PICTORIAL REVIEW

INTRIGUING LYMPHOMA PATTERNS: A RADIOLOGIST'S CHALLENGE

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ABSTRACT

Non-Hodgkin lymphoma (NHL) are a diverse group of tumors of lymphocytes, originating in lymphnodes and sometime from sites other than primary lymphatic organs called extra nodal disease . There is a surge seen in the cases of extra nodal Non-Hodgkin lymphoma, attributed to many factors namely HIV, use of immunos uppressant medications as well as indolent viral infections. There are many subcategories and histological subtypes that are the most important predictor of the outcome. Some of the Non-Hodgkin lymphoma, have site specific predilection as well. Extra nodal Non-Hodgkin lymphoma can present with diverse manifestations and attimes it is difficult to differentiate from other organ related pathologies. That is why thorough knowledge of various imaging presentations of extra nodal Non-Hodgkin lymphoma is crucial. The purpose of this article is to look at a few chosen cases of Non-Hodgkin lymphoma and observe different visceral involvements in those patients, and to find out how lymphomas affect organs other than lymphnodes.

Keywords: Non-Hodgkin lymphoma (NHL), Hodgkin disease (HD),Extra nodal

Introduction

Lymphoma mainly arises from the lymph nodes due to the abnormal proliferation of malignant lymphoid cells as the consequence of genetic aberrations that impair proliferation, differentiation, and ability to undergo a poptosis of lymphatic cells. It is the seventh most prevalent malignancy in both the genders.[1]

The disorders vary in clinical presentation and course from indolent to rapidly progressive disease. It can virtually involve any part of the body. Lymphoma is broadly classified as Hodgkin and Non-Hodgkin disease. Infiltration of organs other than lymph nodes, thymus, and pharyngeal lymphatic ring (primary lymphatic organs) is known as extra nodal lymphoma and it is predominantly seen with Non-Hodgkin Lymphoma. The involvement of spleen in Non-Hodgkin lymphoma is also considered as extra nodal disease.[2] NHL can spread into any organ of the body, however; common sites of involvement are the stomach followed by Waldeyer s ring, lung, liver, spleen, bone, and skin. 43% of cases of NHL with extra nodal spread are seen in gastrointestinal tract, 14% are noted in head and neck region, 2% in lungs, 7% in skin, 5% in bones and brains in 6 to 7%.[3]

The term primary extra nodal lymphoma is used when the tumor arises from non-lymphoid (lymph node) tissue, whereas the hematogenous spread of tumor from lymphoid tissues to other organs is known as secondary extra nodal lymphoma.[4] Non-Hodgkin lymphoma is eight times more prevalent than Hodgkin lymphoma and it has many subcategories.[5]

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The most important predictor of prognosis in extra nodal lymphomas is the histological subtypes and sometimes they present with site-specific distributions e.g almost all cases of diffuse large B-cell lymphoma (DLBCL) are seen in either CNS or testis.[6] NHL is broadly categorized into two groups: B-cell lymphomas and natural killer (NK)/ T-cell lymphomas. The prevalence of diffuse large B-cell lymphoma is 30%, Chronic Lymphocytic Leukemia/ small lymphocytic lymphoma is 18%, and follicular lymphoma is 20% and all other subtypes constitute less than 10% cases.[6] The diffuse large B-cell lymphoma is the most frequently found adult histological subtype and has predilection to liver, kidney, lung, bone and bone marrow.[7] Follicular lymphoma has a more indolent course and extra-nodal involvement is rare. Extra nodal marginal zone B-celllymphoma (EMZBL), previously called mucosa-associated lymphoid tumor (MALT) lymphomas has site-specific extra nodal disease in stomach, lung, ocular, adnexa, breast, skin, softtissue, bowel and dura.[7]

The other less common subtypes of lymphoma are very organ-specific predilection; Burkitt lymphoma involves jaw and facial bones and peripheral T-cell lymphoma (mycosis fungoides) for the skin.

In this review article, various imaging manifestations of extra nodal Non-Hodgkin lymphoma are discussed by observing some cases and few characteristic imaging appearances which could help is differentiation from other possible differential diagnosis will also be briefly reviewed.

HEPATIC INVOLVEMENT (Fig.1-5)

Liver involvement in secondary NHL is quite common, 40% of NHL patients have hepatic disease. It can present in various forms; diffuse hepatomegaly together with splenomegaly is a common finding. However multiple hypodense enhancing focal lesions have also

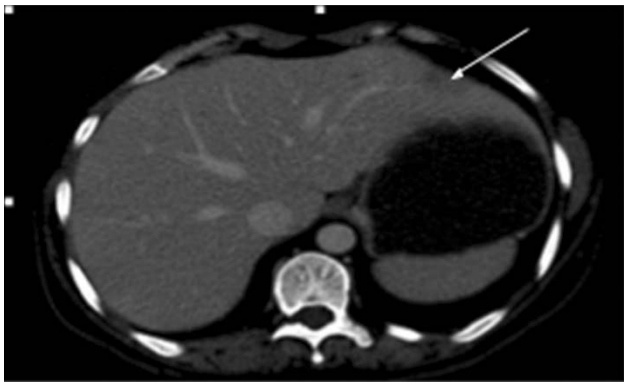


Figure 1: CT with contrast showing hypodense non enhancing lesion in segment 2 of the liver

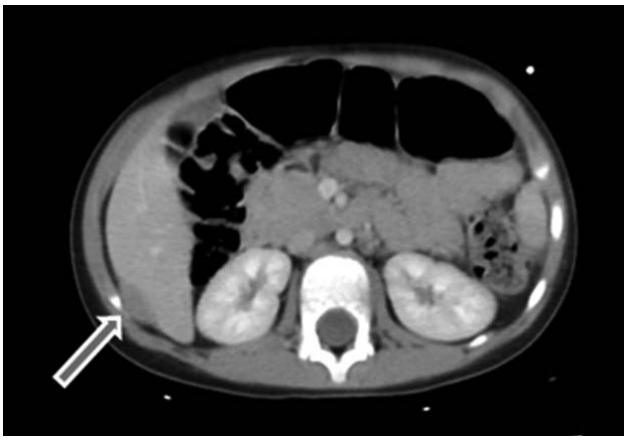


Figure 2: CT with contast showing non enhancing lesion in segment 6 of the liver

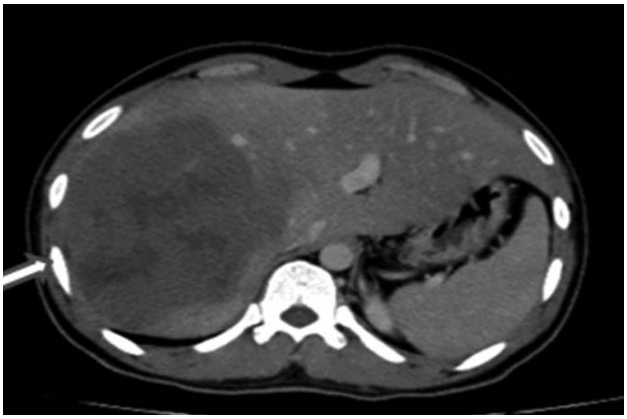


Figure 3: CT with contast showing large enhancing relatively well-demarcated non-enhancing of hte terogeneous focal lesion in right lobe liver on contrast enhanced CT scan (case of diffuse large B cell lymphoma)

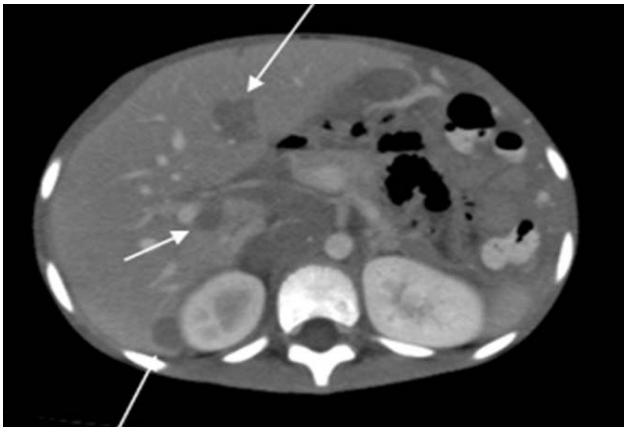
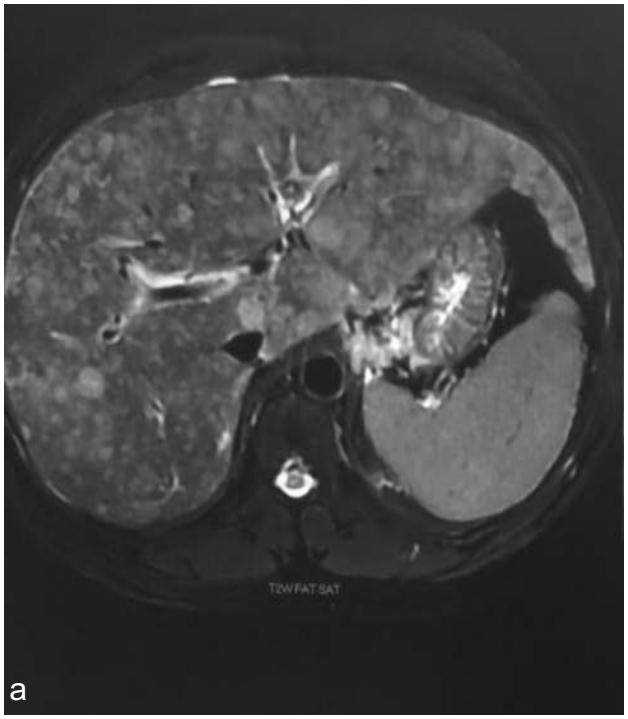
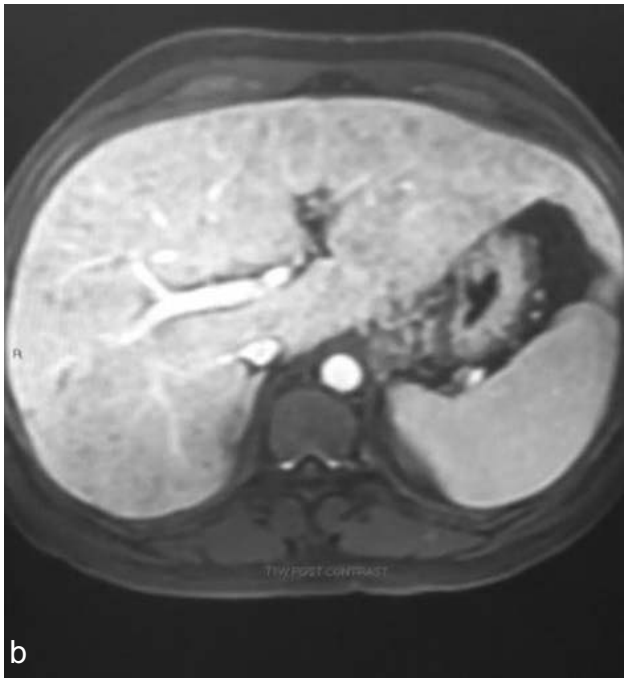
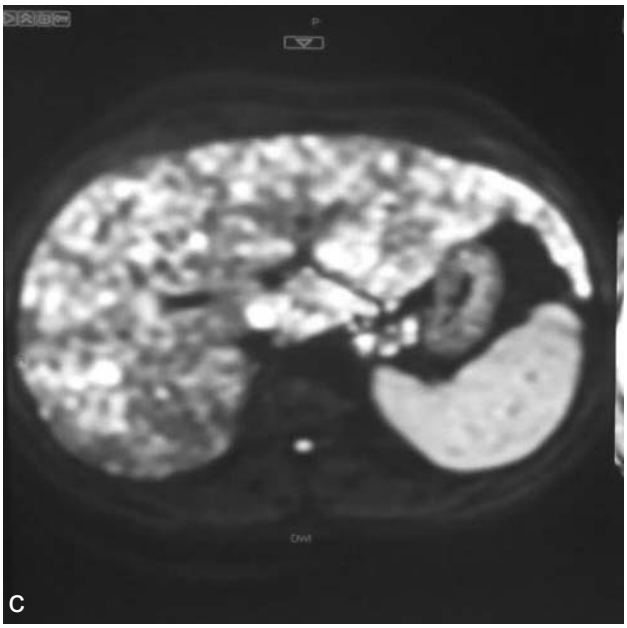


Figure 4: CT with contast showing multiple non focal lesions in liver (case of abdominal burkitt lymphoma)

been described (Fig.1-5). In case of solitary deposit lymphoma is also a differential. Finally periportal infiltration is also reported but usually with Hodgkin disease.[8] Cases showing ring enhancing lesions are also seen particularly in immuno compromised patients, where fungal infection should be ruled out.[9]







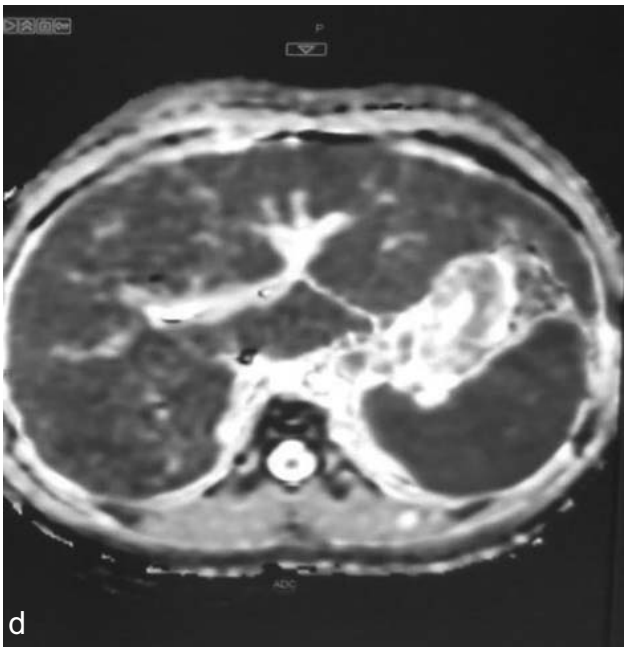


Figure 5a,b,c,d: MRI showing diffusely scattered multiple lymphomatous lesions in liver with T1, hypo: T2 Hyper showing diffusion restriction.

RENAL INVOLVEMENT (Fig.6-11)

There is no lymphoid tissue in kidneys thus the lymphomatous infiltration of the kidney is relatively common either through director hematogenous spread, especially incase of wide spread disease. It can involve one or both the kidneys and can manifest as solitary (10-20%) or multifocal lesion (60-70%) (Fig.6,7,8). Renal lymphoma can be diffusely infiltrative (Fig.10)

or due to contiguous retroperitoneal spread (5-10%).[10] The lymphomatous invasion usually occurs through the renal capsule or sinus; additionally, the aorta may be elevated dueto retro aortic lymphadenopathy.[11] Burkitt lymphoma has the highest incidence of renal involvement in children.

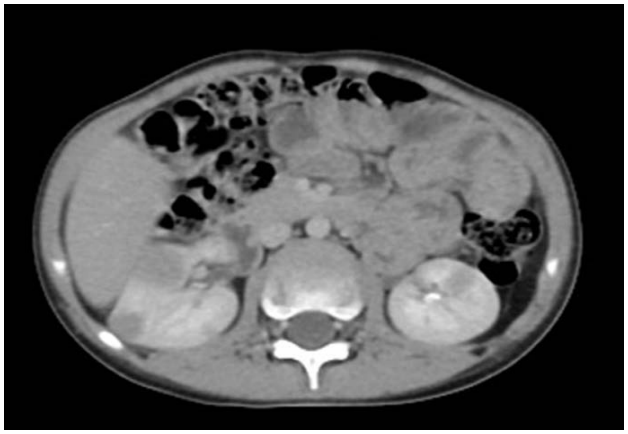


Figure 6: CT with contrast showing bilateral renal non-enhancing focal lesions of variable sizes

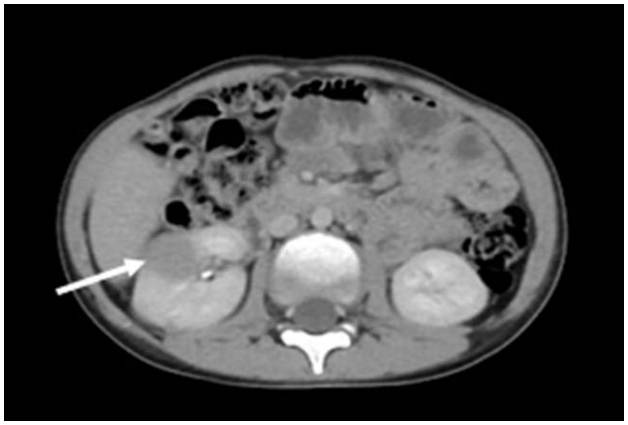


Figure 7: CT with contrast showing unilateral non-enhancing well demarcated focal lesion in anterior lip of right kidney

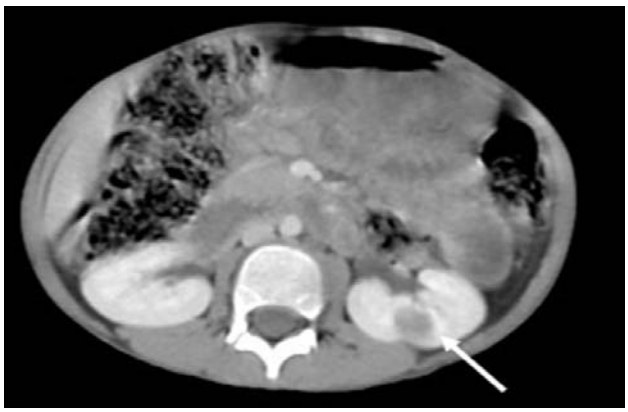


Figure 8: CT with contrast showing unilateral non-enhancing well demarcated focal lesion in the left kidney

Figure 9: CT with contrast showing unilateral non-enhancing focal lesion in the right kidney with bowel related mass (case of abdominal Burkitt lymphoma)

Figure 10: CT with contrast showing bilateral renal non-enhancing tiny focal lesions (case of T-Cell Lymphoblastic lymphoma)

Figure 11: CT with contrast showing bilateral relatively large nonenhancing-hypodensities in both kidneys (case of marginal zone lymphoma)

GASTROINTESTINAL INVOLVEMENT (Fig.12,13,14) The bowel is the most frequently involved extra nodal location of Non-Hodgkin lymphoma seen in about 10% of cases.[12,14]

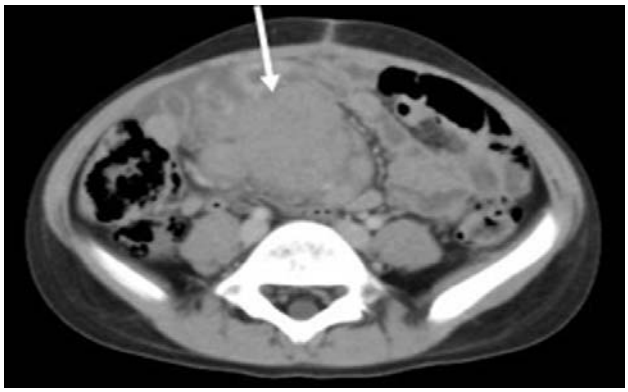


Figure 12: CT with contrast showing lobulated large mass in small bowel lymphoma mesentery

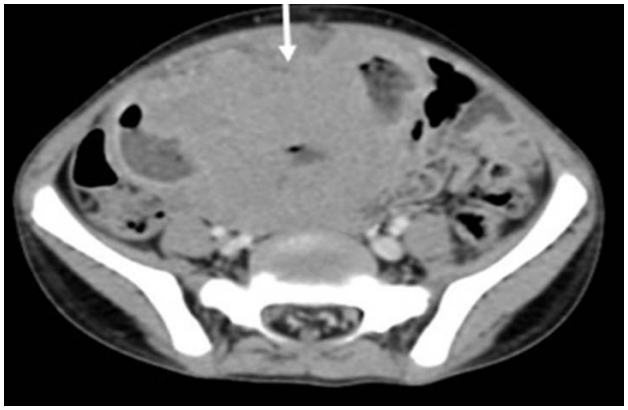


Figure13: CT with contrast showing large lymphomatous mass of Burkitt extending into the pelvis

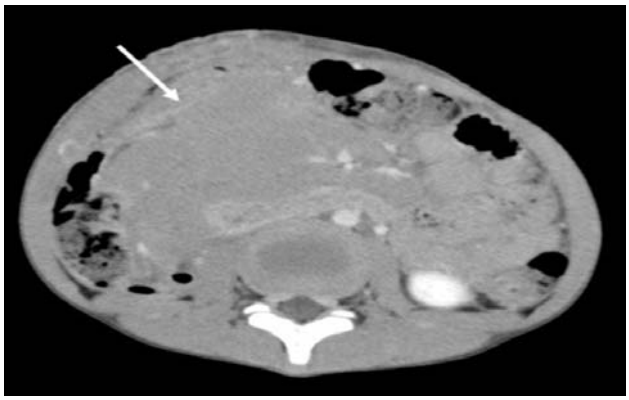


Figure 14: Axial C/E CT scan: large soft tissue density mass centered on right hemi abdomen, involving head of pancreas and duodenal head (case of Burkitt lymphoma)

1. STOMACH

The stomach is the most common site (50%) followed by the small intestine, colon and esophagus.[15] Extra nodal marginal zone B-cell lymphoma (EMZBL), previously known as mucosa-associated lymphoid tissue (MALT) lymphoma, is the most common type. There is a well-known association with H-pylori infection. The tumor can present as polypoidal, ulcerating and infiltrative, that can be difficult to differentiate from carcinoma; however, multiplicity, large cavitations and pronounced focal thickening of mucosal folds can help in differentiation. Also, less desmoplastic reaction is seen in case of lymphoma and extension to nearby viscera is alsorare.

2. BOWEL INVOLVEMENT

Bowel wall invasion is particularly due to T-cell Lymphoma with more chances of perforations.[13] In the caecum polypoidal mass is seen which is indistinguishable from carcinoma, however; associated thickening of terminal ileum is more suggestive of lymphoma. Likewise, in the recto sigmoid larger segment of stricture and irregular excavation of tumor favors the diagnosis of lymphoma rather than adeno carcinoma.[16]

3. MESENTERIC INVOLVEMENT

On imaging it can present as rounded, homogeneously enhancing lesions centered on mesentery. Sandwich sign: bulky mesenteric lymphadenopathy encasing the vessels and bowel is mainly seen in malignant tumors.(Fig.12)

SKELETAL INVOLVEMENT (Fig.15-22)

1. MUSCLES

Around 1.1% of NHL cases show muscle invasion that is seen with disseminated tumors. On MRI, it

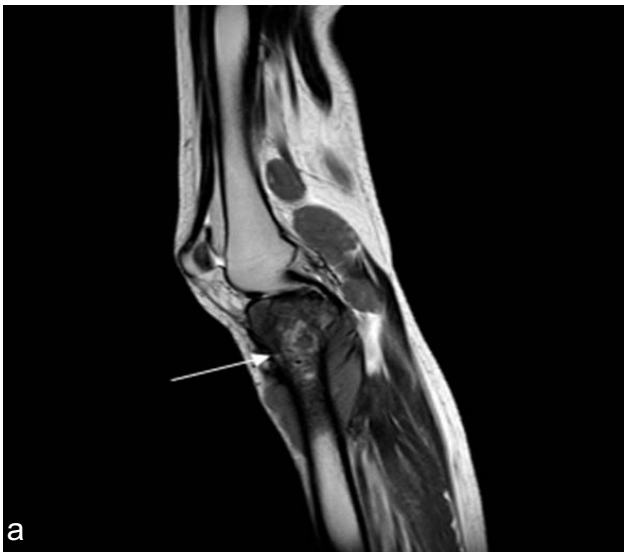


Figure 15(a,b): MRI with contrast T2w showing hete rogeneously enhancing marrow lesion involving upper left tibia (case of DLBCL) and having tumor extension into the adjacents of tissue.

demonstrates diffuse muscle enlargement with contrast enhancement together with diffuse increased trace ruptake.[17,18] (Fig.22)

Figure 16: MRI STIR sagittal images of spine: high signals are seen at the T8, T12 and L2 vertebral level with para vertebral soft tissue. (case of DLBCL)

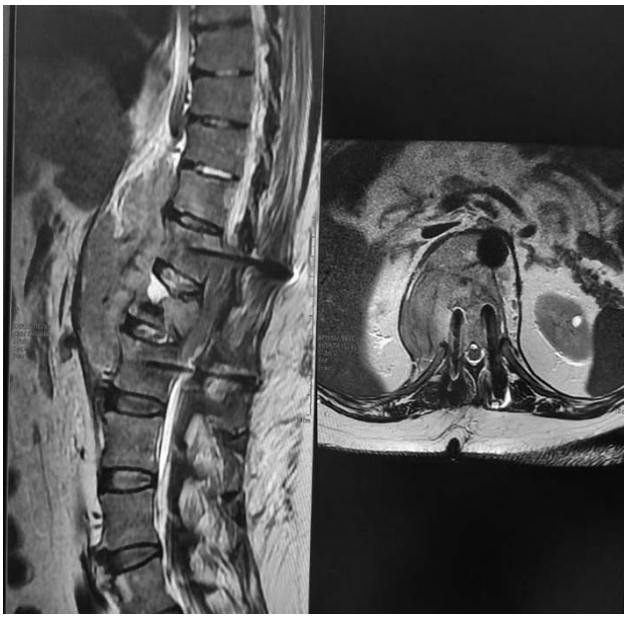


Figure 17: MRI T2W images showing vertebral lymphoma with large para spinal soft tissue mass.

Figure 18: C/E T2w MRI: heterogeneously enhancing large soft tissue mass involving whole of the left thig hand bone and vessels (case of DLBCL)

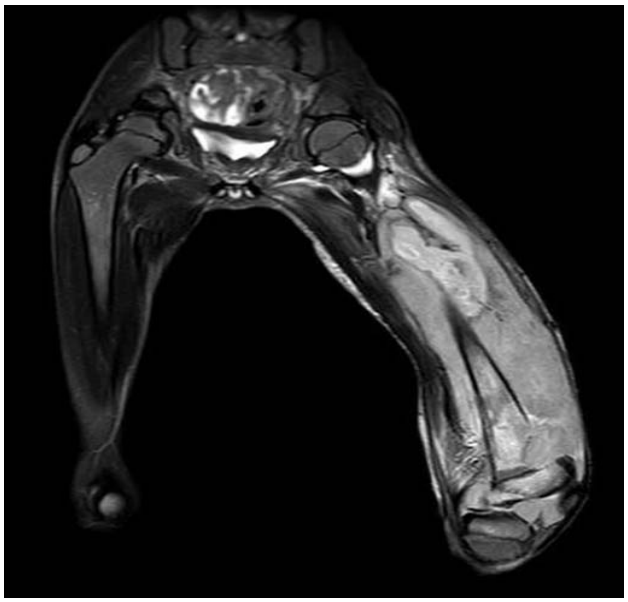


Figure 19: T2w MRI with IV contrast image showing a large soft tissue mass involving the left thigh which is extending to the knee joint with intraosseous extension into distal femoral diaphysis together with marrow edema.

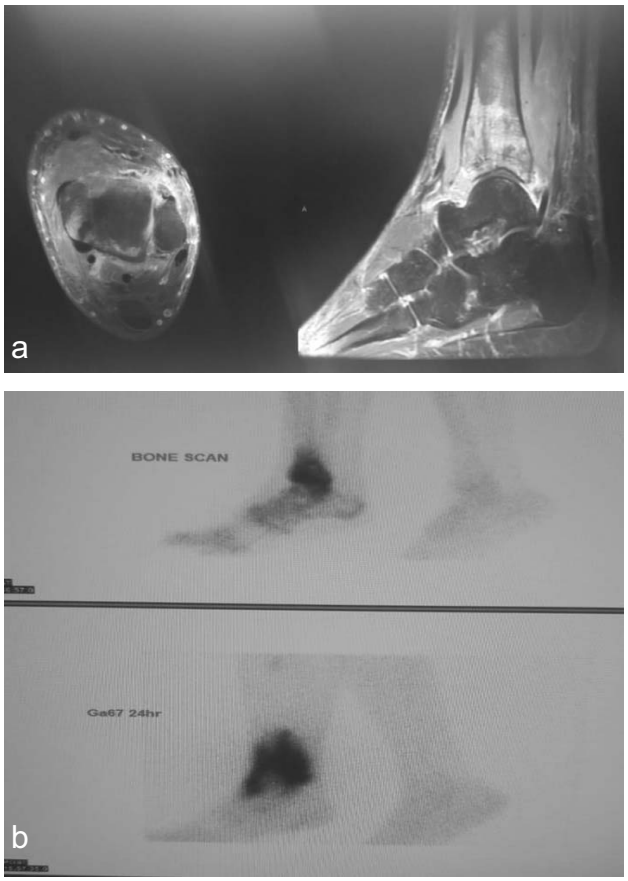


Figure 20a,b: Image A showing MRI with high signal in distal tibial end along with soft tissue mass around it, Image B is increase tracer uptake on bone scan at the cooresponding site.

Figure 21: STIR hyper intense lymphomatous infiltration of proximal right tibia.

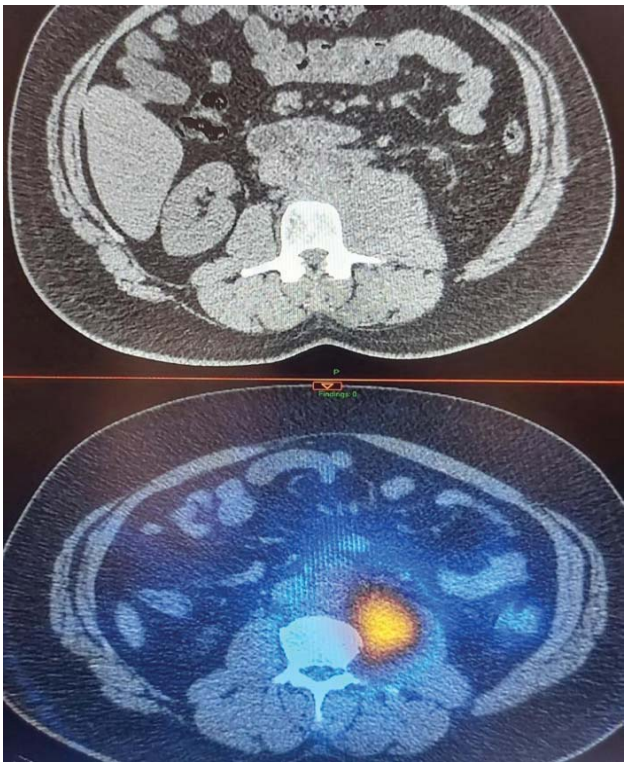


Figure 22: Left psoas muscle involvement with lymphoma showing high uptake on PETCT scan

2. BONES

Secondary extra nodal skeletal involvement usually seen in axial skeleton with diaphyseal predilection in long bones (Fig.15,18,19,21) followed by pelvis and vertebral column (Fig.16,17). The imaging features are usually nonspecific aggressive lytic lesions. FDG PET is reliably more specific and sensitive.[19]

3. BONE MARROW

Bone marrow disease usually shows diffuse or focal involving one or more bones. Although biopsy is considered the gold standard for the diagnosis, 18F-FDG is highly sensitive in detecting bone marrow lesions.[20]

HEAD AND NECK REGION (Fig.23,24,25)

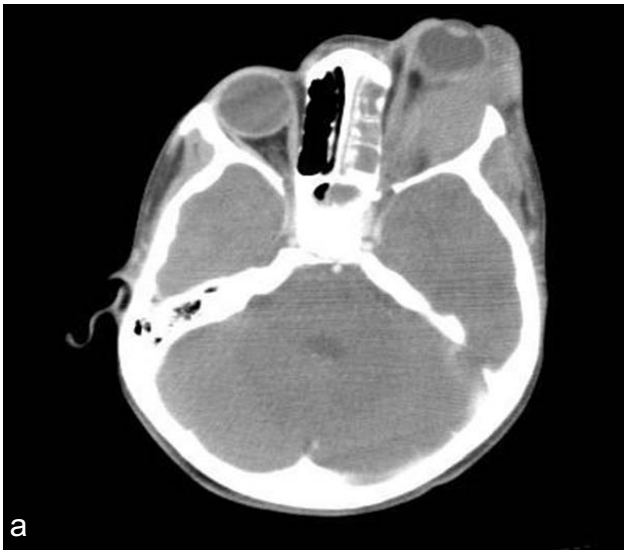
Extra nodal involvement of NHL in head and neck is quite prevalent seen in 25-40% of the cases and it is one of the major differentiating points from hodgkin lymphoma because both the diseases involve contiguous neck lymphadenopathy.[25] The waldeyer s ring comprises almost half of the cases and tonsils being the most frequently involved site.

1. ORBITAL AND EXTRA-OCULAR ADNEXAL INVOLVEMENT

Approximately 55% of cases of orbital masses are lymphoma and 1-10% of these cases are of Non-

Figure 23a,b: C/E CT images of head showing soft tissue mass over vertex causing involvement of skull bone and focal nodular meningeal enhancement

Hodgkin lymphoma.[21] These can be unilateral or bilateral with female preponderance.[22] The term ocular adnexal lymphoma refers to the tumor in the extraocular orbital region that includes involvement of lacrimalgl and, orbital soft tissue, conjunctiva and eyelids.[4] It usually presents as well-defined orbital mass that molds to ocular structures without causing any bony destruction. On CT, it is homogenous and iso or slightly hyperdense to extraocular muscles demonstrating mild enhancement (Fig.24a, b.25). On MRI they are T2 iso to hyperintense with restricted diffusion and homogenous enhancement.[23]



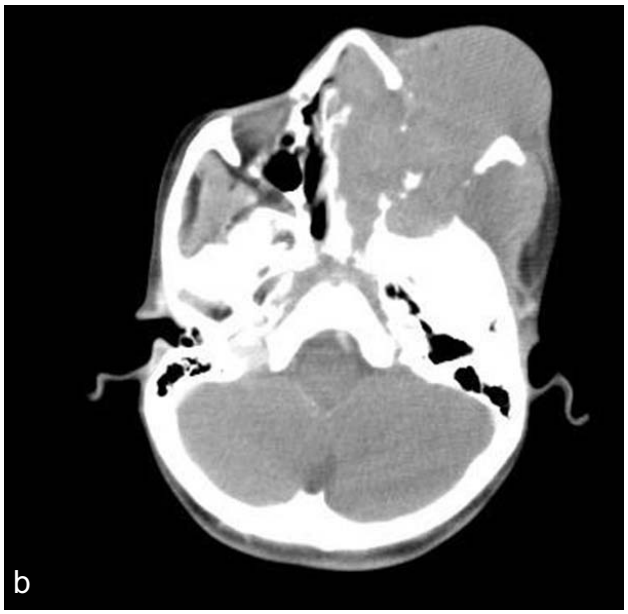


Figure 24: C/E Axial CT showing huge soft tissue isodense mass involving left nasal cavity, left maxillary and sphenoid sinus with left left intraorbital extension of the tumor resulting in proptosis.

Figure 25: C/E Axial CT showing isodense soft tissue mass involving right infra temporal region as well as right extra ocular muscles causing proptosis.

2. SALIVARY GLANDS INVOLVEMENT

2-5% of salivary gland neoplasm are lymphomas and the most frequent site is parotid gland,especially associated with Sjogren s syndrome. The tumor is usually solitary, poorly marginated, isodense on CT, however on MRI, it becomes more conspicuous.[26]

3. CRANIAL VAULT

The lymphoma in the cranial vault may present with cerebral infiltration and orbital involvement. CT is superior to bony evaluation; however, MRI helps in better delineation of intra cranial extension and marrow infiltration.(Fig.23a,b)

4. SINONASAL INVOLVEMENT

NHL represents only less than1% of all the malignant tumors of head and neck. On Imaging, the present with intermediate signal bulky masses on MRI with contrast enhancement (Fig.24a,b). The other pattern could be aggressive lesions that can resemble squamous cellcarcinoma; however, it is more homogenous on T2 and shows less avid enhancement. Nasal cavity and maxillary sinus are more frequent sites.[27]

Conclusion

In the above discussion, we have seen quite a few cases of non-Hodgkin lymphoma demonstrating disease involvement in regions other than lymph nodes which has clearly shown that it is not a very rare finding in the patients of non-Hodgkin lymphoma. Due to its variable presentation at imaging, it is essential that extra nodal disease of NHL should also be considered in the list of differentials. Multimodality imaging is an excellent tool for evaluating the extent and sites of disease involvement that enables a radiologist to accurately stage the disease and to provide essential information required for the thorough management of the patient.

Conflict of Interest: Declared None.

References

1. Altekruse SF, Kosary CL, Krapcho M, et al. SEER Cancer statistics review, 1975-2007. National Cancer Institute, Bethesda, MD.http://seer.cancer.gov/csr/1975_2007/,basedonNovember2009SEERdatasubmission,postedtotheSEERwebsite,2010.

2. Groves FD, Linet MS, Travis LB, Devesa SS. Cancer surveillance series: non Hodgkin's lymphoma incidence by histologic subtype in the United States from 1978 through 1995. J Natl CancerInstitute. 2000; **92:** 1240-51.

3. Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement innon-Hodgkin lymphoma and Hodgkin disease. Radiographics. 2010; **30:** 269-91.

4. Even-Sapir E, Lievshitz G, Perry C, Herishanu Y, Lerman H, Mester U. Fluorine-18 fluorodeoxy glucose PET/CT patterns of extranodal involvement in patients with Non-Hodgkin lymphoma and Hodgkin's disease. Radiol Clin NAm. 2007; **45:** 697-709.

5. Office for National Statistics. Cancer statistics registrations 2007: registrations of cancer diagnosed in 2007, England. London, UK: Office of Public Sector Information, 2010: series MB 1 no. 38

6. Hernandez-Maraver D, Hernandez-Navarro F, Gomez-Leon N, et al. Positron emission tomography / computed tomography: diagnostic accuracy in lymphoma. Br J Haematol 2006; **135:** 293-302.

7. Matasar MJ, Zelenetz AD. Overview of lymphoma diagnosis and management. Radiol Clin North Am 2008; **46:** 175-98.

8. Guermazi A, Brice P, de Kerviler E, et al. Extranodal Hodgkin disease: spectrum of disease. Radio Graphics 2001; **21:** 161-79.

9. Lee WK, Duddalwar VA, Rouse HC, Lau EW, Bekhit E, Hennessy OF. Extranodal lymphoma in the thorax: cross-sectional imaging findings. Clin-Radiol 2009; **64:** 542-9.

10. Sheth S, Ali S, Fishman E. Imaging of Renal Lymphoma: Patterns of Disease with Pathologic Correlation. Radio Graphics. 2006; **26(4):** 1151-68.

11. Cronin CG, Lohan DG, Blake MA, Roche C, McCarthy P, Murphy JM. Retroperitoneal fibrosis: are view of clinical features and imaging findings. AJR 2008; **191:** 423-31.

12. Gollub MJ. Imaging of gastrointestinal lymphoma. Radiol Clin North Am 2008; **46:** 287-312.

13. Ghai S, Pattison J, Ghai S, O Malley ME, Khalili K, Stephens M. Primary gastro intestinal lymphoma: spectrum of imaging findings with pathologic correlation. Radio Graphics 2007; **27:** 1371-88.

14. Zucca E, Conconi A, Cavelli F. Treatment of extra nodal lymphomas. Best Pract Res Clin Haematol. 2002; **15:** 533-47.

15. Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement innon-Hodgkin lymphoma and Hodgkin disease. Radiographics. 2010; **30:** 269-91.

16. Sarah JV, Rodney HR. Reticuloendothelial Disorders: Lymphoma. In: Adam Andy., editor. Grainger & Allison's Diagnostic Radiology A text book of Medical Imaging. 5th ed. Philadelphia: Elsevier Limited; 2003. pp.1733-58.

17. Chong J, Som PM, Silvers AR, Dalton JF. Extra nodal non-Hodgkin lymphoma involving the muscles of mastication. AmJ Neuroradiol. 1998; **19(10):** 1849-51.

18. Chun CW, Jee W-H, Park HJ, Kim YJ, Park J-M, Lee S-H, et al. MRI Features of Skeletal Muscle Lymphoma. AmJ Roentgenol. 2010; **195(6):** 1355-60.

19. Moog F, Kotzerke J, Reske SN. FDG PET Can Replace Bone Scintigraphy in Primary Staging of Malignant Lymphoma. J Nucl Med. 1999; **40(9):** 1407-13.

20. Evan-Sapir E. Imaging of malignant bone involvement by morphologic, scintigraphic and hybrid modalities. J Nucl Med. 2005; **46:** 1356-67.

21. Eckardt A Metal. World J Surg Oncol. 2013; **11:** 73.

22. Ahmed Setal. AmJ Med Sci. 2006; **331(2):** 79-83.

23. Bonemarrow Antigen-Driven Lymphomagenesis and Microbial-Targeted Therapy. Ann Oncol. 2008; **19(5):** 835-46.

24. Maksimovic O, Bethge W, Pintoffl Jetal. Marginal Zone B-Cell Non-Hodgkin's Lymphoma of Mucosa-Associated Lymphoid Tissue Type: Imaging Findings. AJ RAmJ Roentgenol. 2008; **191(3):** 921-30.

25. Aiken AH, Glastonbury C. Imaging Hodgkin and non-Hodgkin lymphoma in the head and neck. Radiol Clin North Am 2008; **46:** 363-78.

26. Zhu L, Wang P, Yang J, Yu Q. Non-Hodgkin lymphoma involving the parotid gland: CT and MR imaging findings. Dentomaxillofac Radiol. 2013; **42:** 20130046 20130046.

27. Das S, Kirsch CF. Imaging of lumps and bumps in the nose: a review of sinonasal tumors. Cancer imaging: the official publication of the International Cancer Imaging Society. 2005; **5:** 167-77.