Primary skull lymphoma: A case report and review of similar cases

Dear Editor,

A true primary malignant lymphoma of the bone is definedas a solitary mass lesion with no evidence of disease at others sites and no systemic dissemination within 6 months of detection of tumor.[1,2] Solitary, diffuse, and multifocal skull lesions fulfilling other criteria of primary malignant lymphoma were kept as selection criteria for our study. The electronic databases (Pubmed and Google Scholar) were searched using key words like extranodal lymphoma, non-Hodgkin lymphoma (NHL) and primary skull lymphoma. Titles and abstracts of the initially identified studies were screened to determine if they satisfied the selection criteria. Full-text articles were retrieved for the selected titles. Reference lists of the retrieved articles were searched for additional publications. We found that sporadic cases have been reported in different journals.[1-23] The patients have variable clinical presentation and management. To our knowledge, this is the largest series of 25 reviewed cases of primary skull lymphoma ever reported.

A 34-year-old male presented to us with history of painless progressive swelling over the left frontal area for the last 1 year. Local examination revealed a 7 × 5-cm, firm, well-defined, smooth surface, non-tender swelling over the left frontal area [Figure 1a]. There was no local rise of temperature or impulse on cough. The overlying skin was healthy. His general and systemic examination revealed no other abnormality. X-ray skull revealed a moth-eaten, lytic lesion over the left frontal area [Figure 1b]. Plain and contrast CT scan of brain revealed a hyperdense, enhancing lesion over the left frontal area having intra and extracranial extension with skull bone erosion [Figure 1c and d]. MRI was not done because of financial constraints. The possibilities of metastatic carcinoma, osteomyelitis, or meningioma were kept in mind. His X-ray chest, ultrasound of abdomen, and bone marrow biopsy revealed no abnormality. Left frontal circumferential craniectomy was done to remove the lesion, with 1-cm healthy skull margin. The tumor was moderately vascular, fleshy in consistency and was found infiltrating the scalp, bone and epidural space [Figure 2a-d]. The extracranial portion was removed along with involved bone, the epidural component was curetted out and the dura was cauterized. Histological and immunopathologic examination confirmed it to be a case of diffuse large B-cell lymphoma [Figure 3a-c]. Post-operatively patient was treated with chemotherapy (CHOP regimen), followed by involved field radiation therapy. After 6 months of surgery patient is doing well, without signs of systemic dissemination.

Comprehensive review of all the published 25 reports in the English literature till date, along with our case is given in tabular form below [Table 1]. All 26 cases are described under the headings of author and year of publication, age/sex, immune status, presenting symptoms, location, radiological findings, treatment given, histological findings, and outcome.

Among 26 reported cases, 15 are female and 11 are male cases. The youngest reported case is of 19-years old and oldest of 80 years with mean age of 50.9 years. Thirteen

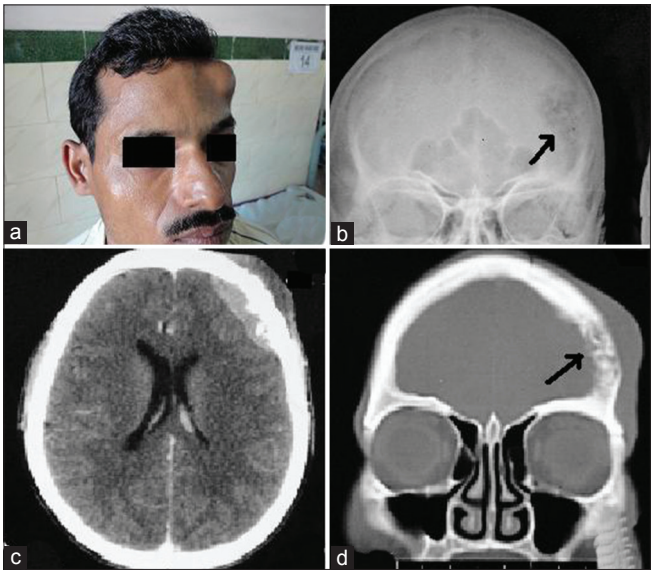

Figure 1: (a) Showing swelling over left frontal area. (b) X-ray skull showing, moth-eaten lytic lesion over left frontal area. (c and d) Contrast CT scan axial view in bone window showing, hyperdence enhancing lesion over left frontal area having intra- and extracranial extension with skull bone erosion

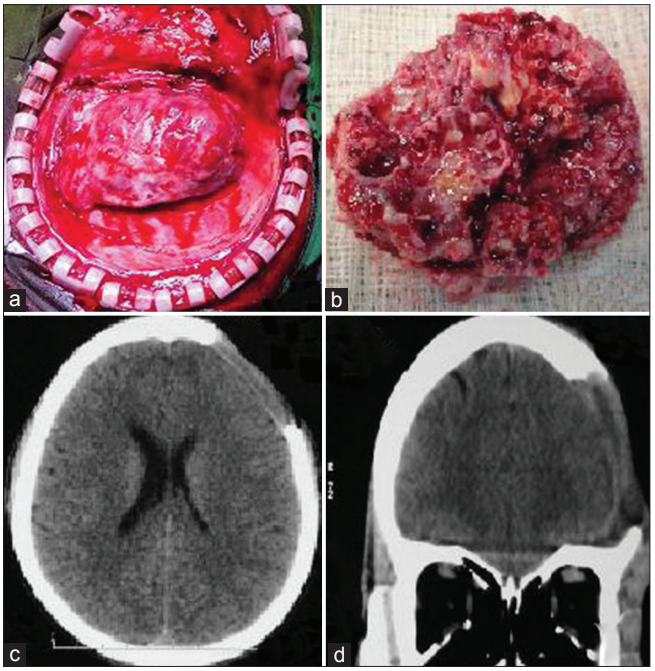

Figure 2: (a) Intraoperative photo showing tumor mass. (b) Intraoperative photo showing eroded skull bone. (c and d) Post-operative CT scan showing no residual tumor and intact dura

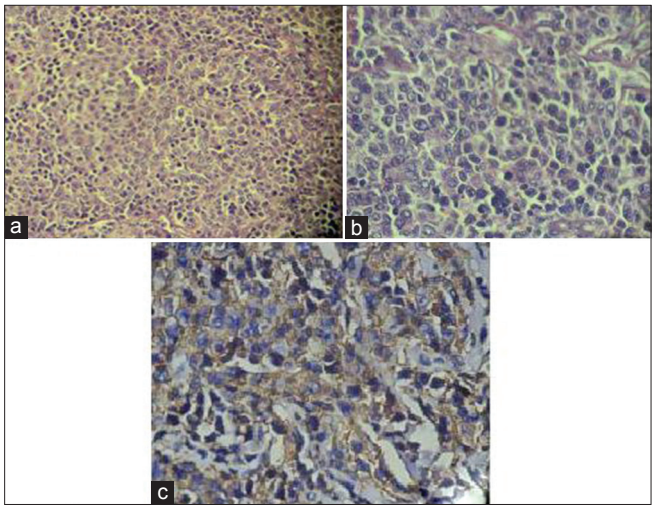

Figure 3: (a) Histopathological slide in low power view showing lymphoid cells in diffuse pattern. (b) Histopathological slide in high power view consisting mostly of large lymphocytes with few small lymphocytes in background. (c) Immmunohistochemestry showing tumor cells, which are positive for CD20

cases presented as scalp swelling without any neurological deficit, seven cases with neurological deficit, three cases with seizure, two cases with progressive proptosis, and one case with multiple cranial nerve palsy. Cases presenting with neurological deficit or seizure had intraparenchymal infiltration. Patients with proptosis had intraorbital extension.[10,17] A case of multiple lower cranial nerve palsies had diffuse primary lymphoma of the scalp that had later eroded the skull.[11] The main clinico-radiological differences between primary cutaneous lymphoma (PCL) of the scalp and primary NHL of the cranial vault include a shorter duration of symptomatology, early onset of focal neurological deficits and large soft-tissue mass in PCL, whereas primary NHL of the cranial vault presents with extensive osteolytic lesions. Twenty cases presented as single-focus lesion whereas rest five cases presented as multiple foci or diffuse lesions.[14] The later five cases were included in our study as the disease process was confined to skull bone only without other sites of dissemination.

All authors have mentioned that incidence of NHLs is more common in immunocompromised (IC) persons than non-immunocompromised (NIC). It has recently been demonstrated that NHLs on the whole are showing a rapid increase in incidence, and over the past 20 years extranodal disease has increased more rapidly than nodal disease. This may be due to the AIDS epidemic, other viral infections, immunosuppressive treatments or environmental factors. But very interestingly we found that among 26 reported cases three cases were IC,[8,9,15] other 23 cases were NIC. This may be due to over reporting of these rare tumors in NIC patients or IC patients may be having lymphoma at multiple sites, there by excluding them from being diagnosed asprimary lymphomas.

Out of 26 cases, radiological finding was available in 24 cases. CT scan was done in 21 cases and MRI in six cases. Hyperdense contrast-enhancing mass was the CT scan finding in all 21 cases. Hyperintense with contrast enhancement in T1W was the MRI finding in three cases and isointense in other three cases. Out of 24 cases, skull bone erosion was found in 15 cases, hyperostosis in four cases and soft tissue component without skull bone erosion in three cases. Because of the characteristic permeating growth pattern of lymphoma, bone destruction was not seen even in patients with a large soft tissue component.[2,10,22] Parenchymal invasion is due to spread of lymphoma cells from diploic space along the emissary veins and cranial nerves to leptomeninges. Radioimaging is not definitively diagnostic because the appearance can mimic that of metastatic carcinoma, osteomyelitis, or meningioma. Therefore, tissue diagnosis is mandatory for proper diagnosis and management. CT scan of neck, chest, and abdomen and bone marrow biopsy should be included in the workup to rule out other evidence of systemic lymphoma.

Histological and immunopathologic examinations confirmed all 26 cases as lymphoma. Revised European American Lymphoma classification was used in recent publications. B-cell NHL was the most common histological subtype. Large T-cell immunoblastic lymphoma was reported in one case.

Out of 26 cases, 10 patients were treated by either surgery or biopsy followed by chemo and radiotherapy. Among these ten patients, intrathecal chemotherapy was given in one case.[4] Eight patients were treated by either surgery or biopsy followed by radiotherapy only. Five patients were treated by surgery or biopsy followed by chemotherapy only. One patient underwent FNAC followed by chemotherapy.[8] Another patient underwent emergency evacuation of the acute intracranial hematoma associated with the tumor mass and biopsy of the tumor.[9] Exact treatment data was not available in remaining one case.[10] CHOP regimen was the most common chemotherapeutic regimen used.

No follow-up data was available in five cases. Even in available 21 cases, it was of variable period ranging from 2 month to 6 years. The outcome was poor in immunocompromised patients and cases having parenchymal infiltration. The survival of patients was found to be better in cases that have undergone surgery followed by chemo and radio therapy.

Although incidence of primary skull lymphoma is very rare, its possibility must be kept in mind in the differential diagnosis of primary skull lesions, irrespective of immune status. Patients can present in various manners ranging from solitary skull lesion to diffuse lesion with or without focal neurological deficit. Although most of the lesions are osteolytic, still few cases could present without lytic lesion. Combined modality of treatment consisting of surgery plus systemic chemotherapy and involved field radiation therapy is considered as optimum treatment for

Table 1: Clinical data of published 25 cases along with present case is given in tabular form below

Publication	Age/ sex	Immune status	Presentation	Location	Radiological finding-Ct/ mri	Treatment given	Histology	Follow-up and outcome
Agbi *et al*., 1983[3]	58 F	NIC	Confusion and neurological deficit for 5 yrs	Rt P single focus. Infiltration of temporalis muscle, dura and cerebral cortex	HO+HD+CE	S+R	Diffuse small cleaved cells	Alive after 7 month
Holtas *et al*., 1985[4]	60 F	NIC	Scalp and facial mass	Lt F, supraorbital mass. Single focus	HO+CE	S+Oral steroid	Diffuse large cells	Alive after 6 month
Holtas *et al*., 1985[4]	20 M	NIC	Seizures	Rt F Single focus, infiltration of dura and cerebral cortex	HD+CE	S+R+Intrathecal Chemotherapy	Poorly differentiated lymphocytic lymphoma	Alive after 5 month
Maiuri *et al*., 1987[5]	51 F	NIC	Headache for 2 months; bilateral papilloedema	Rt P-O, Single focus. Weak adhesion to dura	HD+CE	S+R	Lymphoblastic lymphoma	Alive after 2 years
Parekh *et al*., 1993[6]	65 F	NIC	Headache and neurological deficit for 3 months	Lt P, Single focus. Infiltration of dura	HD+CE	S+R	Malignant B cell NHL	Died after 6 yrs
Isla *et al*., 1996[7]	75 F	NIC	Seizure	Lt F, single focus. Infiltration of dura	HD+CE	S+R+C	Centroblastic centrocytic B cell lymphoma	Alive after 3 years
S. Bhatia *et al*., 1997[8]	50 M	IC	Headache and swelling on scalp for 4 days	Rt P, single focus with epidural component	HI+CE+BE	FNAC+C	Large B cell lymphoma	Died after 7 month
Jamjoom *et al*., 1998[1]	25 M	NIC	Headache for 2 months, bilateral papilloedema	Midline P, single focus. Subgaleal with epidural component	HD+CE+BE	S+R	Large T cell immunoblastic lymphoma	Alive after 5 month
Moragas *et al*., 1999[9]	38 M	IC	Coma, acute frontal and intracerebral Haematoma	Rt F-P multiple foci	NA	Evacuation of haematoma; +Biopsy	Large BCL	Died of pneumonia
S mongia *et al*., 2003[2]	25 M	NIC	Scalp swelling with local pain for 6 months	Large single scalp swelling over Rt F-T-P area.	Scalp swelling without BE	S+R+C	NHL	Disease-free after 2.5 yrs
Kantarci *et al*., 2003[10]	65 M	NIC	Scalp and eye lid swelling with proptosis for 6 months	Diffuse mass in the scalp, bilateral F-P region and invasion of the orbit, dura and parenchyma .	IE+CE without BE.	BIOPSY	Diffuse primary cutaneous BCL	NA
Madan *et al*., 2004[11]	70 F	NIC	Scalp swelling for 1 yr with cranial nerves IX, X and XII palsies	Large diffuse swelling extending from back of Lt ear to nape of neck, forehead and cheeks anteriorly	HD+CE+BE	Biopsy+C	Diffuse primary cutaneous BCL	NA
Agrawal *et al*, 2004[12]	43 F	NIC	Scalp swelling for 8 months with pain	Lt frontal paramedian swelling. single focus	HD+CE+HO	S+R	Diffuse large cell lymphoma	NA
Andrew *et al*., 2004[13]	80 F	NIC	Scalp welling for 6 months	Neck and back of head single focus with intra parenchymal extension	HD+CE+BE	Biopsy+C+R	Diffuse large B-cell NHL	Died after second chemo
K. Aquilina *et al*., 2004[14]	72 F	NIC	Seizures; headaches for 1 year; scalp masses	Diffuse vault infiltration; multiple foci, with intra parenchymal extension	HD/ HI+CE+BE	Biopsy+C	Small to intermediate Cell, BCL	Alive after 6 month
Z. Szucs *et al*., 2005[15]	42 F	IC	Scalp welling with headache	Lt O-P region. single focus, with subgaleal and intra parenchymal extension	HD+CE+BE	Biopsy+R	B-type large cell NHL.	Alive after 8 month

Contd...

Table 1: Contd...

Publication	Age/ sex	Immune status	Presentation	Location	Radiological finding-Ct/ mri	Treatment given	Histology	Follow-up and outcome
Christopher *et al*., 2006[16]	76 F	NIC	Scalp Lump with hemi paresis	Rt O-P region. single focus, with subgaleal and intra parenchymal extension	HD/ HI+CE+BE	Biopsy+R	Diffuse large BCL	Died 2 month after
Amit Agrawal *et al*., 2008[17]	50 F	NIC	Scalp swelling with progressive proptosis for 5 months	Rt F-T area single focus, with subgaleal, intra orbital and parenchymal extension	HD+CE+BE	Biopsy+R	Diffuse and medium size NHL	Alive after 18 months
Saeed H *et al*., 2009[18]	58 F	NIC	Painful scalp swelling for 4 months	Lt F–P area single focus with subgaleal and epidural component	HD+CE+BE	S+C+R	Large B-cell NHL	After 6 month she died
Saeed H *et al*., 2009[18]	60 M	NIC	Headache and painless swelling for 4 months	Rt T-P area single focus, with subgaleal and epidural component	HD+CE+BE	S+C+R	Large B-cell NHL	Alive after 1 yr
D. Renard *et al*., 2009[19]	67 F	NIC	Painful scalp swelling	Rt F area single focus with subgaleal with epidural component	HD/ IE+CE+BE	Biopsy+C	Large B-cell NHL	NA
M. Khalid *et al*., 2010[20]	19 M	NIC	Scalp swelling with headache for 6 months	Lt F-P multifocal skull vault lesion with subgaleal and epidural component	HD+CE+BE	Biopsy+C	Low grade NHL	Alive after 2 yrs
Jovit *et al*., 2011[21]	50 M	NIC	Scalp swelling for 4 months	Diffuse swelling over Lt T-P area with subgaleal and subdural component	HD+BE	S+C+R	BCL	NA
Zouhour *et al*., 2011[22]	4 2F	NIC	Scalp swelling for 10 months	Rt P bone single focus, with subgaleal and epidural component	IE lesion, without BE	Biopsy+C+R	Diffuse Large B-cell NHL	Alive after 9 month
Salunke *et al*., 2013[23]	30 M	NIC	Scalp swelling for 3 months with headache and neurological deficit	Lt F single focus with subgaleal and cerebral cortex infiltration	HD+CE+BE	S+C+R	Diffuse Large B-cell lymphoma	Alive after 6 month
Senapati *et al*., (Present case)	34 M	NIC	Scalp swelling for 1 yr	Lt F single focus with subgaleal and epidural component	HD+CE+BE	S+C+R	Diffuse Large B-cell lymphoma	Alive after 6 month

NIC=Non-immunocompromised, IC=Immuno compromised, F=Frontal, T=Temporal, P=Parietal, O=Occipital, HO=Hyperostiosis, HD=Heperdense, HI=Hyperintense, CE=Contrast enhancing, BE=Bone erosion, S=Surgery, C=Chemotherapy, R=Radiotherapy and BCL=B-cell lymphoma

primary skull lymphomas. In IC, diffuse lesions and those cases who cannot tolerate systemic chemotherapy, biopsy followed by involved field radiation therapy is a reasonable alternate option. Generous reporting of such cases with longer follow-up period will help us in better understanding of such a rare entity.

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