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Case report

A case of primary cervical lymphoma in a patient with abnormal uterine bleeding

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ABSTRACT

Primary lymphoma of the uterine cervix is a rare site of extranodal lymphoma. Many gynecologic oncologists may go their entire career without encountering one. Patients may present with symptoms of abnormal or postmenopausal bleeding, and diagnosis may be challenging as typical office tests such as the pap smear may not detect the abnormal cells. Once a diagnosis is made, management may be debated due to the rarity of the condition and lack of accepted standard treatment. However, most patients respond well to some version of chemotherapy and radiation typically used for standard lymphomas. Prognosis is favorable if the patient is diagnosed early in the disease process.

1. Introduction

Primary cervical lymphoma is an extremely rare malignancy encountered by gynecologic oncologists. It is estimated that less than 1% of extranodal lymphoma arises from the uterine cervix (Komaki et al., 1984). Diagnosis can be challenging as the routine Papanicolaou test often fails to detect the pathologic cells (Dursun et al., 2005). Treatment varies, but high rates of success have been achieved with a combination of chemotherapy, radiation and/or surgery. Here we report a case of primary cervical lymphoma in a perimenopausal woman who presented with abnormal bleeding.

2. Case presentation

Patient presented as a 55-year-old woman who had never ceased menses. She developed daily spotting 4 months prior to presentation. One month prior to presentation, she experienced an episode of heavy bleeding with passage of clots and was referred to a gynecologist for further evaluation. Transvaginal ultrasound showed poor visualization of the uterus and MRI was obtained. The uterus was atrophic. Her cervix was enlarged with abnormal stromal signal that was read as highly worrisome for cervical malignancy. The widest cervical diameter was measured at 5.6 cm. There was no adenopathy, stranding or thickened parametria. Endometrial biopsy was non-diagnostic and patient was referred for gynecologic oncology evaluation. A pap smear was normal, though no transformation zone noted, and HPV testing was not performed.

On physical examination, a left labial cyst was noted and the patient reported that it had been present for several years. The cervix was posterior and difficult to visualize on speculum examination. On bimanual exam, the cervix was barrel-shaped and uterus was non-palpable. Her parametria were smooth and ovaries free from masses.

Patient underwent an exam under anesthesia (EUA), cervical biopsies, and dilation and curettage. On EUA, the cervix was 10 cm in diameter. Pathology showed lymphoma and immunohistochemistry was consistent with diffuse large B cell lymphoma (DCBCL) with high mitotic index on both the cervical biopsies and curettings. Post-procedure evaluation included PET/CT which was negative for metastatic disease (Fig. 1), but did show marked uptake at the cervix consistent with known malignancy (Fig. 2). Bone marrow biopsy was normal.

The patient was initiated on standard DCBCL multi-agent chemotherapy with cyclophosphosphamide, doxorubicin, vincristine, and prednisone with rutiximab (R-CHOP). After cycle 1, she continued to have a markedly enlarged cervix on examination. After cycle 3, the cervix had only minimally decreased in size. The medical oncologist was quite concerned that the size of the cervix had not significantly changed on exam and recommended surgical resection, as it was felt the tumor should have had a better response to chemotherapy. Plan was made for hysterectomy and patient underwent laparoscopic assisted vaginal hysterectomy, bilateral salpingo-oophorectomy without

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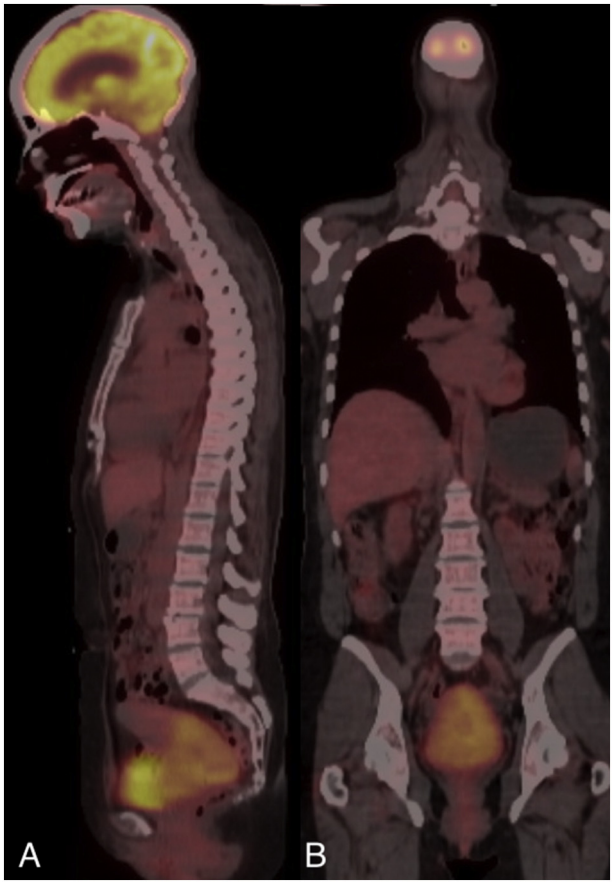

Fig. 1. PET/CT demonstrating large, isolated FDG-avid cervical mass. [A] Sagittal view. [B] Coronal view.

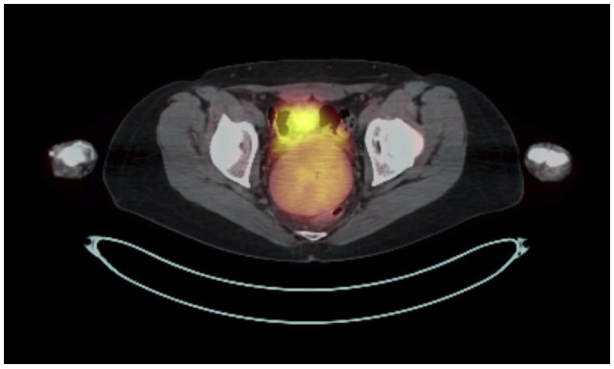

Fig. 2. Axial image of PET/CT revealing large, FDG-avid cervical mass.

complication. Final pathology showed no residual lymphoma and was otherwise benign. Inflammation and lymphocytic infiltrate without evidence of large B-cell component or fibrosis was noted on the pathologic report (Fig. 3). Following surgery, the patient underwent a post-treatment PET/CT which was negative for disease. She then completed surveillance CT scans every 6 months for a total of two years. This was in addition to regular office visits and physical exams. We are happy to announce that the patient has been free from disease for three years at time of publication.

3. Discussion

Primary lymphoma of the uterine cervix is a rare malignancy encountered by gynecologic oncologists. Typically, lymphoma arises in lymphatic organs such as the spleen, thymus, or lymph nodes and spreads to other sites (Groszmann and Benacerraf, 2013). Approximately one third of lymphoma is extranodal in origin and an even smaller number, estimated to be 1 in 175 (0.057%), originates from the female gynecologic tract (Heredia et al., 2005). Non-Hodgkin lymphoma (NHL) is one of the most common types of cancers accounting for 4% of all cancers in the United States (Society AC, 2017).The incidence of NHL has been on the rise in recent decades with a disproportionate number of extranodal lymphomas (Guerard and Bishop, 2012). However, primary cervical lymphoma still remains exceedingly rare. Due to its infrequent presentation, its exact incidence is unknown (Stroh et al., 1995).

The median age of presentation is in the fourth decade although documented cases range from age 20 to 80 (Dursun et al., 2005; Cheong et al., 2000). Initial presenting complaints are typically non-specific and include irregular bleeding, vaginal discharge, or a symptomatic pelvic mass (Korivi et al., 2014). Most patients do not display the classic signs of lymphoma such as fatigue, fever, night sweats, and weight loss (Vijayakumar et al., 2016). Diagnosis may be delayed as pap smear testing of the squamous epithelium often fails to detect the underlying abnormal stromal cells (Dursun et al., 2005). For definitive diagnosis, tissue biopsy with histopathologic examination with or without immunologic analysis is typically required (Kuo et al., 1994).

Differential diagnosis of primary cervical lymphoma should include cervical fibroids, poorly differentiated squamous cell carcinoma, chronic inflammation, and sarcoma (Dursun et al., 2005; Groszmann and Benacerraf, 2013). Radiographic assessment of the lesion may help to differentiate etiologies. Transvaginal ultrasound, a frequent part of initial workup, may reveal a solid lobulated mass with blood flow throughout consistent with malignancy (Dursun et al., 2005). Magnetic resonance imaging (MRI) is typically significant for a uniformly enhancing pattern on T1 imaging which aids in excluding other pathologies such as degenerating fibroid or squamous cell carcinoma (Korivi et al., 2014). Once diagnosis is obtained, PET/CT imaging is helpful to identify additional sites of involvement, but its use as a first line imaging modality is not recommended due to cost and accessibility (Korivi et al., 2014).

There is no accepted consensus for the staging of primary cervical lymphoma. Most commonly, the Ann Arbor staging and the International Federation of Gynecology and Obstetrics (FIGO) systems are used (Korcum et al., 2007). Prognosis is affected by stage at time of diagnosis, and detection of extranodal disease often occurs at a later stage due to inaccurate or delayed diagnosis (Trenhaile and Killackey, 2001). If detected at an early stage, prognosis of cervical lymphoma has a favorable prognosis to many other primary gynecologic malignancies (Korcum et al., 2007).

Given the rarity of the disease, there is no standardized treatment approach once diagnosis is made. However, complete response with remission has been well documented with multiple cases of combination chemotherapy and radiation (Stroh et al., 1995). Most commonly, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) with or without bleomycin has been used successfully. One case report demonstrated success with monoclonal antibody therapy in addition to CHOP chemotherapy (Baijal et al., 2009). Other reports advocates for neoadjuvant chemotherapy followed by surgical resection without radiation (Szantho et al., 2003).

Post-treatment surveillance is also not clearly defined given the rarity of this condition. In our patient who was noted to have a complete response after pathologic examination of the surgical specimen, close observation was deemed appropriate. It is unclear why the patient's cervix remained enlarged after chemotherapy, but if residual disease had been identified at time of resection, an additional 3 cycles of R-CHOP would likely have been administered. If there was ongoing post-treatment FDG uptake on follow up PET/CT, adjuvant radiation could be considered as well.

While primary cervical lymphoma remains a rare condition

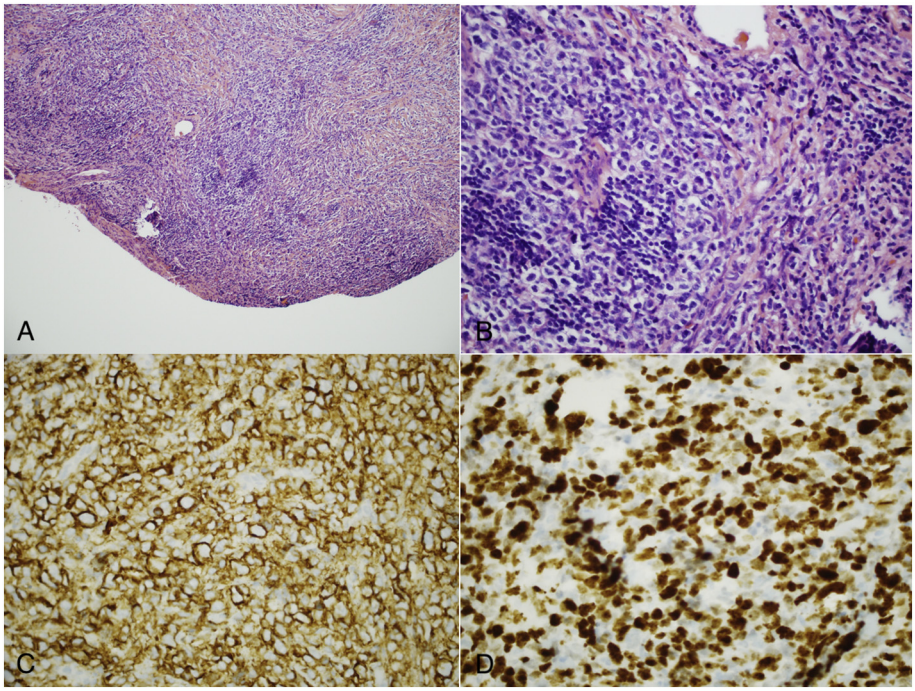

Fig. 3. [A] 40×. H&E. Diffuse lymphoid infiltrate with overlying ulceration involving cervix. [B] 400×. Sheets of centroblasts with irregular nuclear contours and moderate cytoplasm. [C] 400×. CD20 positive neoplastic B-cells. [D] 400×. Ki67 demonstrating increased proliferation rate in the neoplastic cells (approximately 90%).

encountered by few gynecologic oncologists, and even fewer general obstetrician/gynecologists, its recognition and prompt treatment is essential to improve survival. In the case presented, the patient was diagnosed after presenting with symptoms of subnormal uterine bleeding and referred promptly to a gynecologic oncologist. Her evaluation and treatment occurred expeditiously and her resulting favorable prognosis is without a doubt a favorable conclusion.

Conflict of interest statement

The authors declare that there are no conflicts of interest. No funding sources supported this investigative review.

Author contribution section

Both authors were significantly involved the background research, written presentation, and editing of this report and are listed as such.

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