# Asymptomatic cervical stiffness as the sole presenting feature of ovarian follicular lymphoma: The value of hands-on medicine

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#### **ABSTRACT**

A primary care visit is the first encounter of a patient with health care. In context to malignancies, breast cancer and primary ovarian lymphomas are NA clinically and morphologically different malignancies. The rare concurrence of breast cancer and non-Hodgkin lymphoma (NHL) does not warrant any routine surveillance through testing but we present a case of a 71-year-old female with the history of invasive ductal carcinoma of the breast in remission who was diagnosed with follicular carcinoma after an abnormal pelvic examination during her routine primary care visit. This highlights that a routine PC visit with a skilled physical examination can prove to be one of the most cost-effective tools for screening high-risk cancer patients in remission.

**Keywords:** Cancer screening, history of malignancy, primary care

#### Introduction

Breast cancer is one of the most common cancers among US women, only second to cancers of the skin, accounting for 26% of all newly diagnosed cancers in women.[1] Infiltrating ductal carcinoma is the most common type of invasive breast cancer.

Follicular lymphoma is a separate clinicopathologic entity with tumor derived from germinal center B cells and has a propensity to grow in a partially nodular pattern both grossly and microscopically. The concurrent existence of both types of cancer has been extremely rare with less than 10 reported cases in the literature. [2]

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A primary care (PC) visit is the first encounter of a patient with health care and a thorough history alongside a detailed physical exam, even in asymptomatic patients, NA can turn out be a crucial screening/diagnostic tool. PC has proven to play a key-role in the prevention of heart disease, diabetes, colorectal, breast and cervical cancers, with recent trials such as Building on Existing Tools to Improve Chronic Disease Prevention and Screening in Primary Care (BETTER)[3,4] further highlighting this fact. We describe the case of a 71-year-old female with a history of invasive ductal carcinoma, who was found to have follicular lymphoma of the left ovary after a suspicious pelvic examination during a routine PC visit. This case not only exemplifies the key role of PC in the chronic illness and disability payment system (CDPS) but also proves the importance of physical examination in rare malignancies.

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# **Case Report**

A 71-year-old female presented for her annual well-woman exam. Her medical history included confined ductal carcinoma in situ (DCIS) of the left breast treated 30 years prior to lumpectomy and adjuvant radiation. She also developed stage IA (T1a, N0, M0) estrogen receptor (ER)/progesterone receptor (PR) positive, human epidermal growth factor receptor 2 (HER-2) positive invasive ductal carcinoma of the left breast 5 years prior which was treated with bilateral mastectomy and completed 5 years of anastrozole therapy. A family history of breast cancer, in maternal grandmother and maternal aunt, and ovarian cancer, in maternal aunt, was also reported. Because of her age >65 years, Papanicolaou (Pap) smear was not indicated. Due to personal history of breast cancer and family history of both breast cancer and ovarian cancer, she did elect to have a pelvic exam performed. An abnormally firm cervix was appreciated on exam. Transvaginal ultrasound revealed a thickened endometrium measuring 5.6 mm as well as a solid left adnexal mass measuring  $5.6 \times 5.4 \times 3.9$  with internal Doppler flow. A moderate amount of free fluid was also noted in the cul de sac.

The left adnexal mass was highly concerning for malignancy, prompting further workup and gynecology/oncology referrals. The CA-125 was mildly elevated at 51 U/ml (ref range 0–50). A CT of the abdomen and pelvis further revealed an enlarged left external iliac chain lymph node and increased density of the mesentery in the lower right quadrant [Figure 1]. Given the elevated CA-125, CT and ultrasound findings, the patient was recommended to undergo a robotic total laparoscopic hysterectomy with bilateral salpingo-oophorectomy. The patient underwent the procedure 18 days following her initial annual clinic visit.

Intraoperatively, a 5 cm solid left ovarian mass was removed and sent for pathology. The uterus was small and the right fallopian tube and ovary were grossly normal. Liver, stomach and pancreas were grossly normal, but omentum stranding concerning for metastatic disease was identified and pelvic washings were also sent for pathology.

Pathological examination of the left adnexa showed predominantly large lymphoid cells with a vaguely nodular architecture. Immunohistochemical stains of the lymphoid infiltrate were positive for CD20, CD21, Ki-67, PAX5, CD10, BCL6, BCL2, and CD23; stains were negative for CD3, CD5, cyclin D1, and MYC. The morphology and immunohistochemical staining patterns were consistent with a diagnosis of follicular lymphoma, grade 3A, with possible areas of grade 3B. Pelvic peritoneal cell washings were also consistent with follicular lymphoma.

Full body PET/CT and a bone marrow biopsy were performed for staging purposes. Bone marrow biopsy showed normocellular marrow with no signs of involvement by follicular lymphoma. Complete blood count and peripheral blood smear were also



Figure 1: CT scan of the pelvis showing a left-sided adnexal mass and enlarged external iliac lymph node with (a) and without (b) calibrations

unremarkable. Activity on PET/CT in multiple regions was concerning for diseases including cervical and external iliac nodes, left and right submandibular glands, and right parotid gland. The final diagnosis was declared stage IIIA, grade 3A/B follicular lymphoma. A gynecological/breast gene mutation panel was negative for any abnormality including BRCA-1 and BRCA-2.

The patient was started on a cycle of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) regimen with plans to undergo six cycles. After two cycles of R-CHOP, a PET/CT was repeated and revealed remarkable regression of the cervical and inguinal lymph nodes.

#### Discussion

Follicular lymphoma is a type of NHL that typically originates in the lymph nodes. It has an indolent course and is generally diagnosed at later stages with waxing and waning lymphadenopathy. Although less common, a primary extranodal disease arising from solid organs accounts for 25–35% of NHLs and presentation depends on anatomical location. [5] Ovaries are actually the most common location to find extranodal lymphomas in the female genital tract, but still only comprise 0.5% of extranodal lymphomas. [5,6] In our case, the patient did not present with any complaints and the only abnormality throughout the visit was a firm cervix appreciated on pelvic exam. This physical exam finding was most likely due to local spread by the tumor.

Another point of importance was our patient's history of breast cancer. She had a history of both DCIS and invasive ductal carcinoma of the breast. Patients with a history of cancers are at increased risk of developing another malignancy. The association between breast cancer and NHL has been shown to be independent of radiation therapy; however, the risk is even higher in patients with a history of radiation therapy.<sup>[7]</sup>

This case report of a physical exam finding, in a patient with a history of breast cancer, leading to a new diagnosis of cancer highlights the importance of routine health care follow-up with physicals—especially for patients with history of prior cancer. This coincides with recent epidemiological study results, done for the years 2005–2015, that showed reduced cardiovascular, cancer, and respiratory mortality by 0.9–1.4%, alongside a 51.5-day increase in life expectancy, by the addition of 10 primary care physicians per 100,000 population.<sup>[8]</sup>

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### **Conflicts of interest**

There are no conflicts of interest.

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