Asia Oceania Journal of Nuclear Medicine & Biology
http://aojnmb.mums.ac.ir
AOJNMB

Incremental Value of FDG PET/CT in Aggressive High Grade B Cell lymphoma with TdT Expression

Nikita Sampathirao[1], Indirani Muthukrishnan[1], Ann Kurian[2], Jaykanth Amalchandran[1], Asra Patel[1], Shema Mathew[1], Shelley Simon[1*]

[1]Department of Nuclear Medicine and PET/CT, Apollo Hospitals, Chennai, India
[2]Department of Pathology, Apollo Hospitals, Chennai, India

ARTICLEINFO

Article type:
Case report

Article history:
Received: 21 May 2020
Revised: 13 Aug 2020
Accepted: 15 Aug 2020

Keywords:
TdT expression
Extranodal B-cell lymphoma
FDG PET/CT

ABSTRACT

High-grade B-cell lymphoma, an aggressive form of Non-Hodgkin's Lymphoma, is known as a double or triple hit lymphoma based on the presence of MYC and BCL2 without or with BCL6 genetic rearrangements, respectively. It carries a poorer prognosis, compared to other variants of B-cell lymphoma, and its management also differs which requires more intensive chemotherapy in contrast to the routine regimen. Terminal deoxynucleotidyl transferase (TdT), a marker of immaturity is commonly expressed in B-cell lymphoblastic leukemia or lymphoma (B cell ALL) which is absent in mature forms of B-cell lymphoma. The TdT is expressed in high-grade B-cell lymphoma; therefore, it poses a classification and management dilemma, which should be accurately differentiated from B-cell ALL and mandates molecular analysis. Herein, we report a case of a 52-year-old female with biopsy reported as high-grade B-cell lymphoma with TdT expression. She was referred for Fluor-deoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (PET/CT) scan for staging in the absence of molecular analysis for B-cell ALL. It was diagnosed as lymphoma on FDG PET/CT based on its characteristic findings of extensive extranodal involvement of multiple organs with no significant lymphadenopathy establishing the incremental value of FDG PET/CT scan, which helped the clinician to arrive at a conclusion.

Please cite this paper as:

Sampathirao N, Muthukrishnan I, Kurian A, Amalchandran J, Patel A, Mathew Sh, Simon Sh. Incremental Value of FDG PET/CT in Aggressive High Grade B Cell lymphoma with TdT Expression. Asia Ocean J Nucl Med Biol. 2021; 9(1): 45-50. doi: 10.22038/AOJNMB.2020.48887.1332

Introduction

Non-Hodgkin's lymphoma (NHL) is a group of lymph proliferative disorders, which predominantly arise from the lymph nodes (1). High-grade B-cell lymphoma is an aggressive mature B-cell lymphoma, which has been included in the World Health Organization tumor classification of hematopoietic and lymphoid tissues in 2016 (2). When MYC and BCL2 without or with BCL6 genetic rearrangements are present, they are named double or triple hit lymphoma, respectively (3). Terminal deoxynucleotidyl transferase (TdT) expression is usually considered a feature of precursor B-cells and is seen commonly in B-cell lymphoblastic leukemia or lymphoma (B-cell ALL) (4). Its presence in mature form causes a classification dilemma of B-cell lymphoma versus B-cell ALL (5). Both entities have to be differentiated as the management protocol and prognosis since they are very contrasting (2). Herein, we present a unique case report of high-grade B-cell lymphoma with TdT expression referred for Fluor-deoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (PET/CT). Molecular analysis to rule out B-cell ALL was not available at that time. The FDG PET/CT scan was suggestive of lymphoma with its findings, which helped the clinician arrive at the diagnosis in the absence of molecular analysis.

* *Corresponding author:* Shelley Simon. Department of Nuclear Medicine and PET/CT, Apollo Hospitals, 21 Greams Lane, Off Greams road, Chennai, 600006, Tamil Nadu, India.Tel: +91 9884055655; Email: shelleysimon@rediffmail.com

Case report

A 52-year-old post-menopausal female initially presented with a lump in the right breast of 6 months duration with a gradual increase in size. On clinical examination, a firm mass of soft tissue consistency was noted in the areolar region of the right breast. Axillary nodes were not palpable. Mammography was suggestive of multiple lobulated mass lesions in bilateral breasts (Right>left) that were the largest (5.2×3.3 cm) in the retro areolar region of the right breast (Figure 1 a, b, c, d). Routine evaluation with ultrasound (USG) abdomen showed an ill-defined uterine mass. Biopsy of breast and uterine lesions revealed a monomorphous population of atypical mononuclear cells with scant cytoplasm, intermediate-sized round nuclei with coarse chromatin, and a few small nucleoli (Figure 2a-b). The immune-histochemistry (IHC) diagnosed a high-grade B-cell lymphoma with TdT expression since the neoplastic cells showed diffuse positivity for CD20, BCL2, BCL6, CMYC, CD10, TdT, and PAX5 with a high proliferation index negative for CD3, Cyclin D1, CD34, and MUM-1 (Figure 3a-h). Since the USG of the abdomen and mammography were modalities for regional imaging, the patient was further referred for FDG PET/CT scan for staging and evaluation of the disease extent.

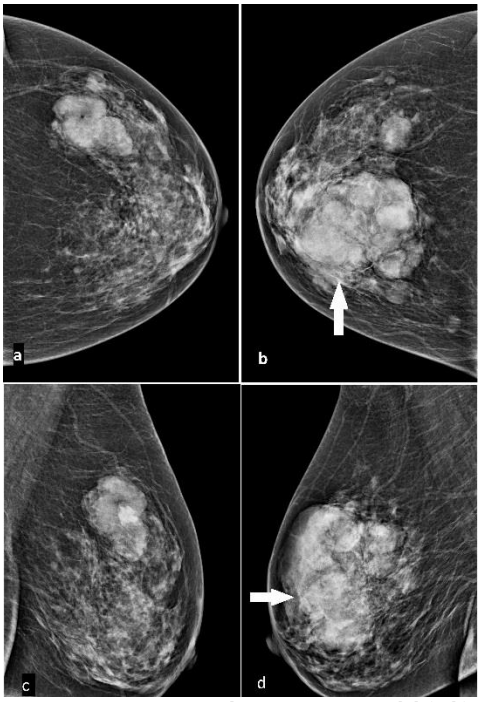

Figure 1. Mammogram showing craniocaudal (a, b) and mediolateral (c, d) views of right and left breasts with multiple homogenous lobulated lesions that are largest in the retro areolar region of the left breast (arrow)- Breast imaging, reporting, and data system IV category

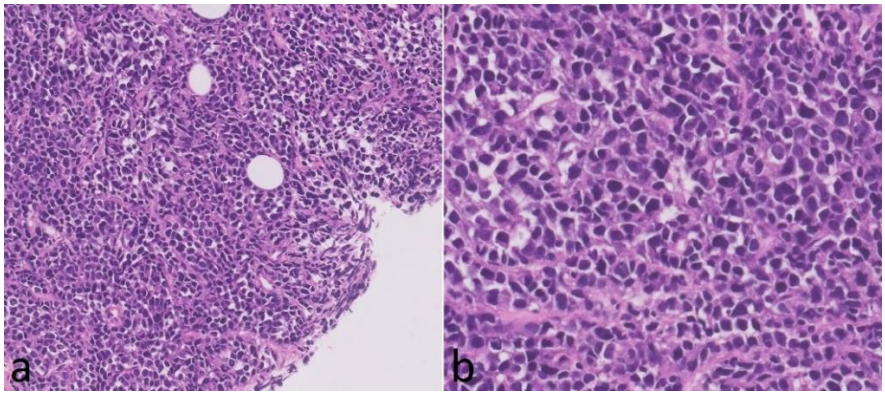

Figure 2(a-b). Microscopy showing the monomorphous population of small to intermediate-sized atypical mononuclear cells with scant cytoplasm, coarse chromatin, and a few small nucleoli a: (H&E, ×100) b: (H&E, ×400)

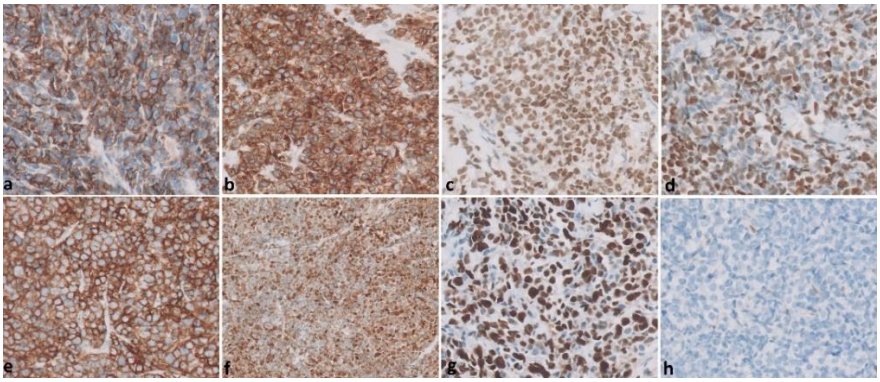

Figure 3(a-h). Immunohistochemistry of atypical cells are diffusely positive for positivity for a: CD20 (×400), b: BCL2 (×400) c: BCL6 (×400), d: C-MYC (×400), e: CD10 (×400), f: TdT (×200), g: High proliferation with Ki-67 labeling index (×400) and negative for h: Cyclin D1 (×400)

The FDG PET scan was performed following a standard protocol after 60 min post intravenous injection of 6 mCi of FDG from the vertex of the skull till toes. The CT with a contrast of the whole body was performed for attenuation correction and anatomical correlation. The maximum intensity projection (MIP) image (Figure 4), as well as axial, sagittal, and coronal sections, showed well-defined enhancing lobulated lesions in the bilateral breasts with intense FDG uptake (Figure 5) and a Maximum Standardised Uptake Value (SUV_{max}) of 20.2 in the lesion and retro areolar region of the right breast. No significant axillary lymph nodes were noted in this case.

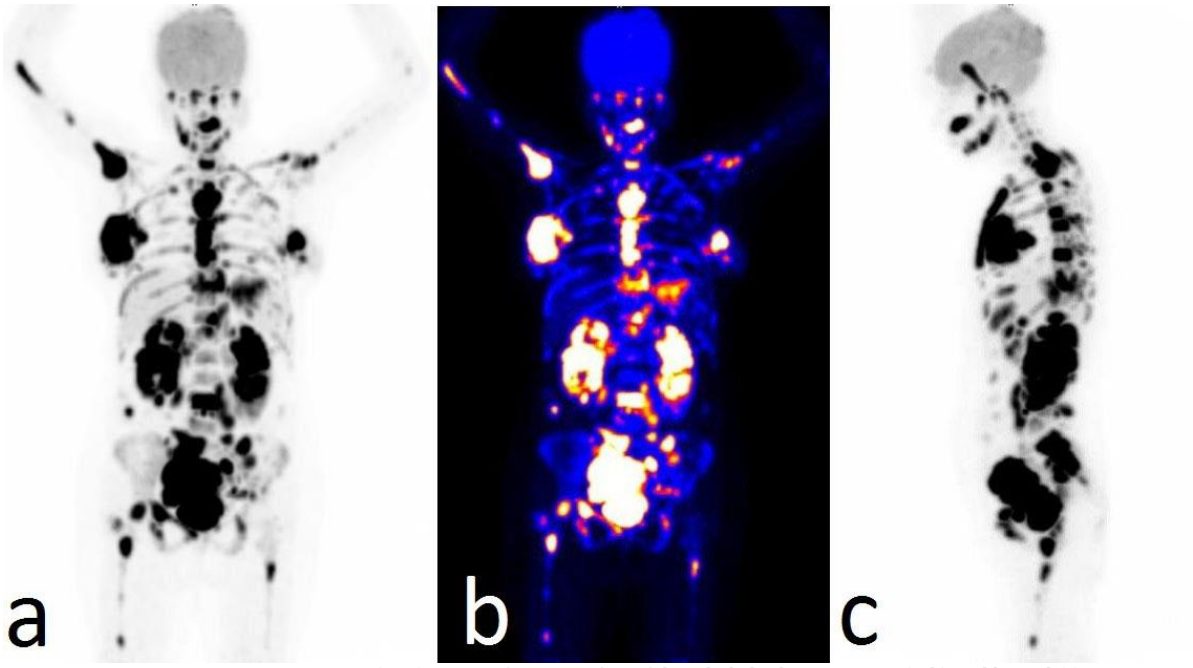

Figure 4. Maximum intensity projection (MIP) image of FDG PET/CT of the whole body in anterior (a, b) and lateral (c) views demonstrating abnormal FDG uptake in bone marrow, breasts, abdomen, and pelvis

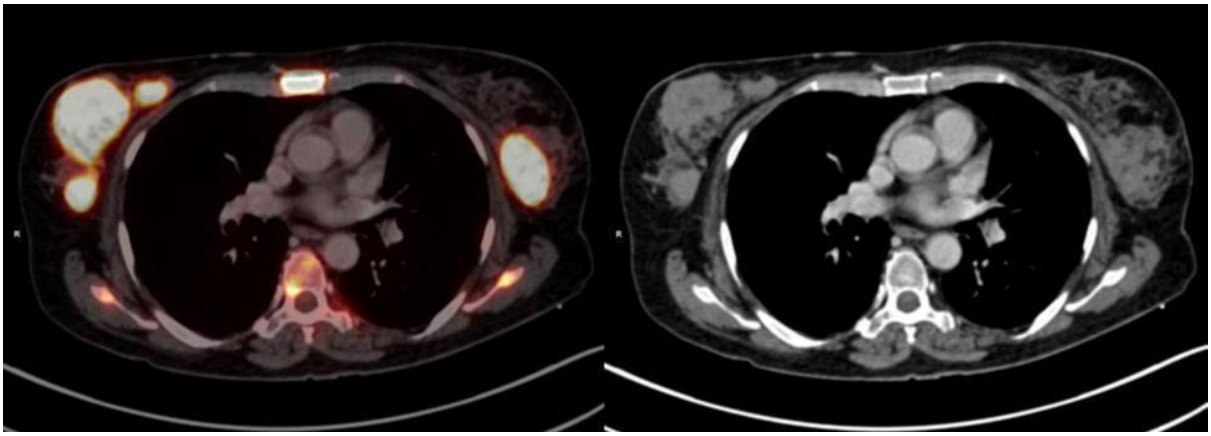

Figure 5. Axial sections of fused FDG PET/CT and contrast CT showing intensely FDG-avid enhancing lobulated lesions in bilateral breasts (Left>right)

Intense hypermetabolic heterogeneously enhancing soft tissue mass was observed involving the entire uterus and bilateral ovaries (Figure 6a-b) with SUV_{max} of 34.8. The mass was seen compressing the distal part of the left ureter resulting in left hydroureteronephrosis. Diffusely thickened left broad ligament with increased FDG uptake was a significant feature (Figure 6c). Bilateral bulky kidneys with multiple intensely FDG-avid hypodense lesions were also noted in this study (Figure 7). Foci of asymmetrical wall thickening with intense FDG avidity were observed involving the fundus and wall of the stomach (Figure 8). The pancreas displayed many foci of increased FDG uptake (SUV_{max}=14.7) with no corresponding CT abnormality.

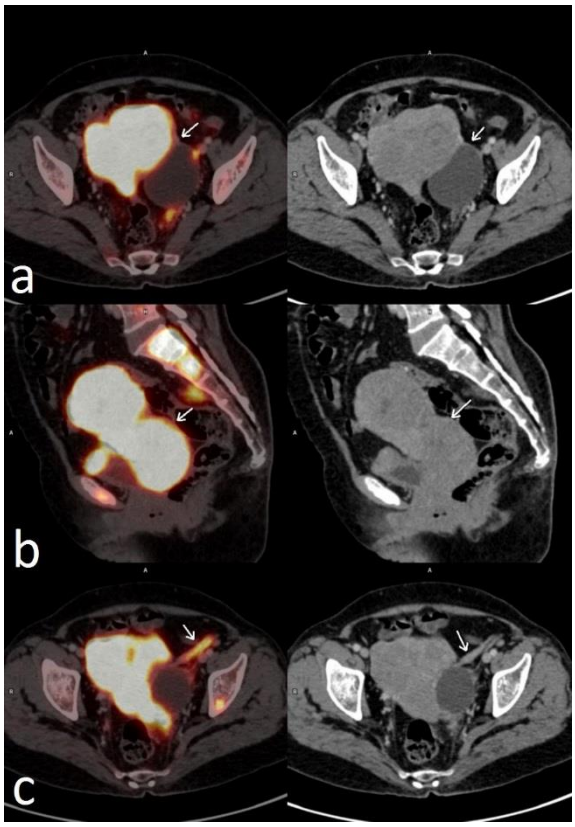

Figure 6. Axial (a) and sagittal (b) sections of fused FDG PET/CT and contrast CT images of the pelvis showing FDG-avid soft tissue mass involving the fundus, body, and cervix of the uterus and bilateral ovaries with a large non-FDG avid cyst in the left adnexa. Diffuse thickening of the left broad ligament (c) is seen with intense FDG uptake

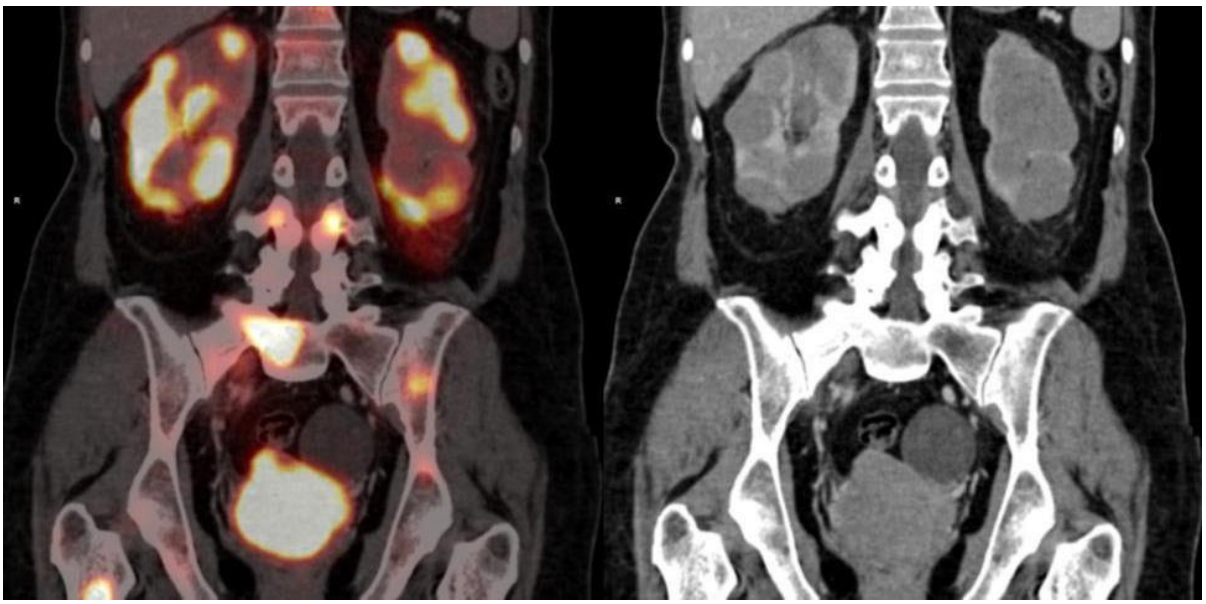

Figure 7. Coronal section of fused FDG PET/CT and contrast CT of the abdomen illustrating bulky bilateral kidneys with multiple hypodense lesions showing intense FDG avidity. Increased FDG uptake is also noted in the marrow of the sacrum and posterior elements of lumbar vertebrae

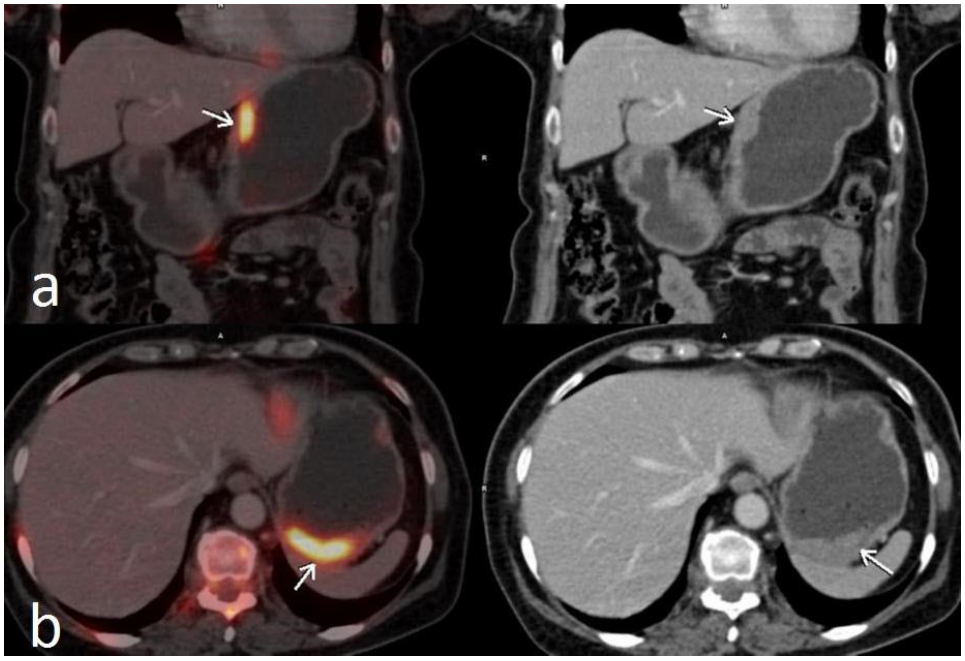

Figure 8. Coronal (a) and axial (b) sections of fused FDG PET/CT and contrast CT images showing multiple foci of asymmetrical wall thickening and nodular elevation in the fundus and along the lesser curvature of the stomach

Multiple peritoneal deposits were noted in the gall bladder fossa (SUV_{max}=9.8), surface of the urinary bladder and ascending colon, as well as presacral and left adnexal regions. The FDG-avid ill-defined soft tissue thickening was also noted in the para-aortic and left periureteric regions. Deposit with high metabolic activity was also noted in the interventricular septum (SUV_{max}=12.2).

Heterogeneous FDG avidity was seen in the marrow of the entire axial and appendicular skeleton, including the skull, maxilla, and mandible. The final impression of the FDG PET/CT was extensive-stage IV extranodal lymphoma with no significant lymphadenopathy. The liver and spleen, which constitute the major part of the reticuloendothelial system, were spared which was an unusual presentation in this case.

Discussion

Extranodal lymphomas constitute around 25% of all NHLs. The most common site is the gastrointestinal tract followed by nasopharynx, testes, uterus, ovary, and thyroid (1). High-grade B-cell lymphoma is incident in the elderly and is characterized by nodal disease and involvement of two or more extranodal sites. It is worth mentioning that more than 50% of the patients present with advanced disease (Stage IV) (3). Moreover, TdT expression in a mature form of lymphoma is very rare and poses a classification dilemma between B-cell ALL and B-cell lymphoma. In this case, FDG PET/CT demonstrated extensive extranodal involvement of major organs, including breasts, kidneys, pancreas, stomach, uterus, cervix, ovaries, peritoneum, and marrow with sparing of liver and spleen followed by no significant lymphadenopathy.

The involvement of mandible is also unusual. Whenever lymphoma occurs in jawbones, it is initially mistaken for a dental infection (6). No oral or dental symptoms were noted in the patient since no skeletal anatomical disease was manifested .

Bilateral bulky kidneys with multiple FDG-avid hypodense lesions are a characteristic picture of renal lymphoma. The most common imaging appearance of renal lymphoma is FDG-avid multiple parenchymal mass of variable sizes. This pattern is noted in 50%-60% of the cases. The lesions are most often bilateral; however, they may also affect only one kidney (7). Gastric involvement was observed as multiple foci of asymmetric nodular thickening which is contrary to the commonly noted pattern of bowel involvement which is characterized by diffuse circumferential wall thickening with aneurysmal dilatation and no proximal obstruction. Lymphoma involving the uterus, cervix, and ovaries is commonly diffuse (8) which is consistent with the findings in the present case. However, the impressive aspect in our case is the diffuse beaded peritoneal thickening over the left broad ligament. With all the features mentioned above, the FDG PET/CT scan of this case stands out with its unique findings of lymphoma.

In total, 80% of the ALL cases are seen in children;

moreover, its incidence in adults is very low at around 1.6 per 100,000 populations (9). Bone marrow is the primary site to be affected in leukemia. Extramedullary involvement can occur in the liver, spleen, and lymph nodes in 20% of the patients. Leukemic infiltration of the central nervous system is seen in 5%-8% of the cases (9). Furthermore, the involvement of other major organs, such as breast, uterus, ovaries, and pancreas that is noted in this case is very rare in the literature.

On the other hand, NHL is prevalent in adults and constitutes only 10% of childhood lymphoma. The NHL is known to occur anywhere in the body with organ involvement in more than 25% of the cases. The characteristic findings of our FDG PET/CT scan with exclusive organ involvement and sparing of lymph nodes, liver, and spleen supports the diagnosis of lymphoma over B cell ALL .

High-grade B-cell lymphoma carries a poor prognosis and a low overall survival (2). In this study, high SUV_{max} of the lesions (largest size: 34.8 in the mass involving uterus and ovaries) on FDG PET/CT scan is indicative of poor prognosis. High metabolic activity and SUV_{max} is known to be the independent prognostic factors in lymphoma (10).

Despite the non-availability of molecular analysis at that time point, the FDG PET/CT scan acted as a clinching tool along with histopathology for arriving at a diagnosis, thereby leading to the management and prognosis. However, histopathology with IHC and molecular analysis is the gold standard.

Conclusion

The FDG PET/CT scan is an important imaging modality, which can help clinch the diagnosis in cases of a clinical conundrum. Exclusively extensive extranodal disease with sparing of liver and spleen is a distinctive feature of this case, which helped the clinician arrive at a diagnosis in the absence of molecular analysis. Accordingly, along with histopathology and IHC, FDG PET/CT acts as a complementary tool for diagnosis, management, and prognostification.

References

1. Pai A, Kannan T, Balambika R, Vasini V. A study of clinical profile of primary extranodal lymphomas in a tertiary care institute in South India. Indian journal of medical and paediatric oncology: official journal of Indian Society of Medical & Paediatric Oncology. 2017; 38(3):251.
2. Tashakori M, Crane G.High grade B cell lymphoma with MYC and BCL2 or BCL6 rearrangements.http://www.pathologyoutlines.com/topic/lymphomabunclassburkitt.html (accessed March 21 2020).
3. Soliman DS, Al-Sabbagh A, Ibrahim F, Taha RY, Nawaz Z, Elkourashy S, et al. High-grade B-cell neoplasm with surface light chain restriction and Tdt coexpression evolved in a MYC-rearranged diffuse large B-cell lymphoma: a dilemma in classification. Case reports in hematology. Epub 2017 Aug 13
4. Kim D-Y, Park H-S, Choi E-J, Lee J-H, Lee J-H, Jeon M, et al. Immunophenotypic markers in adult acute lymphoblastic leukemia: the prognostic significance of CD20 and TdT expression. Blood research. 2015; 50(4):227-34.
5. Ok CY, Medeiros LJ, Thakral B, Tang G, Jain N, Jabbour E, et al. High-grade B-cell lymphomas with TdT expression: a diagnostic and classification dilemma. Modern Pathology. 2019; 32(1):48-58.
6. Steinbacher DM, Dolan RW. Isolated non-Hodgkin's lymphoma of the mandible. Oral Oncology EXTRA. 2006; 42(5):187-9.
7. Sheth S, Ali S, Fishman E. Imaging of renal lymphoma: patterns of disease with pathologic correlation. Radiographics. 2006; 26(4):1151-68.
8. Onyiuke I, Kirby AB, McCarthy S. Primary gynecologic lymphoma: imaging findings. American Journal of Roentgenology. 2013; 201(4):W648-W55.
9. Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: a comprehensive review and 2017 update. Blood cancer journal. 2017; 7(6):e577-e.
10. Oh M-Y, Oh S-B, Seoung H-G, Kim J-H, Kim S-M, Kim T-K, et al. Clinical significance of standardized uptake value and maximum tumor diameter in patients with primary extranodal diffuse large B cell lymphoma. The Korean journal of hematology. 2012; 47(3):207-12.