Case report

B-cell acute lymphoblastic leukemia/lymphoma in relapse presenting as a cervical mass: A case report and review of literature

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ARTICLE INFO

Keywords:
Hematologic malignancy
Diagnosis - relapse
Cervical cancer

ABSTRACT

The involvement of the cervix as a site of relapse for hematologic malignancies is rare. We herein present a case of relapsed B-cell Acute Lymphoblastic Leukemia/Lymphoma (ALL) mimicking advanced cervical cancer. The patient is a 61-year-old female with history B-cell ALL and had multiple relapses confined to the bone marrow and had received several different chemotherapy regimens. She presented with lower abdominal pain after the end of her last cycle for which an MRI abdomen and pelvis was done and it showed the presence of an asymmetrical cervical mass. Further imaging included a PET-CT showing the presence of hypermetabolic cervical mass with left pelvic and retroperitoneal lymph node involvement. She underwent a biopsy of 3 distinct lesions in the cervix and vagina and a diagnosis of relapsed B-cell ALL was confirmed in two out of the three specimens.

1. Case presentation

61-year-old female, G4 P4, presented to the gynecologic oncology clinic after MRI of the abdomen and pelvis showed an asymmetric soft tissue fullness in the region of the cervix measuring 5.7 × 3.9 cm, and extending toward the left, along with a small volume left pelvic and left retroperitoneal lymphadenopathy suggestive of cervical malignancy.

The patient had a history of B-cell acute lymphoblastic leukemia/lymphoma (ALL) initially diagnosed 4.5 years prior to presentation, with BCR/ABL negative but positive for extra chromosome 22 diagnosed since July 2014 and has had two relapses. These two relapses were diagnosed after the patient returned complaining of symptoms of back pain and fatigue. Bone marrow biopsies were done in both cases and confirmed the relapse in each. However, there was no evidence of any extramedullary involvement on imaging in both relapses.

Immunohistochemical stains done on the cervical specimens showed patchy CD34, CD20, CD79a, TdT, CD10, MUM-1, Bcl-2, c-myc (70%). Cells were negative for CD99, CD30, EBV, and had a Ki-67 of 80%. She has initially received Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin) + ofatumumab followed by POMP (6-mercaptopurine, vincristine, methotrexate, and prednisone) maintenance on which she relapsed in June 2018. She was then started on Blinatumomab in August 2018 and had the surveillance imaging six month after treatment due to a complaint of lower abdominal pain and nausea, as shown in Fig. 1. She has no vaginal bleeding, itching, or discharge. She reported no dyspareunia or post-coital bleeding. She has no family history of gynecologic tumors. Her last pap smear was done in 2010, which was normal. She reported a history of one abnormal Pap smear several years ago, colposcopy was negative, and no biopsy was obtained.

On speculum examination, there was an abnormally appearing cervix with two polyps at the cervical os, and a raised lesion on the left vaginal sidewall. On bimanual and rectovaginal examination, a mobile, nontender uterus was felt, in addition to a 4 cm cervical mass extending to left parametria and left proximal upper 1/3 of the vagina. Pap smear was collected, and three biopsies obtained from the anterior cervical polyp, 6 o’clock location and vagina respectively. The purpose of the pap smear was to detect high-risk Human Papilloma Virus (HPV) strains.

PET scan was ordered after the visit to the gynecologist, and it showed hypermetabolic cervical mass consistent with primary cervical cancer, multiple left pelvic and retroperitoneal FDG-avid lymphadenopathy consistent with nodal metastasis, in addition to foci of increased FDG uptake along the thoracic and lumbar spine consistent
Fig. 1. MRI abdomen and pelvis showing the cervical mass.

Fig. 2. PET-CT scan showing hypermetabolic cervical mass with increased FDG-uptake in retroperitoneal and left pelvic lymphnodes.
with metastasis as shown in Fig. 2.

Pathology reported the anterior polyp at the os as a benign endometrial polyp. The other two specimens were reported as recurrent B-lymphoblastic leukemia/lymphoma with Ki67 of 90%. Histologically, the specimens showed medium and large-sized neoplastic cells with regular cytoplasm and irregular nuclear contours, blastoid chromatin, and occasional small nucleoli. Apoptotic bodies and mitotic figures are identified, and no necrosis was seen. Immunohistochemical staining showed positive CD10, CD19, CD34, and TdT. The patient was started on a new chemotherapy regimen HCVD (hyperfractionated-cyclophosphamide, vincristine and dexamethasone) + Venetoclax and has received her first cycle with no complications Fig. 3.

2. Discussion

In this case report, we present a case of extramedullary B-cell ALL involving the cervix with a presentation similar to locally advanced cervical carcinoma. Hematologic malignancies are rarely found in the female genital tract (FGT). The involvement of FGT accounts for less than 1% of the extranodal lymphoma/leukemia, and of that, the cervix accounts for less than 0.5% (Komaki et al., 1984; Vang et al., 2001). In particular, the primary sites of extramedullary disease in Acute Lymphocytic Leukemia (ALL) are central nervous system and testes (Geetha et al., 2015).

Moreover, Acute Myeloid Leukemia (AML) and lymphoma, which are more common to occur in the genital tract, have been documented at autopsy, but acute lymphoblastic leukemia with relapse in the uterine cervix has been rarely reported (Lyman and Neuhauser, 2002). Primary hematologic involvement is common in patients with hematopoietic malignancies in the genital tract. These patients usually present with symptoms of abnormal vaginal bleeding, pelvic mass, or discomfort. The average age of presentation is 40 years (Hanley et al., 2009). Our patient had non-specific pelvic pain at the time of imaging that showed the cervical mass, after she finished the last cycle of her chemotherapy.

Due to the rarity of the disease, the diagnostic workup is often challenging. The traditional pap smear has low sensitivity in detecting lymphoma with an interval value ranging from 20 to 30%. This can be attributed to the lack of involvement of the surface epithelium and the misclassification of malignant cells as being benign inflammatory without the appropriate clinical context (Hanley et al., 2009; Zutter and Gersell, 1990). For that reason, a biopsy is almost always necessary in addition to the clinical correlation and past medical history of the patient, especially that such tumors when symptomatic can mimic a primary cervical malignancy. The differential of cervical lymphoma can include several inflammatory diseases such as chronic lymphocytic cervicitis or follicular cervicitis and sarcoma. Also, the presence of plasma cells and macrophages along with the appropriate context, may help in the diagnosis of an inflammatory process and prevent misdiagnosis (Kazi et al., 2013).

Cytologic features of chronic or follicular cervicitis include a mixture of small and large lymphocytes, polymorphonuclear cells, plasma cells, in addition to reticular histiocytic cells. However, eosinophils and mast cells are rarely observed (Roberts and Ng, 1975). On the other hand, granulocytic sarcoma which occurs as a consequence of granulocytic leukemia is characterized cytologically by the cells with opaque chromatin, sparse cytoplasm, reniform nuclear shapes and the lack of prominent nucleoli (Spahr et al., 1982; Chorlton et al., 1974).

Detecting extramedullary relapse of acute lymphoblastic leukemia/lymphoma by imaging can be hard but often possible when patients are symptomatic. Relapse may occur at various sites with or without bone marrow involvement. The lack of current surveillance protocols for detecting extramedullary relapse and the fact that long-term follow-up with PET-CT and MRI is not routinely used adds to the burden of early detection of disease. Clinical and laboratory correlation require careful consideration when interpreting radiologic findings as radiologic.
findings alone can be non-specific especially in the context of previous leukemia, soft tissue masses include differentials of infection, hemorrhage and secondary neoplasms (Clark et al., 2010; Arrigan et al., 2013).

In patients with a known extrauterine malignancy, the physician should have a high-suspicion of a metastatic disease, in which a tissue biopsy is warranted to achieve an accurate diagnosis. Imaging and physical exam will aid when interpreted in the context of the medical history of the patient, but the biopsy should be done as early as possible to ensure proper management.

Author contribution

Jamil Kazma: Writing – Original Draft; Writing, Review & Editing, Cynae Johnson: Investigation, Writing – Review & Editing, Nitin Jain: Resources, Vasantha Lakshmi Gali: Resources, Ken H Young: Resources, Amir A. Jazaeri: Writing – Review & Editing, Supervision.

Declaration of Competing interest

We have no conflict of interest to declare.

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