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

Dear Editor,

A true primary malignant lymphoma of the bone is defined as a solitary mass lesion with no evidence of disease at other sites and no systemic dissemination within 6 months of detection of tumor.\(^\text{1,2}\) 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.\(^\text{1-23}\) 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
Parenchymal invasion is due to spread of tumor at multiple sites, thereby excluding them from being solitary skull lesion. Other extracranial lymphoma may be due to over-reporting of these rare tumors in NIC patients or IC patients may be having lymphoma. We found that among 26 reported cases three cases were IC, 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 as primary 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. 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. 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 emergency evacuation of the acute intracranial hematoma associated with the tumor mass and biopsy of the tumor. Exact treatment data was not available in remaining one case. 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[9] | 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[10] | 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[11] | 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 | IE+CE without BE | Diffuse primary cutaneous BCL | NA |
| Kantarcı et al., 2003[12] | 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 | Scalp swelling without BE | IE+CE without BE | Diffuse primary cutaneous BCL | Disease-free after 2.5 yrs |
| Madan et al., 2004[13] | 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[14] | 43 F    | NIC            | Scalp swelling for 8 months with pain masses | Lt frontal paramedian swelling, single focus | HD+CE+HO | S+R | Diffuse large cell lymphoma | NA |
| Andrew et al., 2004[15] | 80 F    | NIC            | Scalp swelling 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[16] | 72 F    | NIC            | Seizures; headaches for 1 year; scalp masses | Diffuse vault infiltration; multiple foci, with intra parenchymal extension | HD+HO | Biopsy+C | Small to intermediate Cell, BCL | Alive after 6 month |
| Z. Szucs et al., 2005[17] | 42 F    | IC             | Scalp swelling 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 |
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.

**Satya Bhusan Senapati, Sudhansu Sekhar Mishra, Mannmath Kumar Dhir, Srikantha Das, Subrat Burma**
Departments of Neurosurgery, Pathology, Shrirama Chandra Bhanj Medical College and Hospital, Cuttack, Odisha, India

**Correspondence to:** Dr. Satya Bhusan Senapati
E-mail: satya.bhusan.senapati@gmail.com

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