thrombocytopenia Purpura Masking Hodgkin Disease: A Paraneoplastic Syndrome or Simply a Mere Association?

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Hodgkin disease · Immune thrombocytopenia purpura · Lymphoma

Abstract
We report a 74-year-old female who presented to the emergency department complaining of bruising and stroke-like symptoms. She underwent a negative stroke work-up but was found to have profoundly low platelets and splenomegaly on examination. An abdominal CT scan was ordered, showing pelvic lymphadenopathy. Lymphoma was suspected. However, subsequent bone marrow and lymph node biopsies showed no evidence of this. She was treated for immune thrombocytopenia purpura (ITP) to no avail while a lymphoma work-up continued. Months later, a third and final lymph node biopsy yielded evidence of Hodgkin disease (HD) and she began treatment shortly thereafter. She is currently undergoing standard treatment for this malignancy and her platelet counts have normalized. The case not only outlines the importance of the physician's gestalt in arriving at the proper diagnosis, but it also posits the thought that perhaps ITP should be considered a paraneoplastic syndrome of HD.

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Background

Paraneoplastic syndromes are presentations of malignancy that occur far from the site of the primary tumour or metastatic focus. Their effects are not from the physical interaction of the tumour with surrounding tissue; rather they are secondary to ectopic hormone or autoimmune antibody production, or effects from other factors produced by the malignancy. Hodgkin disease (HD) has been known to have many rare associated syndromes, including pruritus, alcohol-induced pain, haemolytic anaemia, lytic bone lesions, and immune thrombocytopenia purpura (ITP) among many others. Although relatively rare, ITP is still the most common of these associated syndromes. Not only do these syndromes create a diagnostic challenge for the physician, but they have also been the centre of debate regarding whether or not some should be considered as paraneoplastic syndromes and potentially prompt an investigation for an underlying malignancy.

Case Presentation

We present the case of a 74-year-old Spanish-speaking female who presented to a community emergency department with a chief complaint of slurred speech and bruising. She had a past medical history significant for heart failure with preserved ejection fraction, hypertension, type II diabetes mellitus, COPD, and an unremarkable surgical history. Her vitals were stable, her speech deficit resolved, and her physical examination was significant for hyphaemia of her left eye, a palpable spleen, and bruising with a diffuse petechial rash on every extremity.

Investigations

She had a platelet count of 8,000/μL, white blood cell count of 2,100/μL, and haemoglobin of 11.1 g/dL. A contrast CT scan of the chest/abdomen/pelvis found 3 enlarged lymph nodes in the right lower pelvis measuring 3.4 × 3.5 × 3.2 cm, 3.0 × 3.9 × 3.3 cm, and 2.8 × 3.8 × 4.2 cm, and an enlarged lymph node in the left groin area measuring 4.1 × 2.6 × 3.5 cm. Her spleen was moderately enlarged at 13.8 cm. A whole-body PET scan (Fig. 1) was ordered which revealed 4 lower abdominal/pelvic nodal masses predominately in the right lower quadrant with a standard uptake value (SUV) varying from 13.17 to 20.78 along with a left-sided pelvic nodal mass with an SUV of 3.78. A subsequent bone marrow biopsy revealed normocellular marrow with only mild megakaryocyte hyperplasia. A CT-guided biopsy of a right-sided pelvic lymph node found atypical lymphoid infiltrates consisting of small- to medium-sized T-cell lymphocytes, eosinophils, occasional plasma cells, and histiocytes, but no classic Reed-Sternberg cells. Flow cytometric analysis showed no immunophenotypic evidence of a T-cell lymphoma.

Differential Diagnosis

The differential diagnosis for the patient's pancytopenia with pelvic lymphadenopathy included primary ITP, myelodysplastic syndrome, B_{12} and/or folate deficiency, paroxysmal nocturnal haemoglobinuria, HIV infection, myelophthisic anaemia, primary myelofibrosis, acute leukaemia or lymphoma, and multiple myeloma. ITP secondary to an underlying lymphoma was high on the differential diagnosis since the initial encounter, however.

Treatment

The patient was initially treated for primary ITP with intravenous dexamethasone 20 mg b.i.d. for 4 days and concurrent intravenous immunoglobulin 80g q.d. for 3 days with only a modest improvement of her platelet count to 18,000/μL. She later received intravenous rituximab 375 mg/m^2 weekly for 4 total doses along with therapeutic splenectomy which revealed a benign spleen. At a later time, she also received subcutaneous romiPLOStim, up to a maximum dose of 200 μg weekly for several weeks. Despite these interventions, her platelet count remained below 50,000/μL during the majority of her clinical course.

Outcome and Follow-up

This patient underwent a second right-sided pelvic lymph node biopsy approximately 1 month after her initial hospitalization. This study revealed features highly suspicious for peripheral T-cell lymphoma. A final left-sided pelvic lymph node biopsy was performed 2 months thereafter, which showed a mixed cellular infiltrate consisting of Reed-Sternberg cells and variants with CD30, CD15, CD20, and Pax-5 cell markers in a background of CD3- and CD5-positive T cells (Fig. 2). A diagnosis of stage II mixed cellularity HD was established.

She was subsequently started on chemotherapy for her lymphoma, including 4 cycles of Adriamycin, bleomycin, vincristine, and dacarbazine. After her fourth cycle of chemotherapy, her platelet count had normalized to 189,000/μL and her previously enlarged bilateral pelvic lymph nodes has decreased in size to approximately 1 cm in diameter or less. She is currently undergoing 2 additional cycles of chemotherapy with the above-mentioned agents and her platelet counts have remained within normal limits.

Discussion

The presence of ITP with HD is relatively rare, with an estimated prevalence of 0.2–1% among patients with HD according to some studies [1]. The relationship between the 2 diseases may lead one to consider ITP as a paraneoplastic disorder; however, this is still a debated topic in the medical literature.

Paraneoplastic autoimmune syndromes may present prior to cancer diagnosis or concomitantly with diagnosis, or they may be seen after cancer treatment as a sign of recurrence [2, 3]. A literature review revealed multiple case reports of ITP occurring both before and after the diagnosis of HD. In most of these cases, ITP was considered to be a mere association of HD, since much of the time its discovery is encountered long after the diagnosis of lymphoma, sometimes years later while in remission [2]. One large case-controlled study *did* reveal a statistically significant incidence of ITP in patients with HD and concluded that a personal history of certain autoimmune diseases, including ITP, is strongly associated with the risk of developing HD [3].

In this case, the patient's ITP was discovered prior to diagnosis of the underlying malignancy, and it was resistant to first-, second-, and even third-line treatment of ITP. Only proper treatment of the underlying malignancy proved successful in normalizing the patient's platelet count. Given this fact, the authors conclude that ITP was likely an autoimmune paraneoplastic syndrome of the patient's HD. Several other case reports have arrived at similar conclusions [4, 5].

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

No financial support was received for this project and the above-listed authors have no financial or other conflicts of interest to disclose.

Author Contributions

N. Poponea, M. Suede, and M. Muhsin Chisti provided substantial contributions to the conception and design of the study, acquisition of data, and analysis and interpretation of data. N. Poponea and M. Suede drafted the article and revised it critically for important intellectual content. M. Muhsin Chisti gave final approval of the version of the article to be published. All authors listed agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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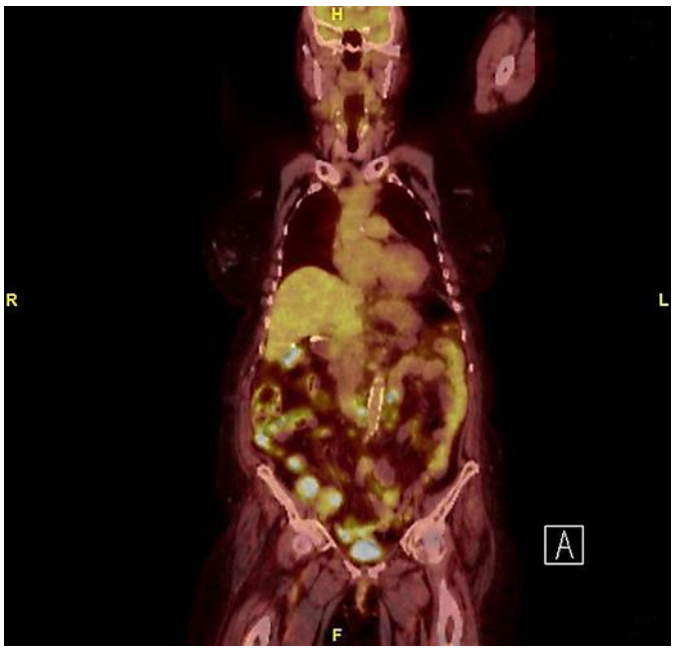

Fig. 1. Coronal whole-body PET scan of the patient showing the presence of bilateral pelvic nodal masses with intense FDG activity.

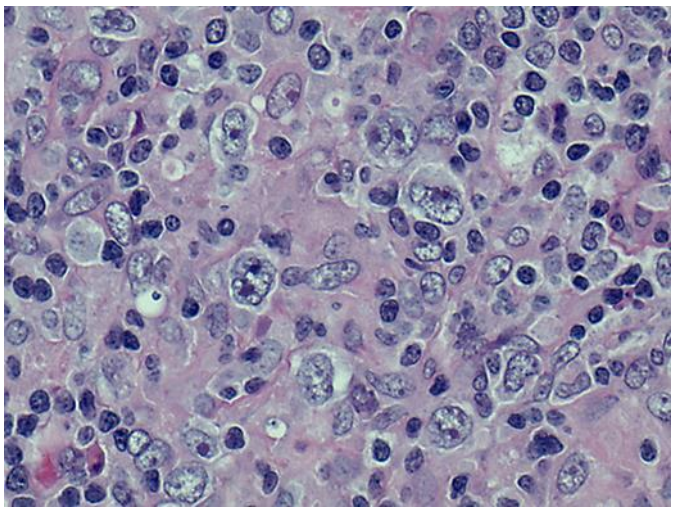

Fig. 2. Histologic section of the patient's left pelvic lymph node biopsy which shows a mixed cellular infiltrate consisting of Reed-Sternberg cells. Stained with haematoxylin and eosin.