

# Utero-Ovarian Involvement in Non-Hodgkin's Lymphoma on 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: A Case Series and Literature Review

## Abstract

Lymphomas are common solid malignancies. They are associated with substantial morbidity and mortality. Hodgkin's lymphoma (HL) and Non-HL (NHL) are subtypes of lymphoma. Lymph nodes are the most common site of involvement, though practically any organ may be involved. NHL has preponderance for extranodal involvement. Primary uterine and ovarian NHL is scarce. However, in advanced systemic disease, secondary utero-ovarian involvement may be seen. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) is a pivotal imaging modality in lymphomas. It abets in pretreatment staging, posttherapy restaging, and surveillance. We present three stage-IV NHL cases with secondary utero-ovarian involvement. FDG PET/CT as a baseline imaging modality established the disease burden and organ involvement.

**Keywords:** 18F-fluorodeoxyglucose positron emission tomography/computed tomography, extranodal lymphoma, female genital tract, staging, utero-ovarian lymphoma

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## Introduction

Lymphoma is a malignant proliferation of lymphoid tissue and frequently commences from Lymph nodes (LNs). Lymphomatous involvement in virtually any organ is described. Extranodal lymphoma (ENL) is the infiltration of malignant lymphomatous cells in organs other than LNs. Approximately one-fourth of the lymphomas arise in extranodal organs. The most frequently involved organ system in ENL is the gastrointestinal tract (The stomach is the most typical site), followed by Waldeyer's ring, lung, liver, spleen, bone, and skin.<sup>[1]</sup> Primary ENL is intriguing as it may have distinct clinicopathologic features, association with underlying immunodeficiency syndromes, autoimmune diseases, and infections.<sup>[2]</sup> Primary Non-Hodgkin's lymphomas (NHLs) of the female genital tract are uncommon. Only 1.5% of all ENL originate in the female genital tract, with ovaries being the most common site.<sup>[3]</sup> Secondary involvement of the female genital system is more common. A patient may present with gynecological symptoms or remain asymptomatic. Conventional cross-sectional imaging has

several constraints in assessing lymphomas. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) is a hybrid imaging modality and has become the standard of care in HL and NHL.<sup>[4]</sup> It accurately identifies disease burden and organ involvement. This case review presents the three NHL patients with secondary involvement of the uterus and adnexa.

## Case Reports

### Case 1

A 60-year-old female presented with complaints of fever for 1 month. The pain was progressive and associated with an inability to walk. On examination, there was a large lump in the right lumbar region. She was menopausal for 12 years and had no significant gynecological history. Her routine blood investigation revealed anemia (Hb-7.6 g/dl), leukocytosis (15,400/uL), and raised serum LDH levels (1140 u/L). Ultrasound (USG) abdomen showed enlarged retroperitoneal LNs. Guided histopathology showed high-grade lymphoma.

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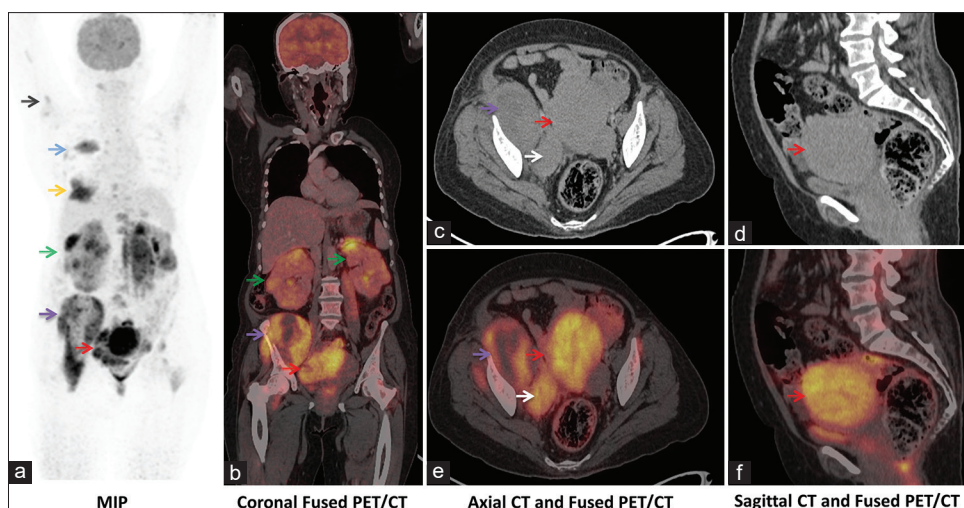
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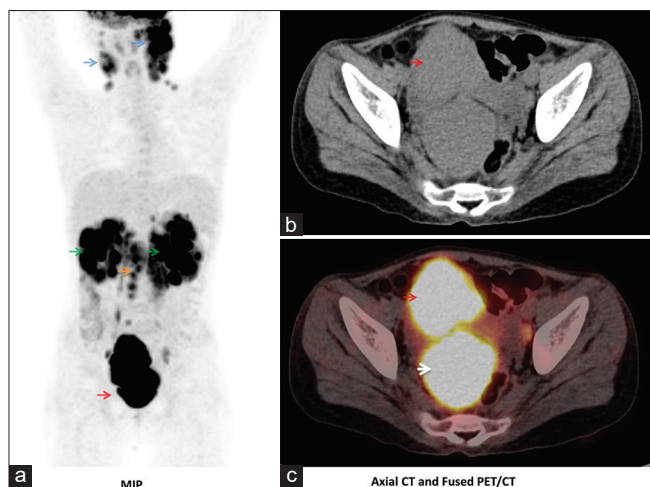
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**Figure 1:** The maximum intensity projection image (a) is showing multiple tracer avid lesions involving the right breast (blue arrow), right lung (yellow arrow), kidneys (green arrow), uterus (red arrow), skeletal (purple arrow), and bone marrow (black arrow). (b) Coronal images show similar findings. A bulky uterus (red arrow) is noted. (c and e) Images showing diffuse increased  $^{18}\text{F}$ -fluorodeoxyglucose avidity in the bulky uterus with right adnexal mass (white arrow). (d and f) Images show an enlarged uterus with increased uptake



**Figure 2:** Maximum intensity projection image (a) is showing multiple bilateral cervical lymph nodes (blue arrow), renal enlargement (green arrow), and retroperitoneal lymph nodes (orange arrow). Apart from them, masses are noted in the pelvis (red arrow). (b and c) Pelvis images are showing  $^{18}\text{F}$ -fluorodeoxyglucose avid enlarged uterus (red arrow). A large mass (white arrow) is noted posterior to it, in the right adnexal region

Immunohistochemistry was noncontributory due to large areas of necrosis and marked degenerative changes. A baseline FDG PET/CT was done [Figure 1]. She received three cycles of the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). Her interim FDG PET/CT after three cycles of chemotherapies revealed a partial response to the treatment (not shown).

### Case 2

An 11-year-old girl presented with swelling on the left side of the neck for 6 months. She had no associated fever or weight loss. On examination, the patient had palpable, firm enlarged cervical LNs. She has not attained

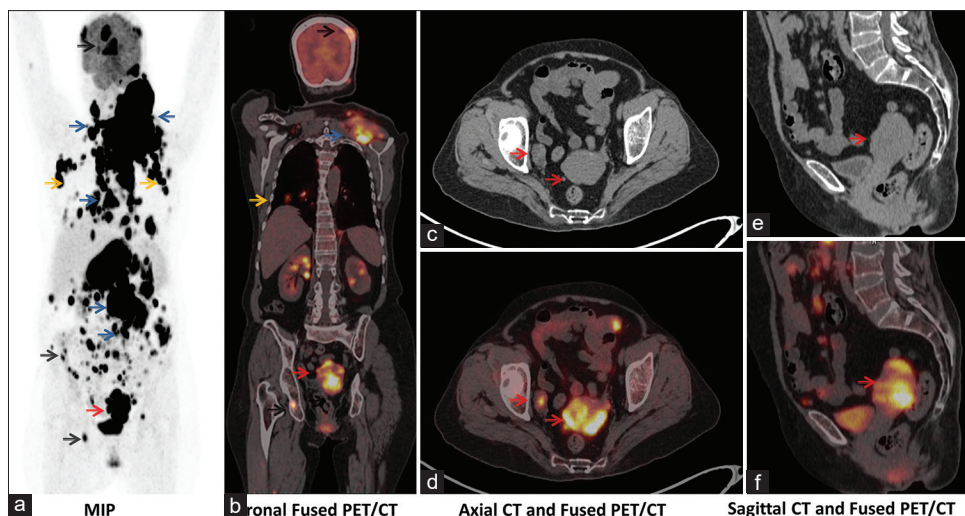
menarche. She had no significant gynecological complaints. Her biochemical investigations were unremarkable. CT suggested bilateral enlarged cervical LNs. Excision biopsy was suggestive of NHL (diffuse large B cell lymphoma). Her baseline FDG PET/CT revealed stage-IV disease [Figure 2].

### Case 3

A 60-year-old female presented with swelling on both sides of the neck for 3 months. It was associated with on and off fever and generalized weakness. On examination, she had multiple enlarged bilateral cervical LNs. Biopsy was suggestive of anaplastic large cell lymphoma. The patient was given three cycles of R-CHOP. However, no clinical response was noted. She was referred to our institute for further management. She had no gynecological complaints. LDH levels were significantly raised (825 u/L). The rest of the biochemical investigations were unremarkable. HPE was suggestive of diffuse large B cell lymphoma (anaplastic variant). On immunohistochemistry, tumor cells were positive for CD-20 and CD-3. FDG PET/CT was done for restaging [Figure 3]. The patient was lost to follow-up during the COVID-19 pandemic.

### Discussion

Lymphomas are common tumors and collectively rank fifth in cancer in incidence and mortality. They are a heterogeneous group of diseases ranging from indolent malignancies to rapidly growing and highly aggressive tumors. The prevalence of NHL has been increasing during the past two decades.<sup>[5,6]</sup> NHLs themselves are varied groups based on clinical presentation, morphological appearance, and response to therapy. Primary lymphomas involving the gynecologic tract are very uncommon. Most of these are NHL, and the most common subtype is diffuse large B-cell.<sup>[7,8]</sup> The secondary lymphomatous involvement of the



**Figure 3:** (a) Maximum intensity projection showing extensive tracer avid lesions involving bone (black arrow), cervical, mediastinal, retroperitoneal lymph nodes (blue arrow), both lungs (yellow arrow). The focal area of increased uptake is noted superior to the urinary bladder (red arrow). (b) Positron emission tomography/computed tomography image show corresponding findings. Axial (c and d) and sagittal (e and f) pelvis images showing <sup>18</sup>F-fluorodeoxyglucose avid bulky uterus and right adnexa with diffuse metabolic activity (red arrow). A focal area of increased uptake is also noted in the small bowel loop

uterus and ovaries is usually associated with disseminated disease.<sup>[9]</sup>

Cross-sectional anatomical imaging plays an essential role in the evaluation of gynecological malignancy. They also access other pelvis and abdominal organs. *In utero-ovarian lymphoma*, CT shows well-demarcated hypodense lesions with mild contrast enhancement.<sup>[10]</sup> On magnetic resonance imaging, uterine lymphoma exhibits homogeneous hypointense signal on T1-weighted images and relatively hyperintense on T2-weighted images. It presents as diffuse and uniform enlargement of the uterine corpus and cervix. The endometrium and cervical epithelium remain unremarkable. However, in some cases, it is indistinguishable from carcinoma.<sup>[11]</sup> The limitations of these imagings are the limited imaging area and low specificity in accessing nonenlarged pathologies.

FDG PET/CT the cornerstone of imaging in both HL and NHL.<sup>[12]</sup> It plays an essential role in staging, restaging, prognostication, planning appropriate treatment strategies, monitoring therapy, and detecting recurrence.<sup>[13]</sup> The advantage of PET over conventional imaging techniques is to access nonenlarged disease involvement. Another crucial aspect is differentiating between viable tumor, necrosis, or fibrosis in residual mass often present after treatment.<sup>[14]</sup> Due to the very low incidence of primary uterine lymphoma, scarce literature is available for management. It involves hysterectomy and bilateral salpingo-oophorectomy, chemotherapy, irradiation, or a combination of these.<sup>[15]</sup> All advanced cases with secondary utero-ovarian involvement are treated with systemic chemotherapy. All three patients had stage-IV disease at presentation, and they underwent systemic chemotherapy. These cases show the rare asymptomatic involvement of the uterus and ovaries in disseminated NHL. FDG PET/CT

could identify all the sites of involvement in one scan, thus helped in staging and prognostication.

## Conclusion

Primary lymphomas of the female genital organs are rare. Even secondary involvement is not well discussed in the literature. FDG PET/CT is a noninvasive imaging modality that discloses disease extent and asymptomatic organ involvement. It helps in staging, prognostication, guiding treatment, and response evaluation.

## 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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