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BRIEF REPORT

Lymphoma relapse; so obvious?

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ABSTRACT

The development of fevers, night sweats and weight loss or 'B-symptoms' are some of the early indications of possible relapse in lymphoma survivors. However, these symptoms are non-specific and could be the result of many other medical conditions.

We report a case of a woman with the prior history of lymphoma who presented with B-symptoms (drenching sweats and weight loss) and hypermetabolic cervical lymph node enlargement. This was highly suspicious for recurrent lymphoma, however, the biopsy of the lymph node was negative. Further evaluation revealed the presence of thyrotoxicosis. As illustrated by this case report, what seems like an obvious relapse is not always a lymphoma. Understanding such possibilities is important for the management of lymphoma survivors.

Key words: lymphoma, late relapse, thyrotoxicosis

Diffuse large B-cell lymphoma patients, who achieve complete remission after initial therapy, are closely followed for possible recurrence.[1] The development of fevers, night sweats and weight loss may indicate a lymphoma relapse. However, as illustrated by this case report, what seems like an obvious relapse is not always a lymphoma.

A 59-year-old woman presented to the lymphoma clinic with complaints of drenching sweats, chills, anorexia, fatigue, cough, and 17-pound weight loss over the preceding 10 weeks. She had been previously treated with oral azithromycin for presumed bronchitis without improvement. Past medical history was significant for diffuse large B-cell lymphoma treated 9 years ago with cyclophosphamide, doxorubicin, vincristine, prednisone and rituximab (CHOP-R). The disease was confined above the diaphragm and she had achieved a complete remission. Physical examination revealed a nontender 1 cm left-sided cervical lymph node. Hemogram and serum lactate dehydrogenase was normal. Chest x-ray was unremarkable and blood cultures did not grow any organism. Integrated 18F-fluorodeoxyglucose positron emission tomography and computed tomography scan of skull to mid-thigh showed single, 0.9 x 0.9 cm left level II cervical lymph node with a maximum standardized uptake value of 4.1. The interpretation of the scan was probable recurrent lymphoma.

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The possibility of recurrent lymphoma led us to perform a biopsy of the lymph node, which showed only reactive hyperplasia. At this point, thyroid function tests were performed, which revealed serum thyroid stimulating hormone of <0.030 mcU/ml (normal range 0.400-5.000 mcU/mL), free T4 of 1.5 ng/dl (0.6-1.5 ng/dL), free T3 of 4.1 pg/ml (2.5-3.9 pg/mL), thyroid stimulating immunoglobulin of 97% (≤122 %) and thyroid microsomal antibody of <0.3 IU/ml (0.0-9.0 IU/mL). Radioactive iodine uptake scan was avoided because of the history of iodine allergy. The patient subsequently developed nausea and vomiting. A possibility of adrenal insufficiency was confirmed by serum cortisol level of 8.3 mcg/dL 60 min after 250 mcg of cosyntropin (expected value: greater than 20 mcg/dL). With the diagnosis of primary hyperthyroidism and adrenal insufficiency, the patient was started on methimazole (20 mg daily) and hydrocortisone (30 mg daily in 2 divided doses). This resulted in clinical improvement. An attempt to taper off hydrocortisone and stop methimazole 2 months later failed, hence she was restarted on these medications. She responded to methimazole but had wide fluctuations in thyroid function tests. Hence, she elected to undergo total thyroidectomy, and remains on levothyroxine supplementation (125 mcg daily). She has been able to taper off hydrocortisone and continues to do well more than 18 months after the initial suspicion of lymphoma relapse.

Patients with diffuse large B-cell lymphoma usually relapse within the first few years after completing therapy. At our institution, among patients with diffuse large B-cell lymphoma treated with a CHOP-like

regimen, who relapsed after a complete remission, 81% did so in the first 5 years.[2] However, patients relapsing as late as 20 years have been described. Patients with late relapse have better prognostic characteristics such as more frequent localized disease and favorable IPI score2,[3] as well as more frequent extranodal disease at initial diagnosis.[3] In most cases, late-relapsing diffuse large B-cell lymphomas are clonally related to original disease.[4]

The majority of relapse is suspected clinically; surveillance imaging for early detection of relapse does not improve outcome. However, imaging is useful in determining the best site for biopsy and for staging relapses.1,5 Although the probability of abnormal surveillance positron emission tomography scan representing relapse is low in asymptomatic disease, the probability is estimated to increase up to 88% in symptomatic patients,[5] as in this case. However, as highlighted by this case, it is crucial to never start therapy for suspected relapse without a biopsy even when both clinical and radiological features concur. At our institution, suspected relapses of lymphoma, on biopsy, have shown fungal or mycobacterial infections, sarcoidosis, or other malignancies.[1] Interestingly, in the patient reported here, the hypermetabolic symptoms from thyrotoxicosis as well as hypermetabolic lymphadenopathy closely resembled localized late relapse of lymphoma. To our knowledge, this is the first reported case of thyrotoxicosis masquerading lymphoma relapse. Adherence to the classic principle of oncology medicine, that is to rely only on histopathology for diagnosis, once again prevented a mishap.

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