

REVIEW

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# Primary sacral non-Hodgkin's lymphoma: report of a case and systematic review of literature

Satya Vijay Chigurupati<sup>1</sup>, Mridula Shukla<sup>2</sup> and Manoj Pandey<sup>1\*</sup>

## Abstract

**Introduction:** Isolated primary sacral diffuse large B cell non-Hodgkin's lymphoma is a very rare entity, and only 11 cases have been reported previously.

**Case presentation:** A 36-year-old man was referred with low backache and radiculopathy pain with a clinico-radiological and cytological diagnosis of sacral metastasis. Histopathological examination and immunohistochemistry of image-guided tissue core biopsy from the sacral mass confirmed it as high-grade diffuse large B cell lymphoma (DLBCL). With normal blood counts and bone marrow, and no lesions elsewhere on imaging, he was staged IAE and received 6 cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) regimen chemotherapy followed by radiotherapy. The patient has completed a 3-year follow-up and is doing well with yearly imaging showing no evidence of active disease or recurrence.

**Conclusions:** The case shows the importance of an image-guided core biopsy and immunohistochemistry over a fine needle aspiration cytology in select cases as it can alter the treatment and outcome in patients. Because of rarity, the treatment and prognosis in primary sacral NHL is not still very clear as it is treated as per the guidelines of treatment of bone lymphoma.

**Keywords:** Primary bone lymphoma, Non-Hodgkin's lymphoma, Sacrum, Diffuse large B cell lymphoma

## Introduction

Primary bone lymphoma is a rare entity constituting less than 2% of all lymphomas in the adult population; it usually involves long bones of extremities [1, 2]. The sacrum is a very rare site for primary diffuse large B cell non-Hodgkin's lymphoma (DLBCL), and a systematic search on PubMed showed only 11 reported cases [3–13]. For tumors to be considered as primary lymphoma of the bone, “it has to be a single skeletal site with or without regional lymph nodes or multiple bones involved with no visceral or lymph node involvement” [14]. We report a case of primary

sacral lymphoma in a 36-year-old male who was referred with complaints of low backache and radiculopathy pain.

## Case report

A 36-year-old man was referred to us with a 30-day history of imbalance while walking, lower backache, tingling, and numbness in the left gluteal region radiating to the left lower limb. He was evaluated outside with a contrast-enhanced computed (CECT) scan suggesting a mass lesion in the presacral region with destruction and involvement of the underlying bone (Fig. 1). He also had an image-guided fine-needle aspiration from lesion suggestive of metastatic deposit.

On clinical evaluation, the patient had an antalgic gait with weight-bearing on the right lower limb.

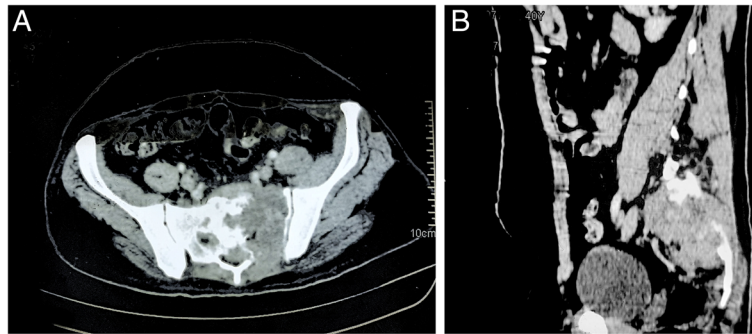
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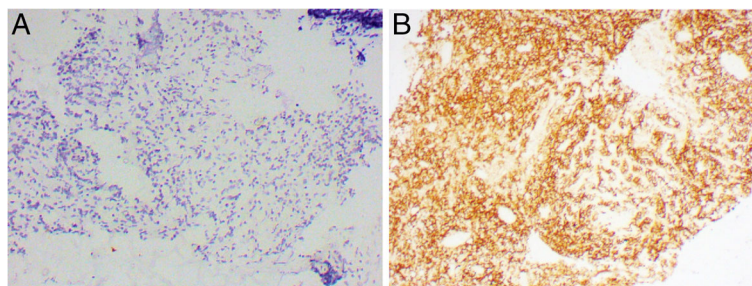
**Fig. 1** Pre-treatment CECT showing mass lesion in presacral region with underlying destruction of the sacrum in **a** sagittal and **b** axial views

Neurological examination showed normal higher mental functions and cranial nerves. Muscle power was 3/5 at left hip, 4/5 at the left knee, and ankle joints. Power in the right lower limb joints was normal. No sensory abnormalities were identified. The straight leg-raising test on the left side was restricted to 40° and was associated with sharp pain. Superficial and deep reflexes were normal in both limbs. The patient had neither bowel and urinary complaints nor history of fever, night sweats, or weight loss. Per abdomen, per rectal, and supraclavicular fossa examination revealed no abnormality. No clinically palpable nodes on systemic examination were found. With a tentative diagnosis of bone secondaries from an unknown primary, he was planned for image-guided core needle biopsy from the sacral mass that was carried out under full aseptic precautions. The histopathology (HPE) was suggestive of malignant round cell tumors. On immunohistochemistry (IHC), cells were positive for CD20 (score 4+), CD10 (score 1+), and ki67 (score 4+). The histological diagnosis was high-grade B cell non-Hodgkin lymphoma (NHL) compatible with diffuse large B cell lymphoma (Fig. 2). Hematology, biochemistry, and bone marrow study

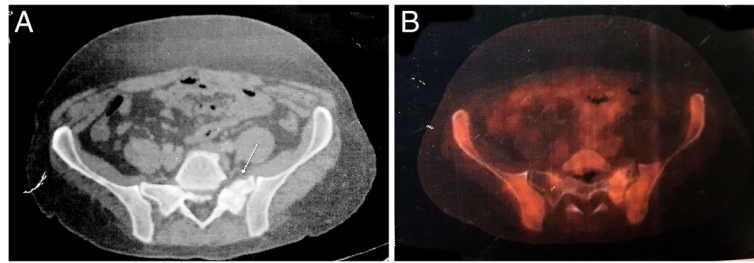
were normal. 18F-fluro-2-deoxy-D-glucose-positron emission tomography (FDG PET) scan showed lytic lesion in the sacrum with no other areas of FDG uptake.

The patient was staged as IAE and started on rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP regimen). After completion of 3 weekly, 6 cycles, the patient was relieved of his pain and numbness and regained 5/5 power in the left lower limb muscles on clinical examination. Reevaluation by FDG-PET was done which showed a mild FDG avid sclerotic lesion of 1.3 × 1.2 cm in the left ala of the sacrum with standardized uptake value (SUV) of 3.22 suggesting a mild active residual disease (Fig. 3). He was started on maintenance rituximab and external photon radiotherapy to the sacrum (45Gy/25#) after multidisciplinary discussion.

Post-treatment FDG-PET was repeated after 3 weeks, which showed metabolically inactive sclerosis at the left sacral ala scored as 1 on Deauville criteria using a 5-point scale as per Lugano classification (Fig. 4). The entire treatment was completed in 2017. The patient was placed on regular 3 monthly follow-up and had no fresh complaints. Follow-up



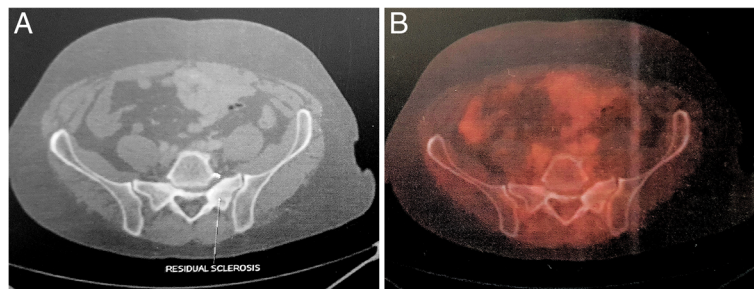
**Fig. 2** Photomicrograph showing **a** malignant round cells on hematoxylin and eosin staining (x10) and **b** cell immunostaining for CD20 (x10)



**Fig. 3** FDG-PET/CT in 2017 after 6 cycles of R-CHOP regimen. **a** Sclerotic lesion in left ala of the sacrum. **b** Mild FDG uptake in the left ala of sacrum (SUV of 3.22)

FDG PET done in 2018 showed a stable ill-defined small sclerotic lesion in the left sacral ala without significant FDG uptake, representing metabolically inactive disease. It also showed FDG uptake (SUV 4) at the site of sacralization of L5 (Fig. 5), which was

showed no significant changes compared to previous FDG-PET (Fig. 7). The patient is asymptomatic without obvious clinical abnormalities and has metabolic complete response 42 months after completion of treatment.

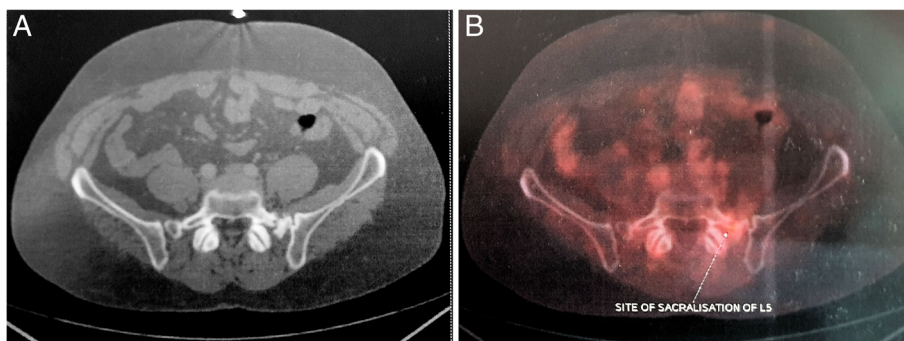


**Fig. 4** FDG-PET in 2017 after 6 cycles of R-CHOP regimen, external beam radiotherapy, and two cycles of maintenance rituximab. **a** Sclerosis at left ala of sacrum **b** with no metabolic uptake

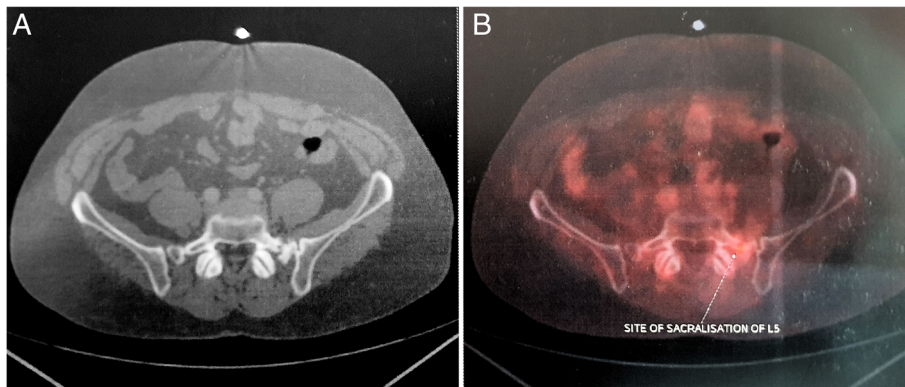
not appreciated in previous scans representing arthropathy due to altered biomechanics. The patient was asymptomatic and clinically no abnormality was noted. Follow-up FDG-PET in 2019 showed non-FDG avid ill-defined sclerosis in the left sacral region and resolution of previously visualized mild FDG at L5-S1 facet (Fig. 6). No fresh complaints were noted. Recent follow-up FDG-PET in June 2020

## Methods

A systematic search was made on PubMed using the string (“sacrale”[All Fields] OR “sacralisation”[All Fields] OR “sacralised”[All Fields] OR “sacralization”[All Fields] OR “sacralized”[All Fields] OR “sacral-s”[All Fields] OR “sacrum”[MeSH Terms] OR “sacrum”[All Fields] OR “sacral”[All Fields]) AND (“lymphoma”[MeSH Terms] OR “lymphoma”[All



**Fig. 5** Follow-up FDG-PET/CT in 2018. **a** Sclerotic lesion in the left sacral ala. **b** Uptake noted at the site of sacralization (SUV 4)

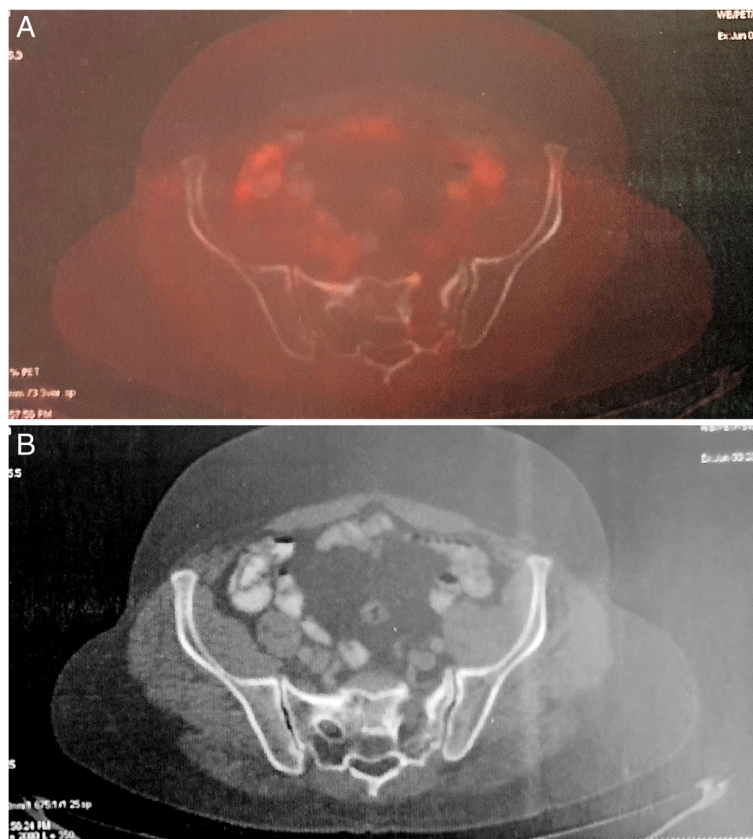


**Fig. 6** Follow-up FDG-PET in 2019. **a** Residual sclerosis in the left sacral ala **b** with the resolution of previous FDG uptake at L5-S1 facet

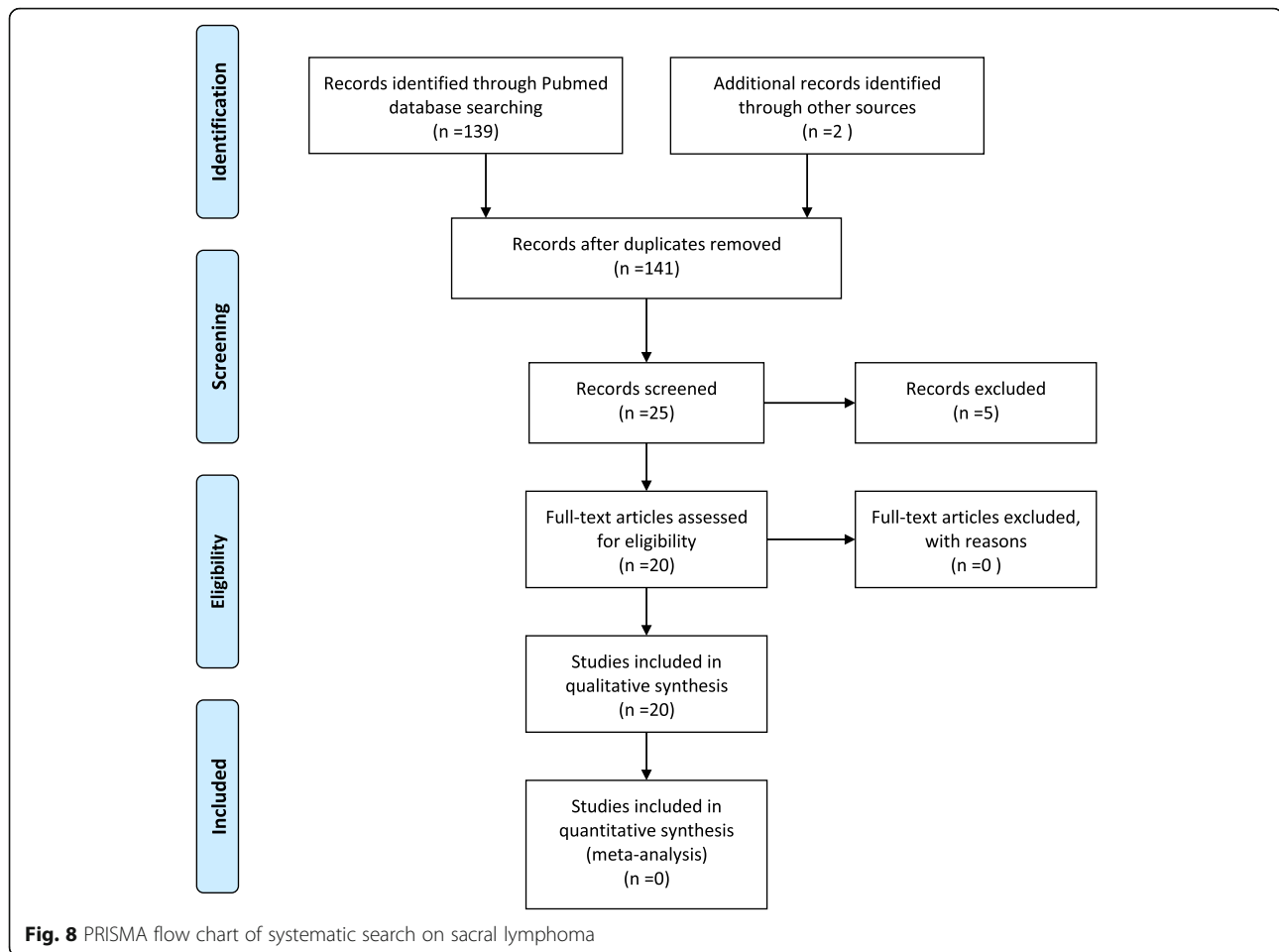
Fields] OR “lymphomas”[All Fields] OR “lymphomas”[All Fields]). The title and abstracts of all the articles were reviewed and for articles wherein no information was provided in abstract and the article that were finally included in review full articles were extracted. Data on age, gender, histological type, treatment, follow-up, and response to treatment was extracted. Data was tabulated.

**Results**

A total of 139 articles were extracted using the search string. Of these, 25 articles were selected and 116 articles were excluded as they did not report on primary sacral lymphoma (Fig. 8). After review of full text, another 5 articles were excluded as they did not report on the primary sacral lymphoma as per the definition reported in introduction. Of the 20 articles, one article reported 2



**Fig. 7** Follow-up FDG-PET in 2020. **a** Subtle sclerosis in the left sacral ala **b** with no FDG avid lesions



cases, and one reported 35 cases, while others reported one case each. In the case series of 35 cases, details of histology and treatment outcome were not reported. In total, 53 cases of sacral lymphoma were identified of which 7 were DLBCL, one DLBCL with EBV and myc translocation, one B cell NHL without further characterization, and 3 cases of Hodgkin's disease while the majority were not characterized and were reported as lymphoma (NOS).

## Discussion

Primary bone lymphomas are rare constituting less than 2% of all lymphomas in the adult population. These tumors mostly involve the femur, other long bones of extremities, and pelvis [1, 2]. Primary tumors of the sacrum are rare, constituting 1–2% of all musculoskeletal tumors [15] and less than 7% of all primary spinal tumors [16]. Metastasis is the most common malignancy in the sacrum, and chordoma is the most common of all primary sacral tumors [17]. Primary bone lymphoma constitutes only 0.4% of all primary bone malignancy [18], of which primary lymphoma has been reported in 53 cases of diffuse

large B cell lymphoma of sacrum which is an extremely rare presentation with only 11 reported cases in PubMed (Table 1). Usually, primary lymphoma of the bone occurs in the middle to elderly age group with male predominance [28]. Lymphoma (NOS) is the most common type encountered [29]. Common clinical symptoms are back pain with or without radiculopathy. Usual B type symptoms like fever, sweating, and weight loss are rarely encountered. The approximate size of the presentation is 2–7 cm, and laboratory findings are usually nonspecific. The most common finding on imaging is osteolytic bony destruction seen in 70% cases [30]. Differential diagnosis of imaging is metastasis, multiple myeloma, and other primary bone tumors. Usual MRI findings are “low signal intensity on T1 weighted images and high signal intensity on T2 weighted images, although not specific of lymphoma of bone” [10]. Sacral chordomas and chondrosarcomas on imaging show calcification specks. In the absence of osteolytic bone destruction and atypical MRI images, FDG-PET is a useful tool. Multiple myeloma and lymphoma have similar characteristics on MRI imaging, but multiple myeloma has

**Table 1** Age, gender, pathological diagnosis, treatment, and outcome in patients with primary sacral lymphoma reported in literature till December 2020

Author and year [Ref]	Age	Gender	Histology	Treatment	Follow-up	Outcome
Nayil K et al. 2011 [9]	56	M	NHL-B cell no further categorization	S1-S2 laminectomy + RT	6 months	Well
Shimada A et al. 2013 [10]	85	M	Non GC type DLBCL, EBV, Myc translocation	R-CHOP	12 months	CR, disease free
Xu T et al. 2020 [13]	84	F	DLBCL	R-CHOP	5 months	CMR
Li GN et al. 2020 [6]	77	M	DLBCL	R-CHOP	1 month	On therapy
Ediriwickrima LS and Zaheer W 2011 [5]	67	M	DLBCL with lupus anticoagulant	R-CHOP	2 months	Disappearance of lupus anticoagulant
Wang J et al. 2020 [19]	35 cases Mean 46.2 years	15 M 20 F	Lymphoma (NOS)	Not described	Not described	NR
Liu JK et al. 2003 [7]	52	M	DLBCL	S2-S3 sacral laminectomy+ RCHOP + RT	4 months	Reduction in size, no metabolic imaging performed
Liu JK et al. 2003 [7]	64	M	DLBCL	3 cycles of CHOP followed by RT	13 months	Reduction in size, no metabolic imaging performed
Thornton E et al 2012 [20]	53	M	Lymphoma (NOS)	Not reported	Not reported	Not reported
Fourati N et al. 2017 [21]	24	-	HD	BEACOPP ×2 ABVD ×4 RT	15 months	CR
Ha-Ou-Nou F et al 2013 [22]	35	M	HD	ABVD	NR	NR
Ezenekwe AM et al 2004 [23]	50	M	Precursor B cell lymphoblastic lymphoma	Carmustine, cyclophosphamide, cytarabine, doxorubicin, etoposide followed by surgical excision	10	CR
Loh JK et al. 2005 [24]	6	M	Lymphoma (NOS)	Subtotal resection	11 years	CR
Hermann G et al. 1997 [25]	NR	NR	Lymphoma (NOS)	NR	NR	NR
Theodorou DJ et al 2000 [12]	58	M	Monostotic primary non-Hodgkin's lymphoma of the bone with intrathecal involvement	Combination chemo Intrathecal MTX RT Peripheral blood stem cell transplant	1 year	CR
Chaari N et al. 2011 [4]	49	F	DLBCL	NR	NR	NR
Kirsch DG et al. 2005 [26]	14	F	HD	Two cycles of vincristine, prednisone, procarbazine, and doxorubicin followed by four cycles of cyclophosphamide, vincristine, prednisone, procarbazine + proton beam RT	2.5 years	CR
Ackerman L et al. 1994 [27]	36	M	Large cell lymphoma	NR	NR	NR
Tazi EM et al. 2009 [11]	45	M	DLBCL	CHOP +RT	10 years	CR, later developed histoplasmosis at

**Table 1** Age, gender, pathological diagnosis, treatment, and outcome in patients with primary sacral lymphoma reported in literature till December 2020 (Continued)

Author and year [Ref]	Age	Gender	Histology	Treatment	Follow-up	Outcome
Amonkar AP et al. 2017 [3]	39	M	GC type DLBCL	RT followed by CHOP	NR	NR same site
Mally R et al. 2011 [8]	24	M	DLBCL	CHOP Intrathecal MTX RT	3 months	NR
Present case	36	M	DLBCL	RCHOP Maintenance R RT	36 months	CR

CR Complete response, CMR Complete metabolic response, NR Not reported, HD Hodgkin's disease, GC germinal center, DLBCL Diffuse large B cell lymphoma

no tracer uptake on isotope scan producing a cold spot. FDG-PET is also useful in disease staging and evaluating treatment response [31]. Histological and immunochemistry is used to confirm the diagnosis. On histology, bony lymphomas show atypical lymphoid cell proliferation. On immunohistochemistry, these tumors are positive for leukocyte common antigen (LCA) and CD20. Primary bone tumors from lymphoma can be differentiated on the basis of histology by their microscopic features for most neoplasms except for small cell osteosarcoma and Ewing's sarcoma, which has to be excluded by IHC for CD99. Small cell carcinoma metastasis from the lung can also be excluded on IHC, as they are positive for cytokeratin and negative for leukocyte common antigen. Treatment of choice is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy regimen followed by radiotherapy. Patients with spinal cord or cauda equina compression features should undergo surgery for decompression and tissue diagnosis followed by radiotherapy [9]. In the present case report, the patient was referred to our department with complaints of low backache and radiculopathy which is quite a very rare presentation. Primary non-Hodgkin lymphoma localized to the bone has a better prognosis than in whom bone involvement is secondary to systemic disease [9]. Because of very few reported cases, and incomplete reporting and reporting after shorter follow-up, the incidence and prognosis of primary sacral lymphoma are not still very clear.

## Conclusion

Primary sacral lymphoma is very rare entity and has imaging similarities with other tumors of sacrum. Definitive diagnosis is made only by HPE, and IHC is required for differentiating it from the rest of bony lesions. Hence, this case demonstrates the importance of insisting on core biopsy and not relying only on fine needle cytology if the diagnosis does not fit the

overall clinical picture; non-Hodgkin's lymphoma has a good response to the R-CHOP regimen and radiotherapy while in a metastatic disease the outcome is dismal. Although few studies show better prognosis in primary bone NHL, the incidence and prognosis of primary sacral lymphoma are not still very clear because of very few reported cases.

## Learning points

- Primary sacral lymphoma is a rare differential diagnosis for primary sacral tumor.
- Definitive diagnosis is by biopsy and immunohistochemistry.
- Treatment options are R-CHOP regimen, radiation therapy, and surgical decompression.
- It is important to obtain a core biopsy and do immunohistochemistry in cases where the imaging and clinical picture does not support the provisional diagnosis.
- Depending upon cytology alone can be disastrous at times.

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None

## Authors' contributions

CSV did the literature search and prepared the draft manuscript. MS did the pathology and drafted the pathological part of manuscript. MP conceived and designed the study and edited the final manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

Not applicable as all information and data are presented in the manuscript.

## Ethics approval and consent to participate

Ethical approval is not required as patient consented for publication.

## Consent for publication

A written informed consent was obtained for publication of this case report and accompanying images. The copy of consent for publication is available with authors.

**Competing interests**

The authors declare that there is no conflict of interests.

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