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RESEARCH ARTICLE

An Unusual Presentation of Primary Extra Nodal Non-Hodgkin Lymphoma

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ABSTRACT

Patients presented with soft tissue lesions without any β symptoms can be a case of Primary extranodal Non- non-Hodgkins lymphoma. According to the World Health Organization classification system, there are two types of Lymphoma with various sub-types of Hodgkins Lymphoma and Non-Hodgkin Lymphoma are classified to assess the disease burden Progression and metastasis Imaging modalities are helpful. Commonest site involvement in Non-Hodgkin Lymphoma in the gastrointestinal tract (44%) followed by Head and Neck and may Involve bone (8%) and Central Nervous System 5%. Diffuse large β-Cell Lymphoma is the most common subtype representing 30%-35% of all Non-Hodgkin Lymphoma Cases. Oral and Para oral sites were involved in 2.5% of the cases. A 27-year-old Male noticed a swelling in the flank which was progressively Increasing in size one year back later it was associated with pain which reduced mobility and pain was increased during walking. Due to the advancement of diagnostic techniques, it is easy to get the radiological picture and correlation with clinical presentation and pathological reports, but these facilities are not available at various centers. Usually, patients are present in very advanced stages because of a lack of awareness about the disease, and how to proceed for diagnosis and treatment resulting in poor outcomes for these patients. This presentation and clinical funding are rare in the case of Lymphoma. This case report allows us to think of another diagnosis rather than usual.

Introduction

According to World Health Organization classification system there are two types of Lymphoma with various sub-types Hodgkin Lymphoma and Non-Hodgkin Lymphoma. Both types of Lymphoma present with different clinical features, and they are helpful in the determination of these two types and subtypes. To assess the disease burden, Progression, and metastasis imaging modalities are helpful. Burkitt's Lymphoma diffuse large β-Cell Lymphoma (DLBCL) and Natural Killer NK/T Cell Lymphoma are aggressive types of Lymphoma and they show destructive patterns of the disease.1 Non-Hodgkin Lymphoma is usually present as extra nodal disease (10%-20%) Commonest site involvement in Non-Hodgkin Lymphoma in the gastrointestinal tract (44%) followed by Head and Neck and may Involve bone (8%) and Central Nervous System 5%. 2 Diffuse large β-Cell Lymphoma is the most common subtype representing 30%-35% of all Non-Hodgkin Lymphoma Cases. 3 Oral and Para oral sites were involved in 2.5% of the cases. 4 Primary extranodal lymphoma is defined as the primary involvement of Non-Hodgkin Lymphoma in any extra nodal tissue or organs. Only a few case reports are available in literature 2,3,4 only 0.5% of extra nodal lymphomas constitute to primary skeletal lymphoma usually found β-Cell or Non- Hodgkin Lymphoma. Clinical features may mimic soft tissue sarcoma or other sarcomas.1

Aim and Objective

The aim of this study is to detect an unusual presentation of primary extra nodal Non- non-Hodgkin lymphoma. The primary objective of this case study is to find patients with soft tissue lesions without any β symptoms, which can be a case of primary extra nodal Non-Hodgkin Lymphoma.

Case Report

A 27-year-old Male noticed a swelling in the flank which was progressively Increasing in size one year back, later it was associated with pain which reduced mobility and pain was increasing during walking. There was no history of fever, weight loss, or sweats. He consulted to local doctor and started symptomatic treatment. FNAC done on the same side showed necrotizing Lymphadenitis and reactive Lymphadenitis. He presented in our department where he was suggested for an Ultrasound biopsy which revealed Non- Hodgkin Lymphoma. The immunohistochemistry report showed CD 45, CD10, CD 20 Positive and the diagnosis was confirmed as Non-Hodgkin Lymphoma. USG's whole report shows Multiple well-defined variable-size hypoechoic nodular lesions in Bilateral Renal Parenchyma. The largest ≃ 2.6×2.1cm^2 on the (R) node at the upper rate and 2.6×4.7cm^2 in (L) Kidney at the lower rate. Localized collection≃20 cc within internal septation in the perihepatic region. Trace ascites present a necrotic parotid lymph node of 4.6×4.4 cm2 is noted.

Positron Emission Tomography Scan Report

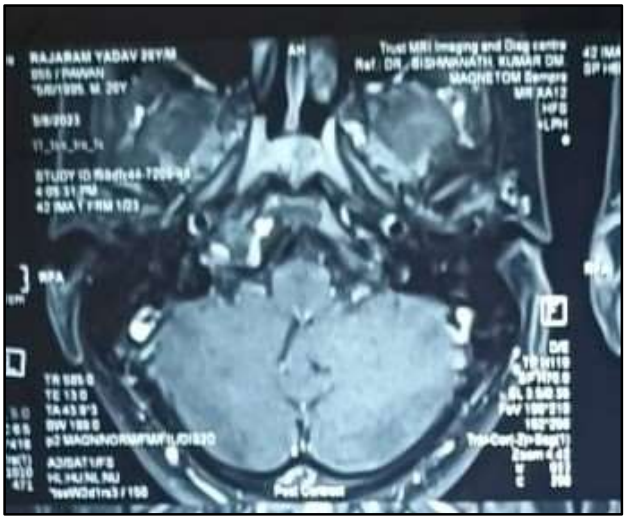

Figure 1 Section of CT scan showing tumor size.

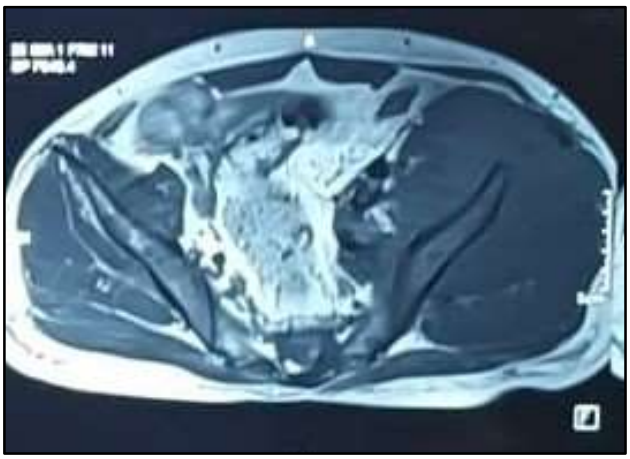

Figure 2 Section of CT scan showing tumor size.

MAGNETIC RESONANCE IMAGING BRAIN AND SPINE

- Varying degree of Dural thickening and enhancement is seen overlying both cerebral hemispheres, predominantly overlying the

parietal lobe and along the posterior fax. The lesion in the posterior falx is compressing/invading the posterior aspect of the superior sagittal sinuses.

• Large soft tissue component is seen superolateral quadrant of both orbits involving lacrimal glands as well.

• Altered signal intensity of lateral walls of both orbits are seen.

• Soft tissue component is also seen in the periorbital region and superficial subcutaneous tissue of the scalp overlying the left parietal region.

• Both cerebral hemispheres are normal in morphology and signal intensity on all pulse sequences.

• Altered marrow signal intensity lesion is seen involving the left iliac bone with large associated soft tissue mass measuring ~ 13.5 x 11.6 x7.4 cm sized seen involving the gluteus muscle as well as left ileo psoas muscle. There is an extension until the anterior aspect of the left sacroiliac joint. The lesion is hypointense on T1 and hyperintense on T2 Short Tau Inversion Recovery (STIR) and post-contrast showing moderate heterogeneous enhancement. The soft tissue thickening shows loss of fat plane with femoral and external iliac vessels however flow voids are maintained.

• Altered marrow signal intensity lesion with patchy enhancement in the left sacral ala around bilateral hip joints, proximal femurs, bilateral acetabulum, and right iliac bone. On STIR images patchy hyperintensity is also seen in a few lumbar vertebrae.

• Mild patchy enhancement is seen in the Cranio Vertebral Junction (CVJ).

• Multiple enlarged lymph nodes are seen on left side of the neck

• Multiple enlarged pre/paraaortic/aortocaval lymph nodes are seen.

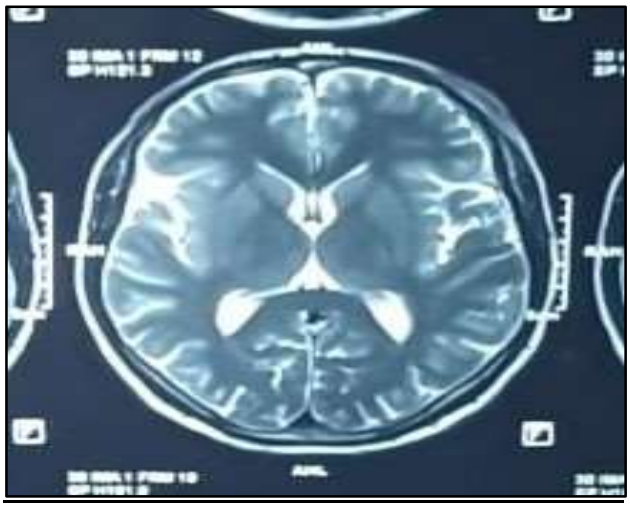

Figure 3. Section of CT scan showing tumor size.

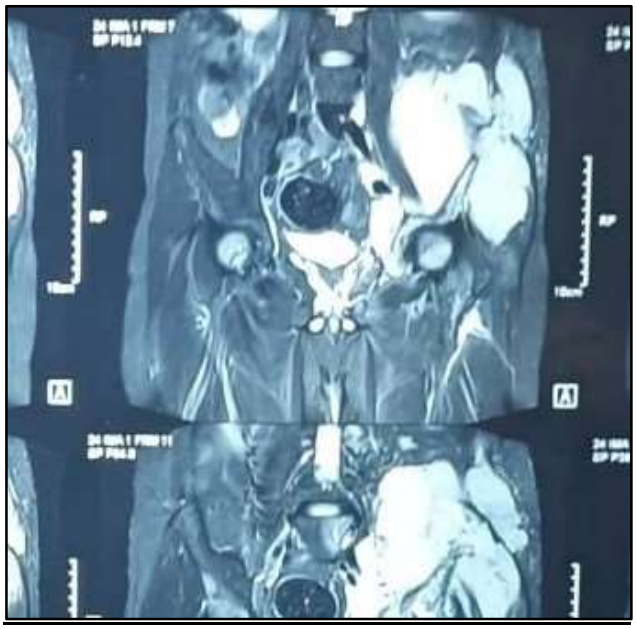

Figure 4 Section of CT scan showing tumor size.

FLUORODEOXYGLUCOSE WHOLE BODY POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY STUDY

Positron Emission Tomography-Computed Tomography Findings:

Brain: fluorodeoxyglucose (FDG) avid (SUV max 9.02) ill-defined hyperdense lesion seen along postero-superior aspect of falx cerebri on either side at parietal convexity.

Head and Neck: fluorodeoxyglucose (FDG) avid (SU max 9.02) ill-defined soft tissue density thickening seen in superolateral aspect of bilateral orbits. Soft tissue component is seen in

peri-orbital region & subcutaneous plane of scalp overlying the bilateral temporal region.

Thorax: Few mildly fluorodeoxyglucose (FDG) avid (SUV max 7.47) discrete & conglomerated lymph nodes seen at left infraclavicular location, larger one measures~15mm in size. Mildly FDG avid (SUV max 6.45) right axillary level I-III nodes seen, larger one measures~19mm in size. Few mildly FDG avid (SUV max 5.89) pre vascular nodes noted, larger one measures~16 mm in size. Mild bilateral (left>right) pleural effusion seen.

Abdomen-Pelvis: FDG avid (SUV max 11.37) soft tissue density lesion (? conglomerated lymph nodal mass) measuring ~4.4x6.0x6.8 (APxTRxCC) with central hypodensity seen in gastrohepatic space, inferiorly abutting body of pancreas with loss of fat plane with it.

FDG avid (SUV max 7.06) multiple other discrete left anterior diaphragmatic, bilateral retrocrural, bilateral paravertebral (dorsal), gastrohepatic, peripancreatic, aortocaval, pericaval, retrocaval, paramortic, presacral, left internal & external iliac and left inguinal nodes noted. Each kidney appears bulky & enlarged in size with lobulated contour. FDG avid (SUV max 15.47) multifocal lesions are seen in bilateral kidneys, the larger one measures 6.3x4.0 cm in the right kidney. Posteriorly lesion is abutting posterior renal fascia on both sides. Mildly FDG avid (SUV max 8.55) soft tissue density nodule ~20x10mm seen along the inferior aspect of posterior renal fascia on the left side. FDG avid (SUV max 8.68) soft tissue density nodular thickening seen along right lateral peritoneal reflection in pelvic cavity. Few mildly FDG avid (SUV max 3.53) omental nodules (larger one~13mm) and mild omental fat stranding noted. FDG avid (SUV max 4.96) ~20×12mm sized module seen in left paracolic gutter.

Musculo-Skeletal System: Intensely FDG avid (SUV max 20.95) lytic-destructive lesion with large soft tissue component seen involving left hemipelvis, left ala of the sacrum and left transverse process of L5. Soft tissue component measuring ~14.2x15.0x18.5 cm (APxTRxCC) seen involving left iliacus, left obturator internus & abuts left psoas muscles anteriorly and posteriorly lesion is involving left gluteal muscles. The superior extension is up to the level of L4 and inferiorly extends into the medial compartment of proximal left thigh. Supero-laterally lesion is involving left external & internal obliques muscles. FDG avid (SUV max 12.48) lytic-sclerotic lesions (few of them with soft tissue component) seen involving clivus, bilateral humeri, bilateral clavicle, bilateral scapulae, sternum, few bilateral ribs, multiple cervico-dorso-lumbar vertebrae (mild intraspinal extensions at DI2 & L3). Sacrum (mild extension into the sacral spinal canal), pelvis, and bilateral femoral. Focal FDG avid intramedullary lesions were seen in bilateral humeri and bilateral proximal femoral.

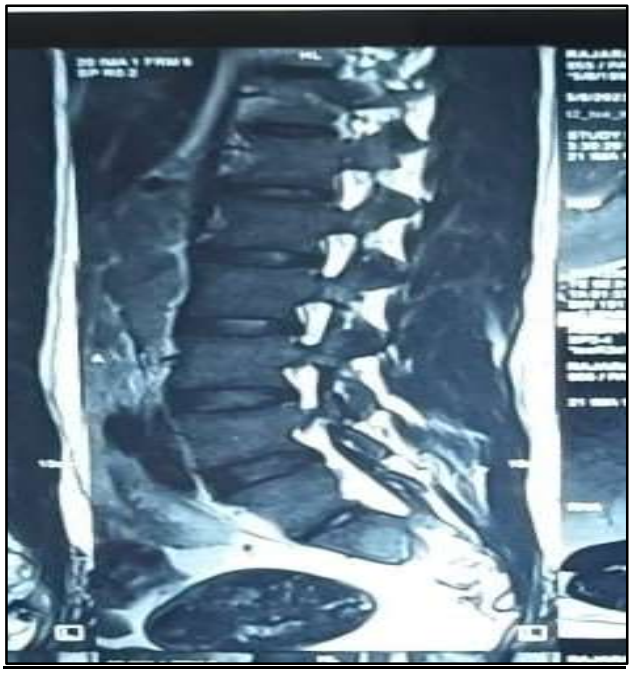

Figure 5 Section of CT scan showing tumor size.

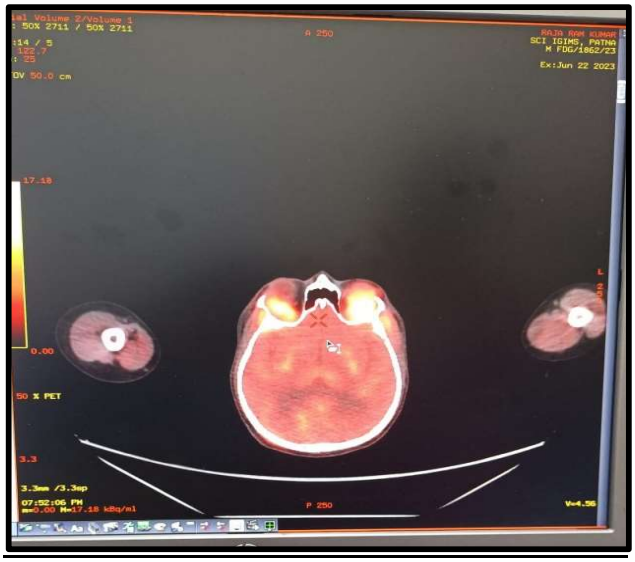

Figure 6 PET Scan of the Brain showing hyperdense lesion.

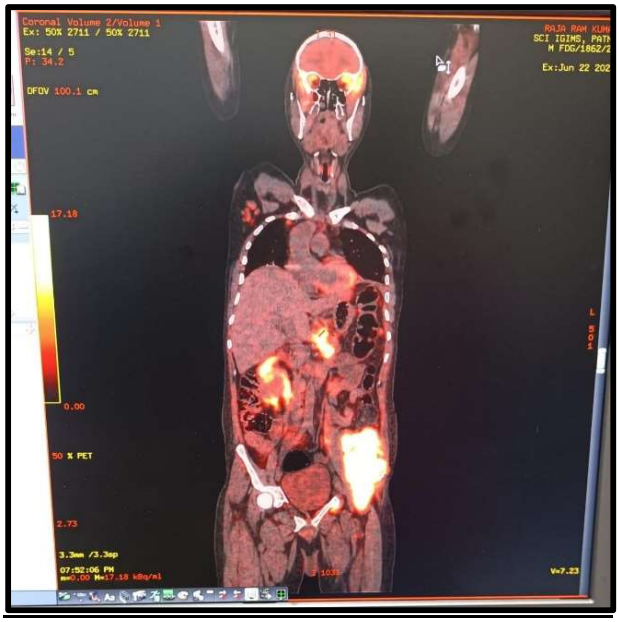

Figure 7 PET Scan showing Thorax and Abdomen Pelvis.

Figure 8 PET Scan of the Abdomen

Table 1 Type of antigens found on leukocytes with their respective results.

IHC Markers	Result
CD 45	Positive
CD 3	Negative
CD 20	Positive
CD 10	Positive
CD 5	Negative
CD 30	Negative

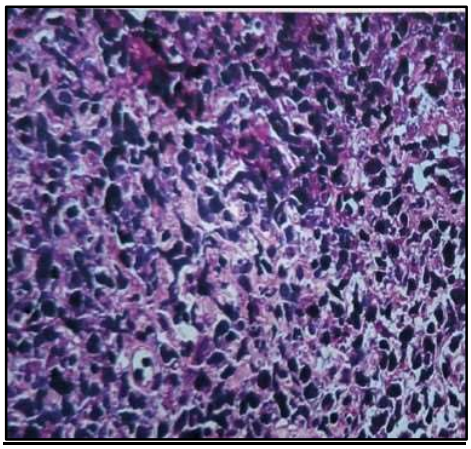

Figure 9 Histopathology of lymphoma cell

Table 2 IHC markers and their result

IHC Markers	Result
Bcl 2	Positive
Bcl 6	Positive
MUM 1	Negative
Ki-67	80%

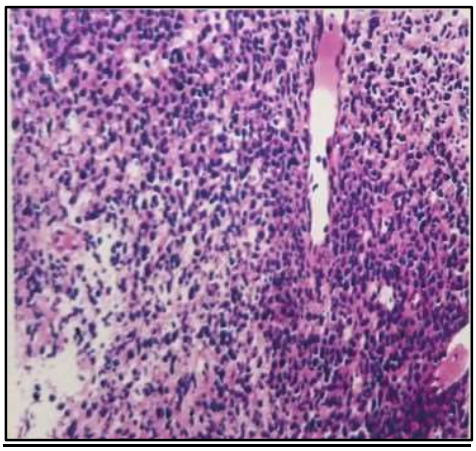

Figure 10 Histopathology of CD 20

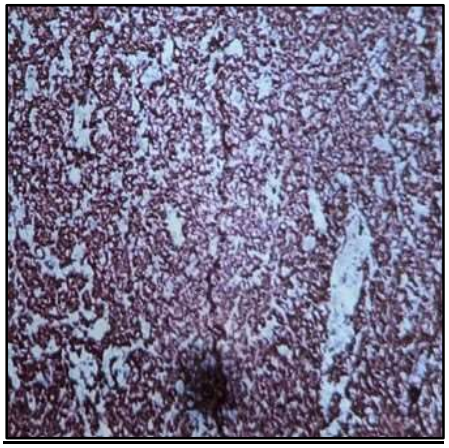

Figure 11 Histopathology of CD 20

Discussion

Non-Hodgkin Lymphoma is a diverse group of Lymphoid Neoplasm which collectively ranked 5th in the incidence and mortality. The prevalence of non-Hodgkin lymphoma has been increasing during the past two decades. 5 The majority of non-Hodgkin lymphoma is originated from β-Cell origin. 2 and more than 90% of the patients have expressed CD20 antigen. 6 Bony involvement is not an uncommon presentation in Lymphoma, but the involvement of the Cranial Vault is extremely rare. 7 A systematic review of 36 articles by EL Ashi with chief complaint of subcutaneous scalp mass. There were various histological subtypes, but DLBCL was the most common type. 8 The diagnosis of extranodal Non-Hodgkin Lymphoma is challenging when there is enhancement of the Renal area, bones, orbits, and para orbital area. Uncommon location of presentation found in 1%-2% of extranodal lymphoma. 3 Common presentations include pain due to bony inducement and later presented with neurological symptoms. A small percentage of patients presented with β-symptoms. 3,9 For diagnosis and confirmation of diagnosis of extranodal lymphoma CT scan, MRI, and PET-CT are advisable. 3

PET-CT is considered essential imaging because large β-Cell Lymphoma has a high affinity for 18F FD9. 10 Selta and Co-workers reported a case of primary cranial vault Lymphoma diagnosed on MRI. 11 Halem reported a case of 79 years old man with (L) triceps involvement. 12 On 221 patients with Head and Neck Lymphoma different sites of organs of Non-Hodgkin Lymphoma with involvement of Lymph Nodes, Tonsils, Major Salivary Gland, Sino nasal tract, and hypopharynx. 13

Scally reported a case of a 51-year-old female presenting with pain in her waist and Left Hip which was misdiagnosed as sciatica. CT Scan showed increased density of buttlock mass and finally, the diagnosis came as β-cell Non-Hodgkin Lymphoma on buttock mass biopsy.14 Utkan reported the case of a 68-year-old male with a histology of swelling and pain in the right buttock. Histopathological examination showed tuberculosis listeriosis Hodgkin's disease.15 Katsura also reported a 52-year-old woman with pain in her left hip. CT scan showed an early-stage mass in the Left gluteus muscle. Finally diagnosed as diffused large β cell Lymphoma after biopsy 16. Skeletal muscle lymphoma generally arises from extremities, more often lower limbs and thighs since these areas are more exposed to injuries 17. Mostly primary extranodal Non-Hodgkins Lymphoma is found in diffused large cell β lymphoma. Many of these are low-grade with good prognosis. Some skeletal lymphoma originates from T cell Lymphocytes and shows poor prognosis 18,19. Radiological investigations like CT scans and MRI are not able to differentiate between soft tissue sarcoma and lymphoma but MRI seems to be superior for the evaluation of soft tissue tumors 20. Definitive diagnosis of primary extra nodal Non-Hodgkin Lymphoma can be made after biopsy and Immunohistochemistry examination recently National Comprehensive Cancer Network (NCCN) guidelines have recommended PET Scan for staging and response evaluation and prognosis of lymphoma 21. Sensitivity and specificality of PET Scan for extra nodal lymphoma were 88% to 97% and 100% respectively 22,23.

TREATMENT OPTIONS AND CHALLENGES

Standard of care for systematic involvement of DLBCL with CNS involvement, chemotherapy with CNS-directed treatment, High dose methotrexate, Procarbazine, Rituximab, and vincristine (RMPV) is expected to have some effect in systemic lymphoma. 24 97% complete response rate shown by previous studies of Non-Hodgkin Lymphoma using Rituximab. 25 Wright et al 2019 published an article on retrospective analysis of 80 patients with synchronous CNS and systematic DLBCL from the UK and Australia who have the ability to control CNS disease. 26 Directly related with survival outcome. High dose of Methotrexate or cytarabine in CNS involvement Non-Hodgkin Lymphoma. Rituximab a chimeric anti-20 monoclonal antibody is the basic drug of targeted treatment of DLBCL showing survival benefits after addition to chemotherapy other target agents for treatment like Obinutuzumab, Ibrutinib, Lenalidomide, and Bortezomib.

None of these agents showed superior efficacy against Non-Hodgkin Lymphoma in comparison to Rituximab. 27 The Challenge is to confirm the diagnosis and early stage of treatment because of the complicated picture of symptoms and presentation most of the time disease progresses to an advanced stage and leads to poor survival outcomes. Due to the advancement of diagnostic

techniques, it is easy to get the radiological picture and correlation with clinical presentation and pathological reports. But these facilities are not available at various centers. Usually, patients present in very advanced stages because of a lack of awareness about the disease, and how to proceed with diagnosis and treatment resulting in poor outcomes with these patients.

Conclusion

Tumors originating from buttock or other soft tissues are commonly diagnosed as soft tissue sarcoma, for such types of cases Primary Extra Nodal Non-Hodgkins Lymphoma should be considered as a differential diagnosis. Early diagnosis and treatment can be offered with curative treatment and improve the prognosis of the disease.

Conflict of interest

None of the authors have any conflict of interest to disclose with regard to the content of this manuscript.

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References

1. Weber AL, Rahemtullah A, Ferry JA. Hodgkin and non-Hodgkin lymphoma of the head and neck: Clinical, pathologic, and imaging evaluation. Neuroimaging Clin N Am. 2003;13(3):371-392. doi: 10.1016/s1052-5149(03)00039-x

2. Moussaly E, Nazha B, Zaarour M, Atallah JP. Primary non-Hodgkin's lymphoma of the spine: a case report and literature review. World J Oncol. 2015;6(5):459-463. doi: 10.14740/wjon947w.

3. Popescu M, Popov V, Popescu G, Dobrea C, Sandu A, Grigorean VT, Strambu V. Spinal involvement with spinal cord compression syndrome in hematological diseases. Rom J Morphol Embryol. 2012;53(4):1069-72.

4. Essadi I, Ismaili N, Tazi E, Elmajjaoul S, Saidi A, Ichou M, Errihani H. Primary lymphoma of the head and neck: two case reports and review of the literature Cases J. 2008;1(1):426. doi: 10.1186/1757-1626-1-426.

5. Chiu BC, Weisenburger DD. An update of the epidemiology of non- Hodgkin's lymphoma Clin Lymphoma. 2003;4(3):161-8. doi: 10.3816/clm.2003.n.025.

6. DeVita VT, Hellman S, Rosenberg SA. Cancer: Principles and practice of Oncology. Wolters Kluwer; 2001;11:1671-1707

7. Nasirmohtaram S, Mesbah A, Mazloom F. An extremely rare presentation of non-Hodgkin lymphoma in the head and neck: a case report. Egypt J Otolaryngol 2022;38:110. doi: 10.1186/s43163-022-00281-3

8. El Asri AC, Akhaddar A, Baallal H, Boulahroud O, Mandour C, Chahdi H, Mikdame M, Gazzaz M, El Mostarchid B, Boucetta M. Primary lymphoma of cranial vault: case report and a systematic review of the literature. Acta Neurochir (Wien). 2012;154(2):257-265. doi: 10.1007/s00701-011-1124-0.

9. Ciftdemir M, Kaya M, Selcuk E, Yalniz E. Tumors of the spine. World J Orthop. 2016;7(2):109-16. doi: 10.5312/wjo.v7.i2.109.

10. Hashi S, Goodwin CR, Ahmed AK, Sciubba DM. Management of extranodal lymphoma of the spine: a study of 30 patients. CNS Oncol. 2018 ;7(2):CNS11. doi: 10.2217/cns-2017-0033.

11. Setta K, Beppu T, Sato Y, Saura H, Nomura J, Sugai T, Ogasawara K. Primary cranial vault lymphoma extending between subcutaneous tissue and brain parenchyma without skull destruction after mild head trauma: a case report and literature review. Case Rep Oncol. 2021;14(2):1118-1123. doi: 10.1159/000516272.

12. Hatem J, Bogusz AM. An unusual case of extranodal diffuse large B-cell lymphoma infiltrating skeletal muscle: a case report and review of the literature. Case Rep Pathol 2016 ;2016:9104839. doi: 10.1155/2016/9104839.

13. Storck K, Brandstetter M, Keller U, Knopf A. Clinical presentation and characteristics of lymphoma in the head and neck region. Head Face Med. 2019;15(1):1. doi: 10.1186/s13005-018-0186-0

14. Scally J, Garrett A. Primary extranodal lymphoma in muscle. Br J Radiol. 1989;62(733):81. doi: 10.1259/0007-1285-62-733-81.

15. Utkan G, Buyukcelik A, Yalcin B, Tek I, Doruk H, Dincol D, Erekul S, Baykara M. Extranodal Hodgkin disease presenting with gluteal mass and hypercalcemia. South Med J. 2006;99(10):1149-50. doi: 10.1097/01.smj.0000240720.24001.77.

16. Katsura M, Nishina H, Shigemori Y, Nakanishi T. Extranodal lymphoma originating in the gluteal muscle with adjacent bone involvement and mimicking a soft tissue sarcoma. Int J Surg Case Rep. 2015;7C:161-4. doi: 10.1016/j.ijscr.2015.01.024.

17. Faraji-Goodarzi M. Sepsis after non-perforated acute appendicitis. Clin Case Rep. 2019;7(3):520-523. doi: 10.1002/ccr3.2030.

18. Masaoka S, Fu T. Malignant lymphoma in skeletal muscle with rhabdomyolysis: a report of two cases. J Orthop Sci. 2002;7(6):688-93. doi: 10.1007/s007760200122

19. Laffosse JM, Gomez-Brouchet A, Molinier F, Chiron P, Roché H, Puget J. A case of malignant primary non-Hodgkin's lymphoma in skeletal muscle treated by exclusive chemotherapy. Joint

Bone Spine. 2009;76(1):86-8. doi: 10.1016/j.jbspin.2008.02.022.

20. Yamada S, Shikata A, Yamazaki M, Makoto O, Kikuo M, Yoichi W, Akio K. Primary non-Hodgkin's lymphoma in the dorsolumbar muscles. Int J Clin Oncol. 1999;4(1):45-47.doi:10.1007/s101470050023

21. Khiewvan B, Macapinlac HA, Lev D, McCutcheon IE, Slopis JM, Al Sannaa G, Wei W, Chuang HH. The value of ^{18}F-FDG PET/CT in the management of malignant peripheral nerve sheath tumors. Eur J Nucl Med Mol Imaging. 2014;41(9):1756-66. doi: 10.1007/s00259-014-2756-0.

22. Schaefer NG, Hany TF, Taverna C, Seifert B, Stumpe KD, von Schulthess GK, Goerres GW. Non-Hodgkin lymphoma and Hodgkin disease: coregistered FDG PET and CT at staging and restaging--do we need contrast-enhanced CT? Radiology. 2004;232(3):823-9. doi: 10.1148/radiol.2323030985.

23. Wang X. PET/CT: appropriate application in lymphoma. Chin Clin Oncol. 2015;4(1):4. doi: 10.3978/j.issn.2304-3865.2014.11.05.

24. Shah GD, Yahalom J, Correa DD, Lai RK, Raizer JJ, Schiff D, LaRocca R, Grant B, DeAngelis LM, Abrey LE. Combined immunochemotherapy with reduced whole-brain radiotherapy for newly diagnosed primary CNS lymphoma. J Clin Oncol. 2007;25(30):4730-5. doi: 10.1200/JCO.2007.12.5062.

25. Carruthers MN, Topazian MD, Khosroshahi A, Witzig TE, Wallace ZS, Hart PA, Deshpande V, Smyrk TC, Chari S, Stone JH. Rituximab for IgG4-related disease: a prospective, open-label trial. Ann Rheum Dis. 2015;74(6):1171-1177. doi: 10.1136/annrheumdis-2014-206605.

26. Wight JC, Yue M, Keane C, Johnston A, Linton K, Chin C, Wai SH, Talaulikar D, Gasiorowski R, Cheah CY, Gregory GP, Dickinson M, Minson A, Coombes C, Ku M, Lam S, Hawkes EA. Outcomes of synchronous systemic and central nervous system (CNS) involvement of diffuse large B-cell lymphoma are dictated by the CNS disease: a collaborative study of the Australasian Lymphoma Alliance. Br J Haematol. 2019;187(2):174-184. doi: 10.1111/bjh.16064.

27. Wang L, Qin W, Huo YJ, Li X, Shi Q, Rasko JEJ, Janin A, Zhao WL. Advances in targeted therapy for malignant lymphoma. Signal Transduct Target Ther. 2020;5(1):15. doi: 10.1038/s41392-020-0113-2.