

Assessment of Extranodal Lymphoma by ^{18}F -FDG PET/CT – A Report of two years in NINMAS

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ABSTRACT

Extranodal lymphoma, characterized by lymphomatous infiltration beyond typical lymphatic structures, poses a diagnostic challenge due to its diverse clinical presentations. This cross-sectional study conducted at the PET/CT division of the National Institute of Nuclear Medicine and Allied Sciences, Dhaka, aimed to explore the prevalence and distribution of extranodal involvement in 517 lymphoma patients (252 Hodgkin's lymphoma [HL] and 265 non-Hodgkin's lymphoma [NHL]) referred for ^{18}F -FDG PET/CT scans from January 2022 to December 2023.

Results revealed extranodal involvement in 9.12% (n = 23) of HL cases and 34.71% (n = 92) of NHL cases. Skeletal system manifestations were most common, accounting for 28.7%, followed by pulmonary (23.4%), gastrointestinal tract (19.1%), and muscular (13.9%) involvement. Other sites collectively constituted 15.6% of extranodal lymphoma cases.

These findings underscore the significance of ^{18}F -FDG PET/CT scans in assessing extranodal lymphomas, providing valuable insights into their distribution patterns. Understanding the prevalence and locations of extranodal involvement is crucial for accurate diagnosis, staging, and effective treatment planning in lymphoma patients.

Keywords: Extra nodal lymphoma, ^{18}F -FDG PET/CT.

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INTRODUCTION

Extranodal lymphoma refers to the lymphomatous infiltration at anatomical sites other than the lymph nodes, thymus and the pharyngeal lymphatic ring. The commonest sites of extranodal involvements include the stomach, spleen, Waldeyer ring, central nervous system, lung, bone, and skin. Extranodal involvement is less common with Hodgkin's lymphoma (HL) than non-Hodgkin's lymphoma

(NHL). It could be a primary extranodal disease or a disseminated lymph nodal disease affecting an extranodal location. ^{18}F -FDG PET/CT scan plays an important role in the evaluation of extranodal lymphomas (1).

PATIENTS AND METHODS

This cross-sectional study was carried out in the PET/CT division of the National Institute of Nuclear Medicine and Allied Sciences (NINMAS), Dhaka, from January 2022 to December 2023. The study included a total of 517 lymphoma patients, including those with Hodgkin's (HL) and non-Hodgkin's (NHL) lymphomas, who were referred for an ^{18}F -FDG PET/CT scan in NINMAS. After a fasting period of six hours, each patient received an intravenous administration of 5–6 mCi of ^{18}F -FDG. Serum blood glucose was measured before administration of FDG, preferably within 6.0 to 10.0 mmol/L. Subsequently, the patient rested quietly in a shielded room for 60 minutes to allow for the distribution and uptake of the radiotracer. Imaging was conducted using a Philips Dual Modality Ingenuity TF PET/CT system equipped with an integrated 128-slice LYSO crystal scanner. A low-dose CT scan with contrast was conducted for attenuation correction prior to PET acquisition. The PET scan was performed from vertex to mid-thigh with nine bed positions, taking one minute per bed. The standardized uptake value (SUV) was calculated as SUV body weight in grams per milliliter. Image evaluation was performed in the transaxial, coronal, and sagittal planes. Each study was meticulously assessed by three expert physicians to evaluate disease status in new patients, detect any new lesions, and assess therapy response in follow-up patients.

RESULT

Age range of the 517 lymphoma patients was 5 to 80 (42 ± 19.6) years, with a predominance of men (M:F=4:1) than

women. There were 252 patients with HL and 265 patients with NHL. Extranodal involvement was found in 9.12% (n = 23) in HL and 34.71% (n = 92) in NHL (Table 1) patients.

Table 1: Extranodal distribution of Hodgkin’s and non-Hodgkin’s lymphoma

Type of Lymphoma	No. of patients	Extranodal involvement
Hodgkin’s Lymphoma	252	23 (9.12%)
Non-hodgkin’s Lymphoma	265	92 (34.71%)
Grand Total	517	115 (22.24%)

The most common site of involvement was the skeletal system, with 33 patients (28.7%), followed by pulmonary (n = 27; 23.4%), gastrointestinal (n=22; 19.1%), and muscular

(n=17; 13.9%) sites among total lymphoma patients. Manifestation at other sites comprise 15.6% (n=18) of total patients (Table 2 and Figure 1)

Table 2: Distribution of extranodal lymphomas in different sites

Involved organ	No. of patients	Percentage (%)
Bone	33	28.7
Lung	27	23.4
GIT	22	19.1
Skeletal Muscle	17	13.9
Others	18	15.6

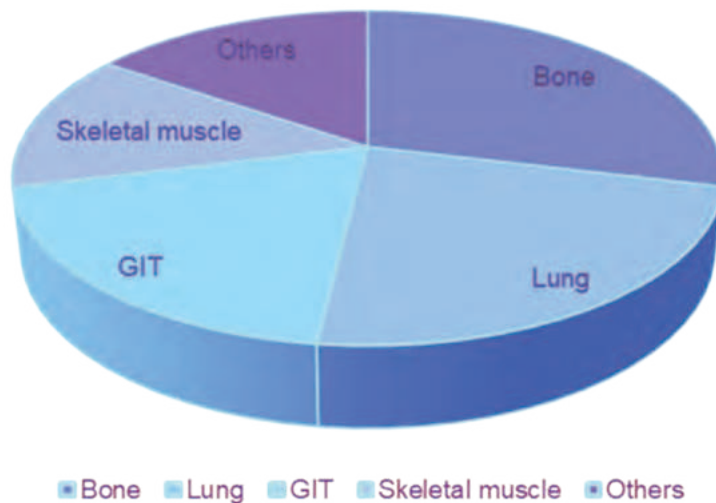


Figure-1: The distribution of extra nodal lymphoma demonstrating bone as the most commonly involved site followed by lung.

DISCUSSION

Extranodal lymphoma refers to the involvement of tissues or organs outside the primary lymphatic organs, such as lymph

nodes, spleen, thymus, and the pharyngeal lymphatic ring. Unlike nodal lymphoma, which primarily affects the lymph nodes, extranodal lymphoma can manifest in a variety of

extralymphatic sites throughout the body. It ranks as the seventh most prevalent malignancy in both genders combined. This form of lymphoma can occur in approximately 25–40% of cases, and nearly any organ may be affected, leading to a wide range of clinical presentations. Hodgkin disease (HD) typically exhibits less extranodal involvement compared to non-Hodgkin lymphoma (NHL), with HD involving adjacent organs in 15% and hematogenous spread in 5–10% (2).

The distinction between disseminated lymph nodal disease at an extranodal site and primary extranodal disease can be a complex task. Generally, primary extranodal lymphoma is associated with more favorable outcomes compared to cases where extranodal involvement is secondary to widespread nodal disease. The use of ¹⁸F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) or computed tomography (CT) is crucial in diagnosing and staging lymphoma, aiding in the identification of the disease's extent and location. Our study involved a review of lymphoma cases referred to the PET/CT division of NINMAS, providing an overview of their distribution across various extranodal sites within a one-year period.

Skeletal Lymphoma

Of all bone malignancies, malignant lymphoma accounts for 7% and extranodal lymphomas for 5% (3). The most common type of lymphoma infiltration in bone is diffuse large B-cell lymphoma. Bony involvement is uncommon in HL. Primary bony lymphoma less frequently occurs and is observed in the appendicular bone, usually affecting the femur, tibia, and humerus metadiaphysis. Oppositely, secondary osseous lymphoma usually affects the axial skeleton, including the ribs, face bones, pelvis, spine, and skull (4). Skeletal involvement is the most common extranodal involvement site in our study, comprising 28.8%.

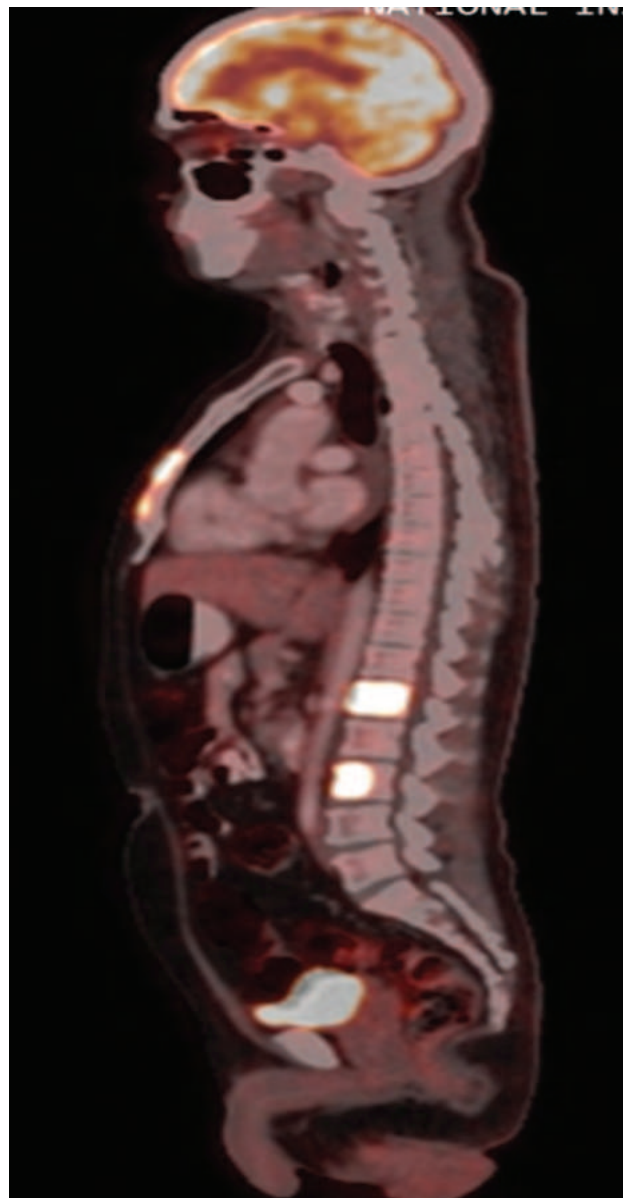


Figure 2: Sagittal section of ¹⁸F-FDG PET/CT scan of a 55 years old male lymphoma patient showing intense FDG avid lesions in sternum and vertebrae (yellow arrow) suggesting skeletal infiltration of lymphoma.

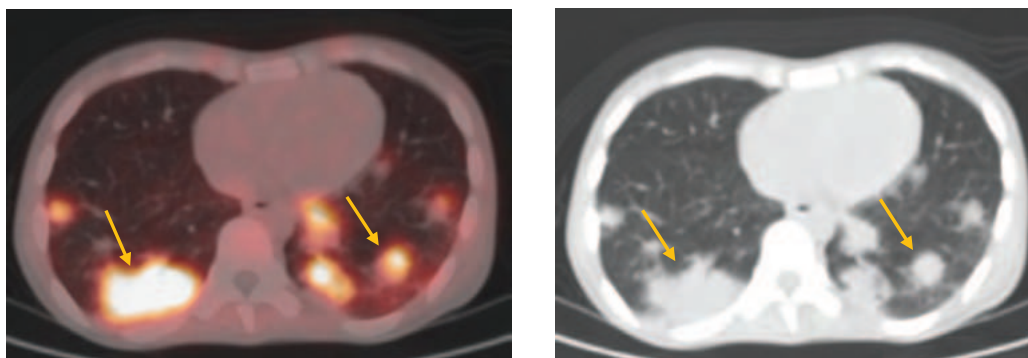


Figure 3: ¹⁸F-FDG PET/CT and CT axial image of a 48-year-old lymphoma patient showing multiple hypermetabolic lesions of variable sizes in both lungs (yellow arrow) suggesting pulmonary lymphoma.

Pulmonary Lymphoma

Pulmonary involvement of lymphoma can be primary or secondary. Secondary changes are much frequent. This study found 23.1% cases with pulmonary manifestations secondary to HL. Lung involvement more commonly occurs in HL having 85% cases with intrathoracic disease at presentation and usually associated with mediastinal nodal disease. (5) NHL can present with lung disease alone. Lymphoma-associated pulmonary parenchymal involvement is documented at rates of 3.7% in extranodal non-Hodgkin's lymphoma (NHL) and 12% in Hodgkin's disease (HD) (6,7).

Gastrointestinal tract (GIT)

The gastrointestinal tract (GIT) is a prevalent extranodal location for non-Hodgkin's lymphoma (NHL), accounting for about 10%–15% of all NHL cases and comprising 30%–40% of all extranodal lymphomas. Notably, primary GIT lymphoma (PGIL) is exceptionally rare, making up only 3%–4% of all gastrointestinal malignancies (8,9).

GI lymphoma is most common in the stomach, with primary NHL more common than Hodgkin's disease, and second most common in the small intestine. (10). Interestingly, nearly all GIT lymphomas of this study are of the DLBCL type and are assessed after surgery.

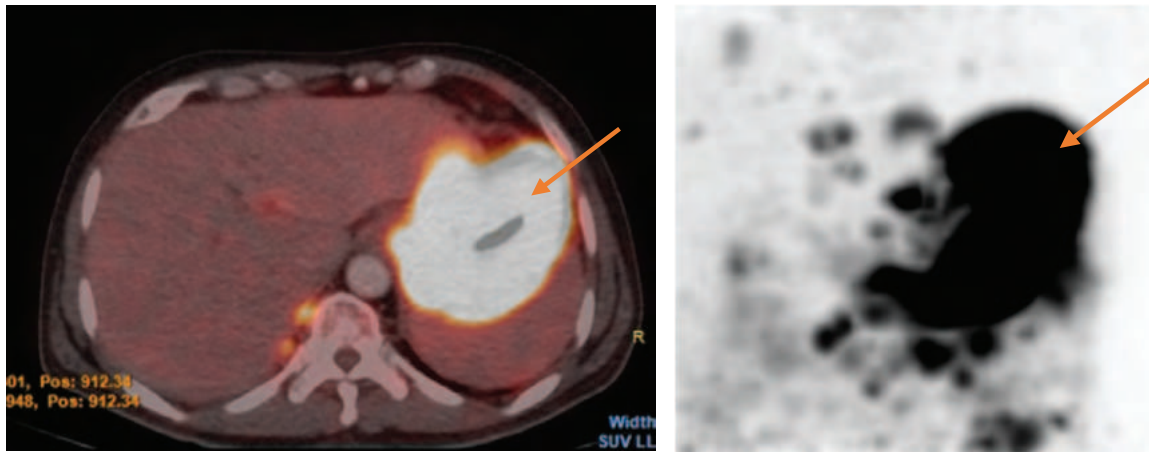


Figure 4: ¹⁸F-FDG PET/CT & CT axial image of a 52-year-old female patient with NHL showing intense FDG uptake in thickened walls of stomach (yellow arrow) suggesting stomach involvement of lymphoma.

Skeletal Muscle

There is no lymphoid tissue present in healthy skeletal muscle. Skeletal muscle lymphoma is less common in HL cases, comprising 0.3%, compared to non-Hodgkin's disease

(1.3%) (11) and is the 4th most common extranodal site in this study, while PET/CT scans are crucial for treatment planning (12). Figure 5 shows skeletal muscle involvement secondary to HL (Figure 5).

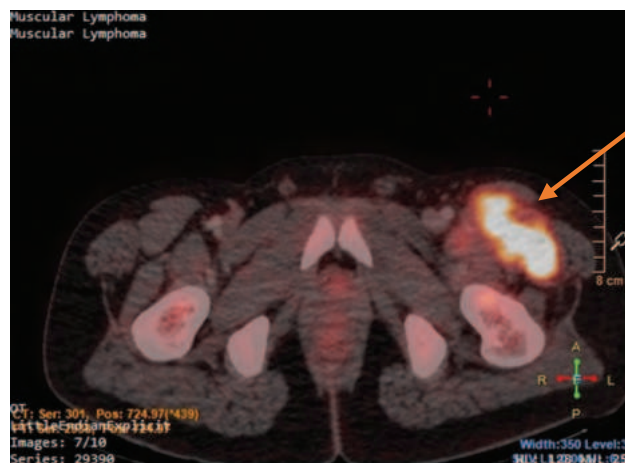


Figure 5: Axial image of ¹⁸F-FDG PET/CT scan showing hypermetabolic area in left iliopsoas muscle (yellow arrow) in a patient of HL representing skeletal muscle involvement.

Others

In the current analysis 15.4% cases comprise in other groups involving spleen, liver, CNS and some extremely rare sites like skin, breast, uterus and kidneys.

Spleen

Splenic involvement in HD represents one-third of all HL and is considered as nodal disease but it is regarded as an extranodal site in case of NHL with 30-40% presentation (13). Splenic lymphoma can be primary or secondary, with predominant involvement. 18F FDG PET/CT scans may show focal or diffuse presentation, with secondary involvement potentially linked to nodal infiltration (14). Figure 6 (a) shows splenomegaly with diffuse intense FDG uptake in a HL patient which resolved completely after chemotherapy.

Liver

This study found few cases of secondary hepatic involvement from lymphoma, primarily NHL type, and rare secondary involvement, presenting as hepatomegaly or nodular lesions. (Figure 6 b).

Central Nervous System (CNS)

CNS lymphoma is a rare, aggressive disease affecting the brain, meninges, spinal cord, and orbit, with primary lesions occurring in 93% of cases. Usually, metastatic CNS lymphomas are Diffuse large B cell type as well as Burkitt type of lymphoma. Figure 6 (c) shows left temporal lobe involvement secondary to DLBCL of neck nodes, suggested by PET/CT scan. The patient expired within three months of the study.

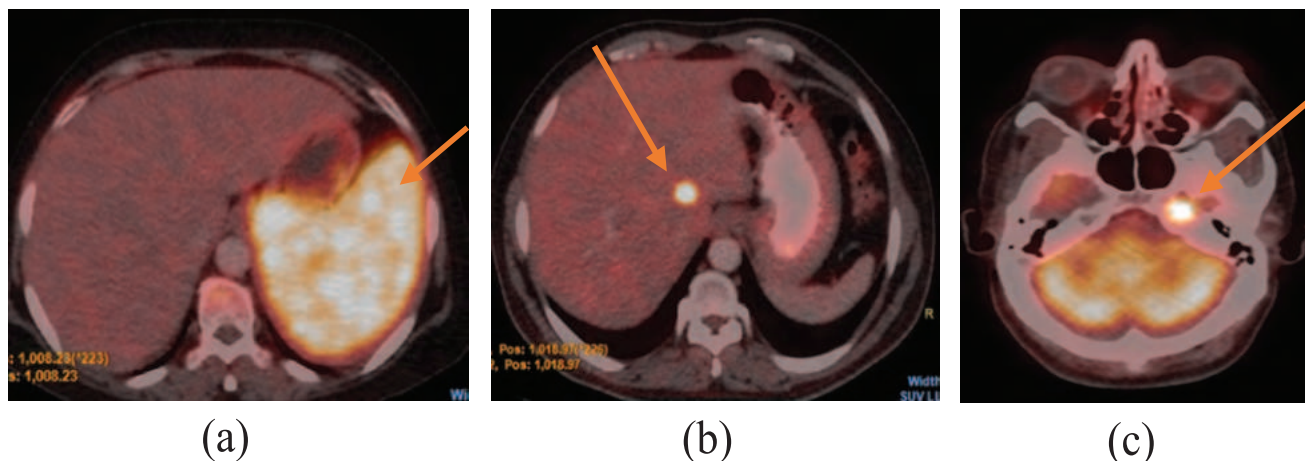


Figure 6: ^{18}F -FDG PET/CT & CT axial image of abdomen showing intense FDG uptake (yellow arrow) in spleen secondary to NHL (a), focal FDG avid lesion in right lobe of liver which is due to hepatic infiltration of lymphoma (b) and axial section of skull showing focal intense FDG avid area in left temporal lobe of brain suggesting CNS involvement from DLBCL of neck node (c).

Skin

Cutaneous lymphomas, primarily NHL-type primary cutaneous lymphoma (PCL), are rare and common in the mantle cell subtype, with over 45 cases reported by Tuknayati et al (18). 18F-FDG PET/CT scans are very useful for staging and to see therapy responses in PCL and also mantle cell lymphoma (17, 19). The case in Figure 7 (a) was suspected as metastatic cutaneous lymphoma associated with multiple hypermetabolic abdominal LNs and pulmonary nodules, which was histopathologically proven later as secondary mantle cell lymphoma of the skin.

Breast

Breast lymphomas, both primary and secondary, are uncommon. Less than 1% of all breast cancers and less than 2% of all extranodal non-Hodgkin lymphomas are breast lymphomas (20). The most frequent kind of breast metastasis (17%) is secondary lymphoma (21). The hypermetabolic lesion in the right breast shown in Figure 7 (b) was suggested as metastatic lymphoma or a second primary lesion, as both primary and secondary breast lymphoma often exhibit imaging characteristics that resemble those of primary breast carcinoma (21). Histopathology of the breast lesion proved it to be secondary breast lymphoma from the NHL.

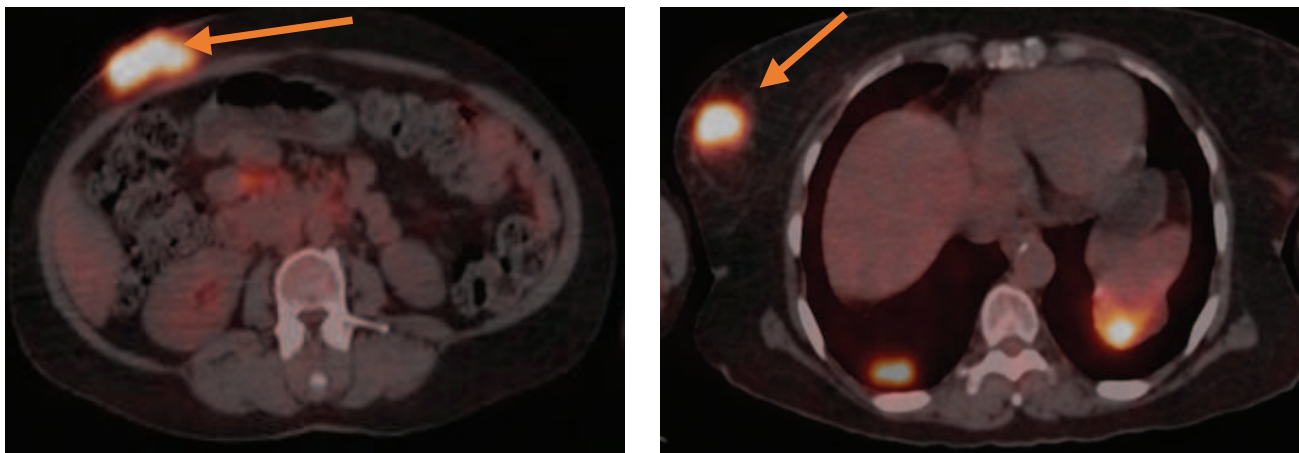


Figure 7: Axial image of ¹⁸F-FDG PET/CT showing hypermetabolic lesion (a) in right side of anterior abdominal wall and (b) in right breast (yellow arrow) representing secondary mantle cell lymphoma of skin and breast involvement from NHL respectively which were proven histopathologically.

Uterus

Primary lymphomas that originate in the female genital tract make up a small proportion, ranging from 0.2% to 1.1%, of all extranodal lymphomas. Most cases of uterine lymphoma are linked to the secondary spread of the disease (22). The ¹⁸F-FDG PET/CT scan of a patient with non-Hodgkin's lymphoma (NHL) indicated a hypermetabolic lesion in the uterine body, accompanied by bony involvement (Figure 8a). Subsequent to chemotherapy, a follow-up PET/CT scan revealed complete regression of the lesion.

Kidney

The kidney is not a lymphoid organ, so renal parenchyma

involvement is a secondary occurrence, either through direct extension or hematogenous spread in disseminated disease cases (23). Primary renal non-Hodgkin's lymphoma is a rare condition, characterized by renal enlargement and deterioration, accounting for less than 1% of all lymphomas. (24). Multiple intense hypermetabolic soft tissue density masses involving both kidneys were found in an ¹⁸F-FDG PET/CT scan of a DLBCL patient with associated FDG-avid pulmonary nodules, skeletal lesions, and retroperitoneal involvement (Figure 8 b). A renal biopsy was done to differentiate between secondary lymphoma and renal cell carcinoma, revealing lymphoma infiltration.

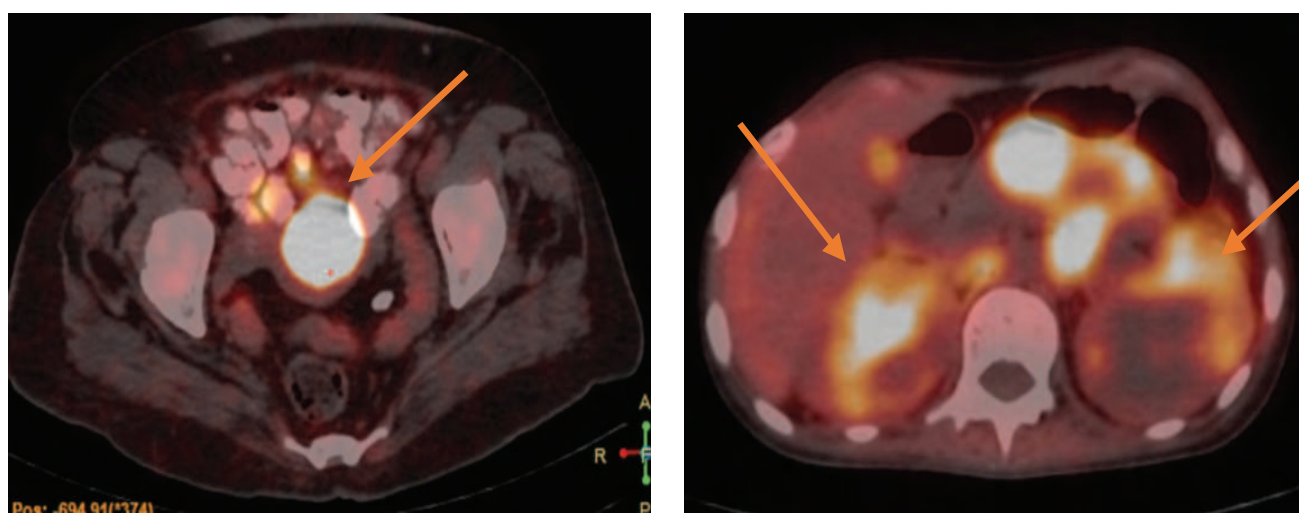


Figure 8: Axial image of ¹⁸F-FDG PET/CT showing hypermetabolic lesion (yellow arrow) involving (a) the body of uterus and (b) both kidneys suggesting uterine and bilateral renal lymphoma respectively.

CONCLUSION

The study highlights the importance of 18F-FDG PET/CT scans in identifying and assessing extranodal lymphomas, with the bone being the most affected site. This imaging method helps suspect rare entities and confirms them through histopathological examination, facilitating early detection and diagnosis.

REFERENCES

- Kashyap, R., Mittal, B.R., Manohar, K., Harisankar, C.N.B., Bhattacharya, A., Singh, B., Malhotra, P. and Varma, S., 2011. Extranodal manifestations of lymphoma on [18F] FDG-PET/CT: a pictorial essay. *Cancer Imaging*, 11(1), p.166.
- Parra, C., Tomich, G., Quaranta, A., Staffieri, R. and Villavicencio, R., 2012. PET/CT of extranodal involvement in lymphoma. *Imágenes*, 1, p.39.
- Fletcher C, Unni K, Mertens F. Lyon, France: International Agency for Research on Cancer; 2002. Pathology and genetics of tumours of soft tissue and bone: World Health Organization classification of tumours; pp. p. 306–308.
- Lim, C.Y. and Ong, K.O., 2013. Imaging of musculoskeletal lymphoma. *Cancer imaging*, 13(4), p.448.
- Angirish, B., Sanghavi, P. and Jankharia, B., 2020. Pulmonary manifestations of lymphoma: A pictorial essay. *Lung India: Official Organ of Indian Chest Society*, 37(3), p.263.
- Fujimoto, Y., Nomura, K., Shimizu, D., Okuda, T., Yoshida, N., Matsumoto, Y., Taki, T., Horiike, S. and Taniwaki, M., 2006. Pulmonary relapse of non-Hodgkin's lymphoma in bilateral upper lobes. *Internal Medicine*, 45(16), pp.971-973.
- Lewis, E.R., Caskey, C.I. and Fishman, E.K., 1991. Lymphoma of the lung: CT findings in 31 patients. *AJR. American journal of roentgenology*, 156(4), pp.711-714.
- Bautista-Quach, M.A., Ake, C.D., Chen, M. and Wang, J., 2012. Gastrointestinal lymphomas: Morphology, immunophenotype and molecular features. *Journal of gastrointestinal oncology*, 3(3), p.209.
- Ghimire, P., Wu, G.Y. and Zhu, L., 2011. Primary gastrointestinal lymphoma. *World journal of gastroenterology: WJG*, 17(6), p.697.
- Suresh, B., Asati, V., Lakshmaiah, K.C., Babu, G., Lokanatha, D., Jacob, L.A., Lokesh, K.N., Rudresh, A.H., Rajeev, L.K., Smitha, S. and Anand, A., 2019. Primary gastrointestinal diffuse large B-cell lymphoma: A prospective study from South India. *South Asian journal of cancer*, 8(01), pp.57-59.
- Parra C, Tomich G, Quaranta A, Staffieri R, Villavicencio R. PET/CT of extranodal involvement in lymphoma. *Imágenes*. 2012; 1:39. 2. Binici DN, Karaman A, Timur O, Tosun Tasar P, San AV. Primary skeletal muscle lymphoma: a case report. *Molecular and Clinical Oncology*. 2018 Jan 1;8(1):80-2
- Mandal, T. ., Mutsuddy, P. ., Ahmed, M. ., Nath, K. K. ., Siddique, A. B. ., & Begum, S. M. . (2023). Rare Presentations of Muscular Infiltrations in Classical Hodgkin's Lymphoma-A Case Series. *Bangladesh Journal of Nuclear Medicine*, 25(2), 143–146.
- Paes, F.M., Kalkanis, D.G., Sideras, P.A. and Serafini, A.N., 2010. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. *Radiographics*, 30(1), pp.269-291.
- Saboo, S.S., Krajewski, K.M., O'regan, K.N., Giardino, A., Brown, J.R., Ramaiya, N. and Jagannathan, J.P., 2012. Spleen in haematological malignancies: spectrum of imaging findings. *The British journal of radiology*, 85(1009), pp.81-92.
- Alves, A.M.A., Torres, U.S., Velloni, F.G., Ribeiro, B.J., Tiferes, D.A. and D'Ippolito, G., 2019. The many faces of primary and secondary hepatic lymphoma: imaging manifestations and diagnostic approach. *Radiologia brasileira*, 52, pp.325-330.
- Lynch, D.T., Koya, S., Acharya, U. and Kumar, A., 2022. Mantle cell lymphoma. In *StatPearls [Internet]*. StatPearls Publishing.
- Qiu, L., Tu, G., Li, J. and Chen, Y., 2017. The role of 18F-FDG PET and PET/CT in the evaluation of primary cutaneous lymphoma. *Nuclear Medicine Communications*, 38(2), pp.106-116.
- Tuknayat, A., Kundu, R., Kucheria, M. and Thami, G.P., 2020. Secondary Cutaneous Mantle Cell Lymphoma. *The Journal of Clinical and Aesthetic Dermatology*, 13(5), p.31.
- Albano, D., Treglia, G., Gazzilli, M., Cerudelli, E., Giubbini, R. and Bertagna, F., 2020. 18F-FDG PET or PET/CT in mantle cell lymphoma. *Clinical Lymphoma Myeloma and Leukemia*, 20(7), pp.422-430.
- Vizcaino, I., Torregrosa, A., Higuera, V., Morote, V., Cremades, A., Torres, V., Olmos, S. and Molins, C., 2001. Metastasis to the breast from extramammary malignancies: a report of four cases and a review of literature. *European radiology*, 11, pp.1659-1665.
- Raj, S.D., Shurafa, M., Shah, Z., Raj, K.M., Fishman, M.D. and Dialani, V.M., 2019. Primary and secondary breast lymphoma: clinical, pathologic, and multimodality imaging review. *Radiographics*, 39(3), pp.610-625.
- Ensor, A.M., Sanchez, C.G., Ensor, J.E. and Anand, K., 2021. Primary diffuse large B-cell lymphoma of the uterus: A SEER database analysis. *Medicine*, 100(40).
- Poitou-Verkinder AL, Francois A, Drieux F, et al. The spectrum of kidney pathology in B-cell chronic lymphocytic leukemia / small lymphocytic lymphoma: a 25-year multicenter experience. *PLoS One*. 2015;10:e0119156.
- Pelin Ozcan Kara,et.al, "A Rare Case of Bilateral Renal Lymphoma on FDG PET/CT Imaging". *ARC Journal of Radiology and Medical Imaging*. 2017;2(2):14-16.