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RESEARCH ARTICLE

# Unusual Presentation of Diffuse large β-cell Lymphoma (DLBCL) Lymphoma with diagnostic challenges

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## ABSTRACT

### Introduction:

Worldwide diffused β cell lymphoma is the commonest type of non-Hodgkin lymphoma about 31% of all non-Hodgkin Lymphoma. Median age reported for diffuse large β-cell lymphoma 60 to 70 years of age. Extra nodal diffuse large β-cell lymphoma reported in about 30% cases and most common site were found gastrointestinal tract skin and soft tissue bone or Genito urinary tract, head and neck region. Extra nodal non-Hodgkin lymphoma only represented in 10% cases.

### Case Study:

Patients presented with complaint of focal neurological deficit vomiting, headache nausea and status seizures with behavioural and mental change and 27-year-old male presented with difficulty pain while walking for last 1.5 months.

### Discussion:

Musculoskeletal Lymphomas are predominantly a manifestation of lymphoma dissemination. Extra nodal Lymphomas commonly involved skin, head and neck and gastrointestinal tract. Lymphomas rarely involved skeletal system. Most common radiological finding with Extra-Nodal lymphoma are blastic lesion and lytic lesion, sometimes mixed lesion with lytic and blastid. Primary central nervous system lymphoma usually originates from cerebellum, spinal cord, Pia matter, Retina or optic nerve. Manifestation of lymphoma in skeletal muscles is rare, usually they involve gluteal muscles and pelvis.

### Conclusion:

Primary Central Nervous System (CNS) Lymphoma often misdiagnosed as Brain tumour and this delays proper treatment and confirmation of diagnosis. Immunohisto-chemistry examination is mandatory to achieve confirm diagnosis.

### Keywords:

Lymphoma, β-cell lymphoma, CNS Lymphoma.

## Introduction

Worldwide diffused β-cell lymphoma is the commonest type of non-Hodgkin lymphoma about 31% of all non-Hodgkin Lymphoma[1].

Median age reported for diffuse large β-cell lymphoma (DLBCL) is 60 to 70 years of age. Extra nodal DLBCL reported in about 30% cases and most common site were found to be gastrointestinal tract skin and soft tissue bone or Genito urinary tract, head and neck region[2].

Extra nodal non-Hodgkin lymphoma only represented in 10% cases.

Primary central nervous system (CNS) lymphoma is rare non-Hodgkin lymphoma limited to central nervous system[3].

They represent less than 1% of all non-Hodgkin lymphoma and 2% to 3% of all brain tumour[4].

Primary central nervous system lymphomas mostly represented by DLBCL. It is characterised by single or multiple contrast enhancing lesion mainly at supratentorial region[3].

In recent years, rising trend of incidence has been reported specially in older patients, incidence rate 0.5 per 100000 per year reported[5].

These tumours usually have better response with chemotherapy and radiotherapy as compared to brain tumour, but survival reported inferior as compare to other lymphoma cases[6].

Primary Central Nervous System Lymphoma commonly presents as sub-acute typical symptoms like headache, focal neurological deficit, nausea, vomiting, cognitive or personality changes seizure are less frequent (10-20%) as compared to brain tumour[7]. Sometimes lepto meningeal involvement also reported about in 15-20%[8]. Other symptoms may occur due to area of involvement like ocular leads to blurring of vision in 30% cases[9].

Manifestation of Lymphoma in skeletal muscles is rare. Usually, they involve glutaeal muscles and pelvis. Only 0.5% of extra nodal Lymphomas diagnosed as a primary skeletal muscle Lymphoma. Involvement of skeletal muscles and bone may mimic as a soft tissue sarcoma, bone tumours or metastasis cancerous which have different diagnostic criteria and treatment[10]. Involvement of muscle and metastasis to brain and other parts is extremely uncommon. Accurate diagnosis of these cases is a challenge for clinicians. Pathologist and Radiologist despite the advancement of radiological and pathological devices. Here we present two cases of DBCL with rare presentation with the belief that our cases will add evidence to diagnose DBCL with rate sites of presentation.

## Case Study

CASE-1

A 35-year-old male presented with sudden onset of headache and vertigo with loss of consciousness one month ago. After few minutes he gained consciousness but developed Hemiparesis and had multiple episodes of seizures. On Magnetic resonance imaging (MRI) 33x34x31 $mm^3$ mass with perilesional oedema and mass effect.

Right frontal Parietal craniotomy with excisional Biopsy done which suggested Papillary meningioma. After immune-histochemistry confirmed as a diffuse B-cell. Lymphoma with CD 20, CD 45, KI 67.70-75%.

Positron emission tomography (PET) scan shows post-operative evidence of right frontal parietal craniotomy. Non-FDG avid mild to moderate vasogenic oedema seen in right frontal lobe with no significant mass effect noted. However, no abnormal focal fluorodeoxyglucose (FDG) avid/ enhancing lesion seen in operated bed/right frontal lobe.

Patient has been planned for Radiotherapy, now he is on follow up.

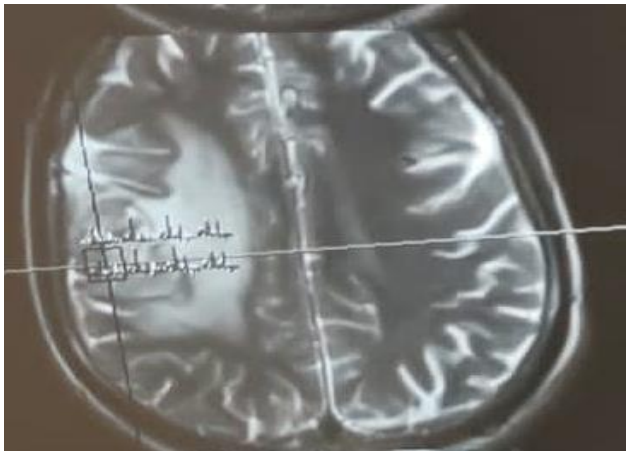

Figure 1

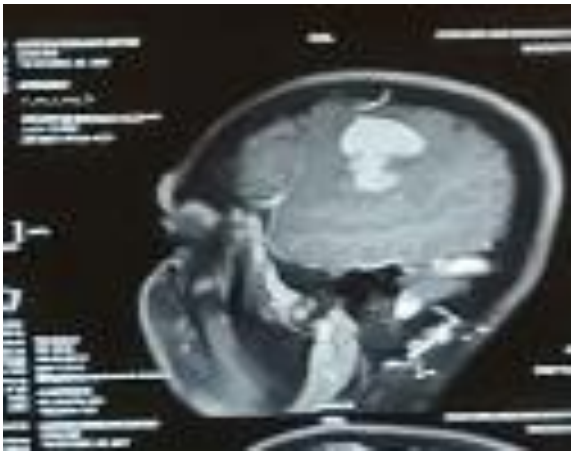

Figure 2

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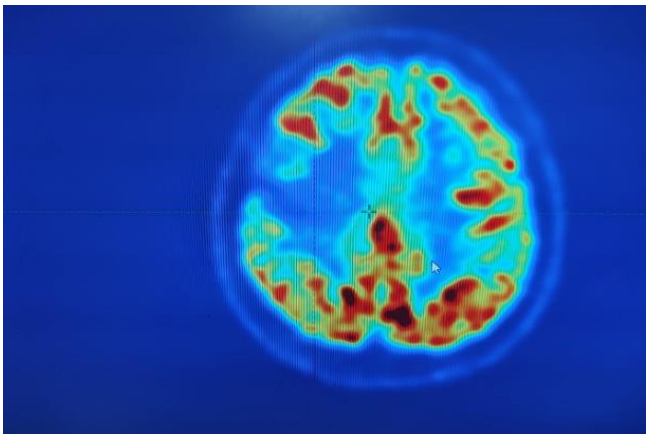


Figure 3

Figures: MRI Reports

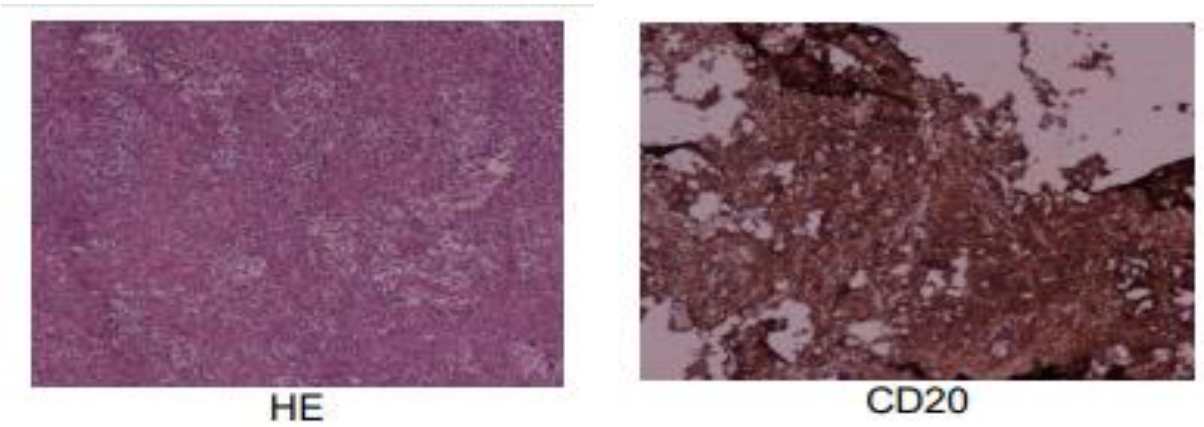



**Figure 1:** Immunoreactive, score 4+ in lesional cells

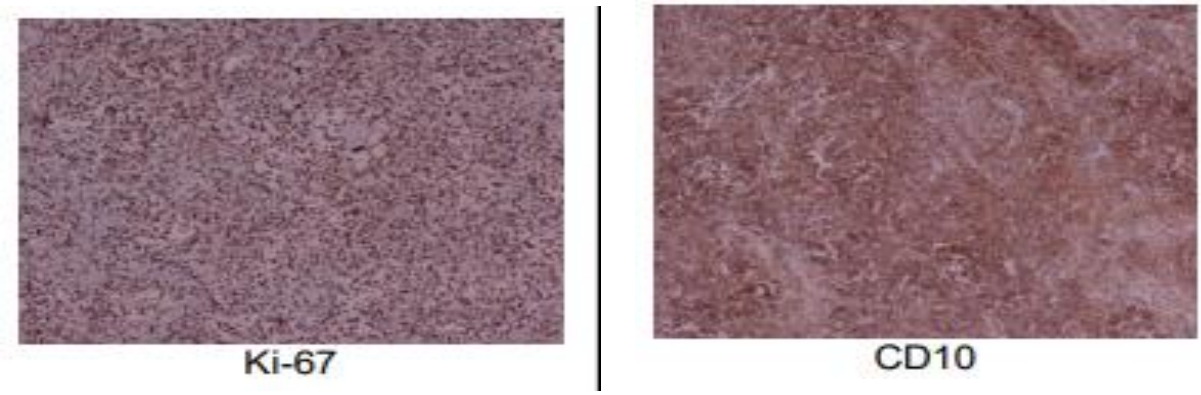



**Figure 2:** Immunoreactive in 70-75% of lesional cells, Immunoreactive, score 4+ in lesional cells

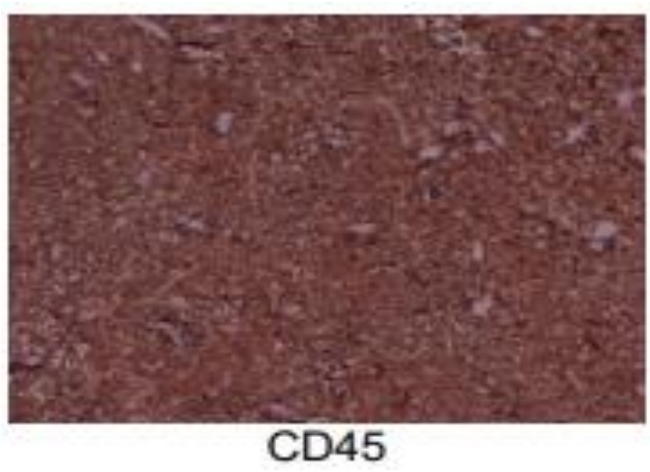



**Figure 3:** Immunoreactive, score 4+ in lesional cells

Table 2: HISTOPATHOLOGY FINAL DIAGNOSIS PANEL (Immunohistochemistry)

| IHC MARKER(S) | RESULT |
|---|---|
| CD20 | Immunoreactive, score 4+ in lesional cells. |
| CD45 | Immunoreactive, score 4+ in lesional cells |
| Ki-67 | Immunoreactive in 70-75% of lesional cells |
| CD-10 | Immunoreactive, score 4+ in lesional cells |
| BCL-6 | Immunoreactive, score 2+ in lesional cells |
| MUM-1 | Immunoreactive, score 1+ in lesional cells |
| CMYC | Immunoreactive in 1-2% |
| BCL-2 | Immunoreactive, score 1+ in lesional cells |
| PAX-5 | Immunoreactive, score 4+ in lesional cells. |

CASE-2

A 27-year-old male presented with difficulty and pain during walking for last one and half month. On examination, tender swelling was felt in left pelvis. Core biopsy from left iliac mass shown Large cell Lymphoma. On immune histochemistry examination it confirmed as diffuse B-cell lymphoma shown CD 45, CD 20, CD 10, BCL 2, BCL 6 positive. On MRI Brain and skeletal system shown.

PET scan shown varying degree of Dural thickening and enhancement is seen overlying both cerebral hemispheres, predominantly overlying partial lobe and along posterior fix, Lesion in the posterior falx is compressing/invading posterior aspect of superior sagittal sinuses.

Fairly large soft tissue component is seen superolateral quadrant of both orbits involving lacrimal glands also altered signal intensity of lateral wall of both orbits are seen, soft tissue component is also seen in periorbital region and superficial tissue of scalp overlying left parietal region.

Both cerebral hemispheres are normal in volume and signal intensity on all pulse sequence.

Altered marrow signal intensity lesion is seen involving the left with large associated soft tissue mass measuring 13.5x11.6x7.4cm size seen involving the gluteus muscle as well as left ileo psoas muscle. There is extension until the anterior aspect of left sacroiliac joint. The lesion is hypointense on T1 and hyperintense on T2 STIR and post contrast showing moderate heterogeneous enhancement. The soft tissue thickening showing loss of fat plane with femoral and external ilia 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, right iliac bone. On STIR images patchy hyperintensity is also seen in few lumbar vertebrates. Mild patchy enhancement is seen in the CVJ (Carme vertebral junction).

Patient has been planned for chemotherapy with R-CHOP – 6 Cycle.

Figure: PET scan images

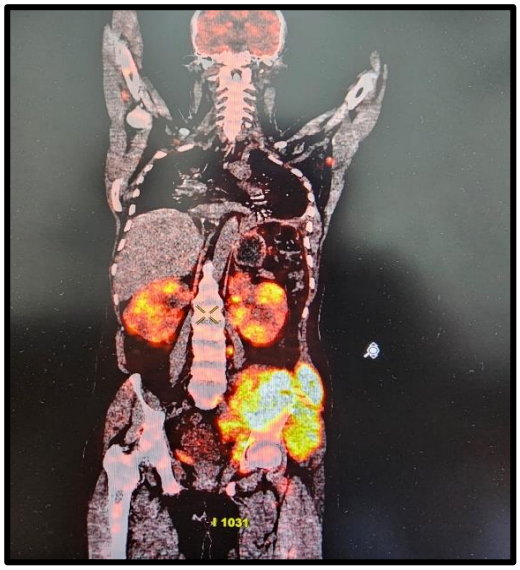


Figure-1

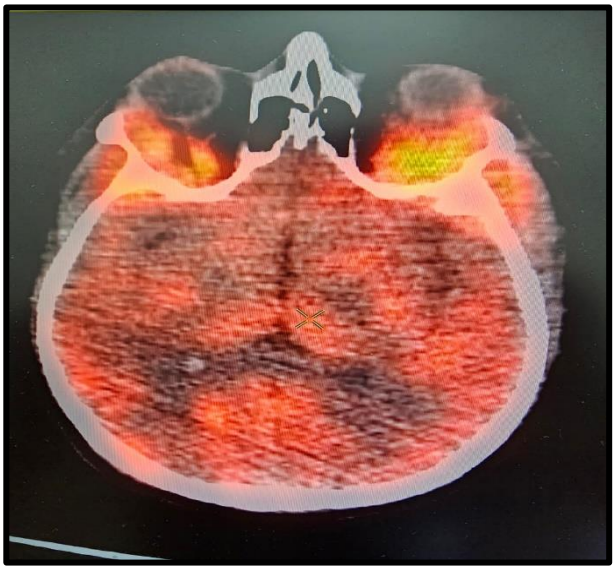


Figure-2

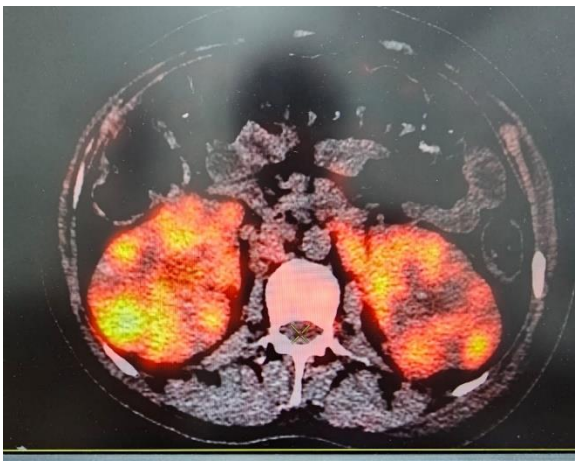


Figure-3

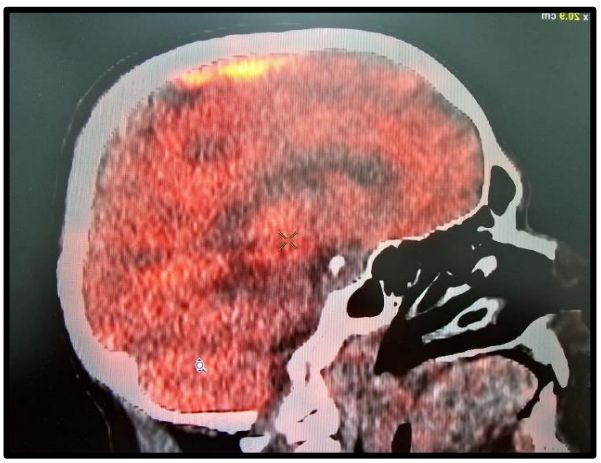


Figure-4

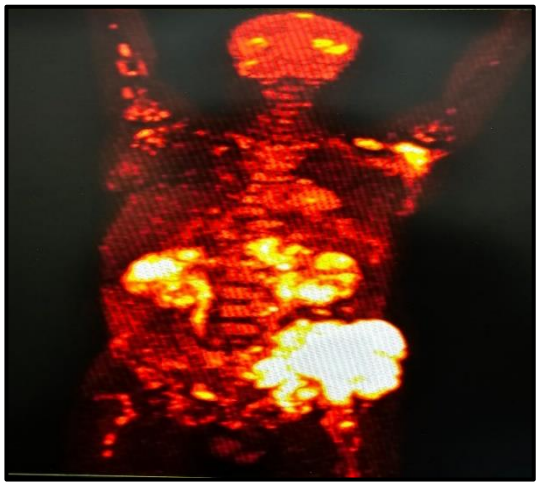


Figure-5

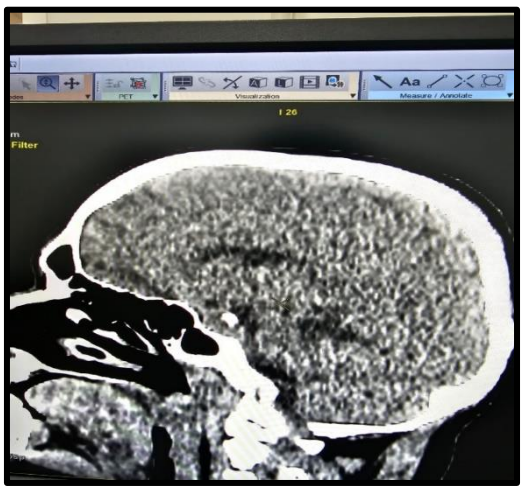


Figure-6

Table 4: HISTOPATHOLOGY FINAL DIAGNOSIS PANEL (Immunohistochemistry)

| IHC Marker | Result |
|---|---|
| CD 45 | Positive |
| CD20 | Positive |
| CD10 | Positive |
| BCL 2 | Positive |
| BCL 6 | Positive |
| Ki 67 | 80% |

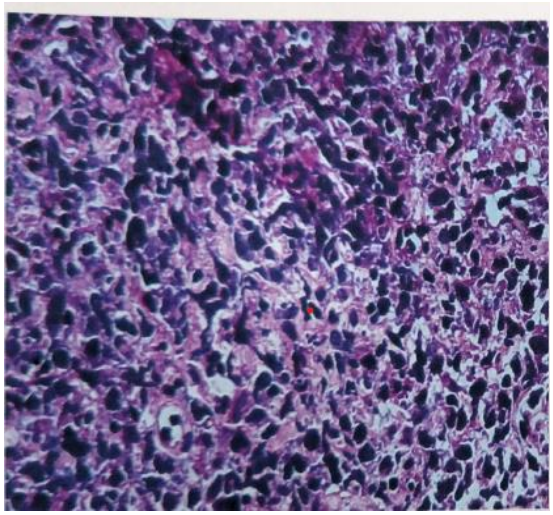
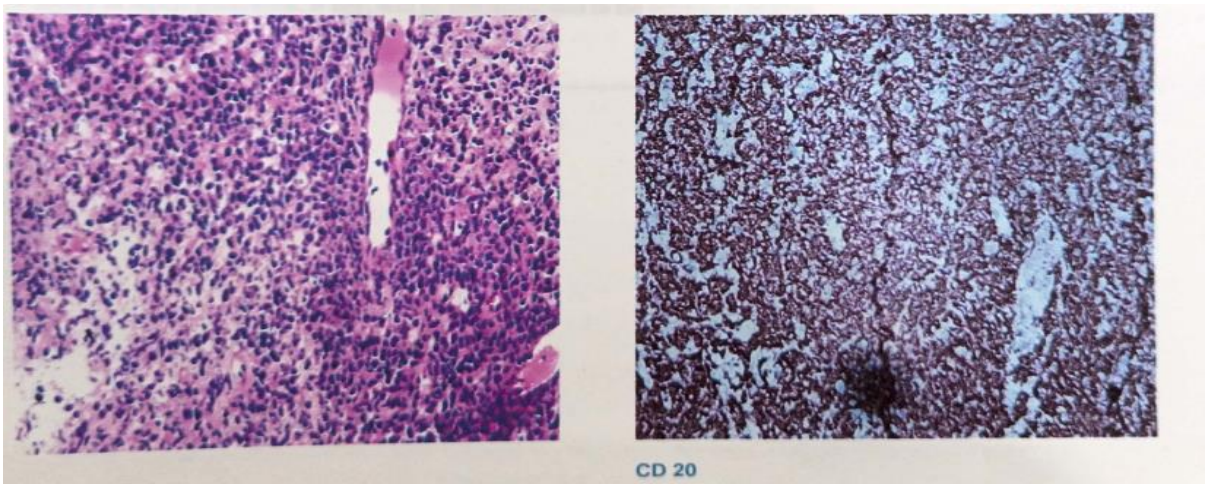


**Figure 4:** Large Cell Lymphoma-Biopsy (L) lilac mass.




Small Biopsy for Histopathology

## Discussion

Musculoskeletal Lymphomas are predominantly a manifestation of lymphoma dissemination[11-12]. Extra nodal Lymphomas commonly involved skin, head and neck and gastrointestinal tract. Lymphomas rarely involve skeletal system[13-14].

Most common radiological finding with Extra-Nodal lymphoma are Blastic lesion and lytic lesion, sometimes mixed lesion with lytic and blastic[11,15-16].

Involvement of muscle and metastasis to Brain and other part is extremely uncommon. Accurate diagnosis of these cases is a challenge for Clinicians, Pathologists and Radiologists despite the advancement of Radiological and Pathological devices[16].

Primary central nervous system lymphoma usually originates from cerebellum, spinal cord, Pia matter, Retina or optic nerve[17-18]

Usually, Primary CNS Lymphoma characterized by supratentorial localization and clinical manifestation are very similar to other intracranial tumour, with the symptoms of intracranial tumours like headache, vomiting and focal neurological deficit[17].

Commonest location in MRI images found periventricular white matter, basal ganglia, or corpus callosum and less commonly areas are cerebellum, brainstem, and spinal cord[14]. In 70% cases single lesion presented multifocal lesion presented more frequently in immune compromised patient. Commonly differential diagnosis found with high grade glioma and less often metastasis or infectious granuloma[18].

Tumour diagnostic finding of primary intracranial lymphoma are hypointense T1 or hyperintense T2 signals. On diffusion weighted imagining there may be homogeneous or heterogeneous and high circular signals and PET scan findings may reveal single or multiple high metabolic signals[19-27].

Role of surgery in primary intracranial lymphoma is debatable[28-29]. Diagnosis is confirmed by pathological analysis. MRI stereotactic biopsy can be considered by confirming the diagnosis[30].

Radiation and chemotherapy can be considered for treatment. A previous study reported 90% response rate with high dose methotrexate and procarbazine and can provide survival up to 5 years[24] Other combination are used in these cases are Temozolomides high dose of methotrexate, Rituximab[31-32].

Temozolomides can cross blood brain barrier and have a high oral bioavailability. The national comprehensive cancer network has recommended the use of Temozolomides in refractory intracranial lymphoma[33-34].

Radiotherapy in Intracranial lymphoma usually prescribed as 40 to 50 GY to whole brain followed by boost of 10gy in 5 fraction to localized area[35].

Without treatment intracranial lymphoma survival is 3-6 months and with comprehensive treatment, progression free and overall survival can be improved. 5-year survival in these cases remains 20-25%[36].

Recurrence reported 35-60% within 2 years and overall survival reported about 8-18 months[37].

Mamorska-Dyga et al. reported a case which was initially diagnosed as a sarcoma on physical and radiological examination, after biopsy it was diagnosed as DLBCL[38]. Another case was diagnosed as a sarcoma reported by Mayo at al., who presented as a subcutaneous swelling on shoulder, diagnosed as a case of DLBCL after surgical excision[39].

Gupta et al. reported a case of cutaneous Lymphoma which was presented as a swelling in inguinal swelling and mimicked as a sarcoma[40]. Primary extra nodal Lymphoma is rare about 0.1 to 0.5 of all non-Hodgkin's Lymphoma cases[41-42]. Generally skeletal muscle Lymphoma arises in lower extremities and thighs[43]. It can occur after treatment at lower extremities. Sometime skeletal muscle Lymphoma arises from T-cell and have poor prognosis[44-45].

Sometimes DLBCL shows aggressive growth pattern and present as a large necrosed masses that may infiltrate and surround's structure[13,46-47]. A recent study shown association of SUV (max) on FDC 18 PET and survival[48-49]. SUV (max) can be considered as a good Prognostic factor (20) for progression and treatment response[48-49].

For confirmation of diagnosis, histological examination of specimen and imaging studies are required. A recently published studies shown PET-CT fusion is more. Sensitive and Specific (88% and 100%) as compared to CT scan (50% and 90%) [50-52].

Utkan et al. reported a 68-year-old male presented with mass in (R) bullock for last 2 month. After Biopsy and histopathological examination of this Inguinal Lymph nodes and mass shown tuberous sclerosis Hodgkin disease[53]. Katsina et al reported a case of 52-year-old female who presented with pain for last 21 days, CT scan shown mass in (L) gluteus muscle. After Biopsy, she was diagnosed a case of DLBCL[54].

Scally et al reported 51-year-old female presented with pain in left hip and diagnosed as Sciatica, a lump approved on her left hip with severe pain, CT showed bullock mass and after biopsy she was diagnosed as B cell NHL[55].

## Diagnostic Challenges

Immune response of Lymphoid tissue causes Proliferation and differentiation of various immune cells associated with non- Hodgkin Lymphoma. Malignant transformation of immune system usually presented in the form of solid tumours of Lymphoid organs and tissues like Lymph nodes, Tonsil, spleen and bone marrow. These tumours can originate from any part of Lymphoid tissue and other organs[56].

Primary lesion occurs in any extra nodal is called as extra nodal Lymphoma. Commonly involved extra nodal tissues are gastrointestinal tract, Waldeger's ring, nasal cavity. It rarely involves mediastinal soft tissues[53-55].

## Conclusion

Neoplasm of extremity many times misdiagnosed as a sarcoma and confirmation of diagnosis delay the treatment and chances to treat and survival decreases as the time prolongs for confirmation of diagnosis. Aggressive disease reduces the chances of survival. Primary CNS Lymphoma often misdiagnosed as Brain tumour and this delays proper treatment and confirmation of diagnosis. Immuno histo-chemistry examination is mandatory to achieve confirm diagnosis.

## Conflict of Interest:

None

## Acknowledgements:

None

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