

Isolated Primary Malignant Lymphoma Arising from the Skull Base

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Abstract Primary skull base lymphoma is quite rare entity, accounting for 1% - 2% of all skull base tumors. Due to its rarity and its similarity to other tumors skull base lymphoma remains a diagnostic challenge. We present a 3-year-old previously healthy boy presented with blindness and exophthalmos revealing a primary skull base lymphoma. The clinical and the radiological features of the lesion have been described as well as the pathologic findings. Lymphoma, although uncommon, should be included in the differential diagnosis of such neoplasms of the skull base. Early diagnosis and treatment as prompt management are crucial for both a visual and vital prognosis.

Keywords: Lymphoma, skull base, optic chiasma, Biopsy

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1. Introduction

Lymphomas comprise approximately 11.5% of all pediatric malignancies, making them the third most common cancer. Primary skull base lymphoma is quite rare entity, accounting for 1% - 2% of all skull base tumors [1,4,5]. Approximately 60% of pediatric lymphomas are non-Hodgkin's lymphoma (NHL). Boys are affected more often than girls with a 3:1 ratio and the peak incidence of NHL is between the ages of 7 and 11 years. Atypical presentations involving the skull or cranial base exclusively have been reported, due to its rarity and its similarity to other tumors skull base lymphoma remains a diagnostic challenge. Although lymphomas of the skull base have been classified previously as non-CNS, or extracerebral lymphomas, recent reports described these lesions as atypical intracerebral or primary CNS lymphomas {PCNSL} [1,4,5,6].

We present a 3-year-old previously healthy boy presented with blindness and exophthalmos revealing a primary skull base lymphoma.

2. Case Report

A 3-year-old previously healthy boy rapidly developed progressive bilateral visual loss and exophthalmia. The otolaryngology examination revealed a voluminous tumor in the cavum. Magnetic resonance imaging revealed a

bulging appearance of the optic chiasm, with homogeneous enhancement after gadolinium administration.

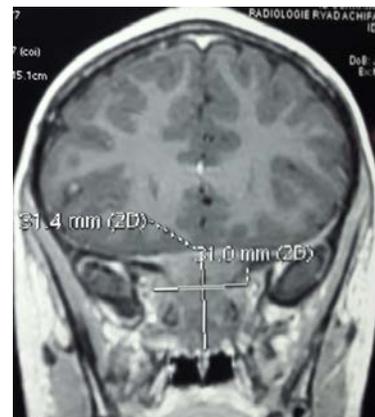


Figure 1. Coronal cranial MRI demonstrating a tumour of skull base



Figure 2. sagittal cranial MRI demonstrating a tumour of skull base

In the absence of clinical clues for a specific diagnosis despite extensive investigation, an endonasal biopsy was performed, resulting in a high-grade malignant b-cell lymphoma. Further evaluation (including ct chest, abdomen, pelvis, cerebrospinal fluid (CSF) analysis, serological investigations and bone marrow biopsy showed no evidence of immunosuppression of systemic disease, or of other tumours. Therefore the conclusion was that this immunocompetent child had a primary central nervous system lymphoma isolated in skull base and the optic chiasm. Treatment included two cycles of polychemotherapy (rituximab, methotrexate, carmustine, etoposide, methylprednisolone). Subsequently, the patient exhibited significant improvement in vision, and was still disease-free at the 1-year follow-up examination.

3. Discussion

Lymphoma are the third most common malignancy in childhood, and account for 11.5% of all childhood malignancy. IT can involve any structure in the head and neck region enlargement of the cervical or other lymph nodes is the most common manifestation of NHL, extra nodal involvement of NHL is more frequent in children than in adult. Primary skull base lymphoma is a quite rare entity, accounting for 1% - 2% of all skull base tumors [1,4,5,6].

There is an increased risk for the development of NHL in children with some form of T-cell deficiency, such as those with congenital immunodeficiency syndromes, acquired immunodeficiency syndrome (AIDS), or prescribed immunosuppressive therapy. Lymphoma of chiasm has been reported in patients with AIDS [2,3], in whom the incidence of PCNSL is increased. Gray et al [7] reported a patient with headaches, loss of hearing, and loss of vision, who had a PCNSL of the optic chiasm.

Nearly 30 cases of skull base lymphoma have been reported in the literature, with less than 10 reported in children [4-8]. The majority of the patients were male, with male to female ratio 5:3. The interval from presentation to diagnosis varied from just over a week to nearly a year. Those with cranial nerve involvement often seek medical attention sooner, as compared to other patients who present late due to raised intracranial pressure symptoms from mass effect. The differential diagnosis of a destructive lesion in the anterior skull base, as described in this case, includes squamous cell carcinoma arising from the paranasal sinuses, chordoma, metastasis, intraosseous meningioma and esthesioneuroblastoma. Lymphoma, although uncommon, should be included in the differential diagnosis of such neoplasms of the skull base.

Both CT and MRI are essential for the complete assessment of skull base lesions, The imaging characteristics of NHL that involve the cranial base have previously been described [9].

But MRI with gadolinium is in fact considered as the imaging method of choice for the intracranial lymphoma diagnosis, which usually shows an isointense to gray matter on T1-weighted images and slightly hypo-, iso, or hyperintense on T2-weighted or protondensity images. Skull base NHL often shows heterogeneous enhancement with gadolinium. Lesions in the intracranial epidural space

may enhance en plaque (dural tail) or homogeneously; both features are reminiscent of meningioma. But, unlike meningioma, NHL does not induce hyperostosis of the adjacent bone. However there are limited numbers of published descriptions of the imaging features of lymphoma affecting the central skull base.

Histologic varieties of NHL are divided into low-, intermediate-, or high-grade categories based upon their clinical behavior and over 90% of children have high-grade disease at presentation. High-grade lesions include large cell, lymphoblastic and small cell noncleaved lymphomas. Large cell lymphomas constitute about 27% of pediatric NHL and have been demonstrated to have a t(2;5) chromosomal rearrangement in 50% of cases that results in the production of a novel chimeric protein.

Although the histopathologic characteristics of PCNSL and NHL metastatic to the intracranial space are practically indistinguishable, PCNSL most often involves the brain parenchyma, typically near the ventricles, whereas NHL with secondary central nervous system (CNS) involvement usually presents in the leptomeninges or dura [8,10,11]. The lack of dural or meningeal involvement in our patient, together with the absence of any extracranial manifestations of NHL noted on his systemic workup, suggests that his lymphoma falls into the category of PCNSL. The differential diagnosis is best resolved by surgical biopsy, as was performed in our patients.

In our patient, the relatively rapid and progressive visual loss in both eyes in a previously healthy child, coupled with the imaging abnormalities, suggested malignant glioma of the optic nerve and chiasm. This case demonstrates the importance of considering the diagnosis of lymphoma in this setting.

The evaluation of the child suspected to have a lymphoma begins with a complete history and physical. Definitive diagnosis requires tissue for pathologic evaluation, which may be obtained by a tumor biopsy. The tissue should be sent fresh to the pathologist to allow for flow cytometry; additional studies may also include immunohistochemical staining or electron microscopy. Because most pediatric patients with NHL present with disseminated disease, a complete staging work-up must be undertaken.

This would include laboratory studies (to include LDH, LFT's, and HIV), LP with CSF analysis, bilateral iliac crest bone marrow biopsy, CT of the chest, abdomen and pelvis, and bone scan.

The reasoning for such an extensive work up is that accurate clinical staging is of utmost importance in assigning patients to an appropriate treatment protocol.

Several different staging systems exist for NHL, probably the most widely used is the Ann Arbor system. In this system, Stage I indicates involvement of a single lymph node region or extralymphatic organ. Stage II implies involvement of two or more lymph node regions on the same side of the diaphragm or one lymph node region and one extralymphatic organ on the same side of the diaphragm. Stage III includes cases that involve lymph node regions on both sides of the diaphragm with or without extralymphatic organ or splenic involvement.

Finally, Stage IV indicates diffuse involvement of one or more extralymphatic organs with or without lymph node involvement.

Multiagent chemotherapy is the mainstay of treatment for NHL. The most commonly used agents include cyclophosphamide, doxorubicin, vincristine, and prednisone. Some protocols for Stage III and IV disease add methotrexate and additional agents may be utilized for recurrent disease.

Patients with a second relapse may be candidates for ablative therapy followed by bone marrow transplant. Radiotherapy is not routinely used for treatment of NHL but may be employed in cases where mass lesions are causing life-threatening problems [7,8,9,10].

With new and continuously evolving chemotherapeutic regimens, the overall event-free survival (EFS) for NHL in a Swedish pediatric population improved from 19% in

the time period from 1975-1979 to 74% from 1980-1994. [11,12].

In this study population another significant prognostic factor was stage of initial disease. In the later time period, patients with Stage I or II disease demonstrated EFS of 86%, while patients with Stage III or IV disease were found to have EFS of 64% and those patients with bone marrow or CNS involvement at presentation had EFS of only 38% and 20% respectively [10,11]. Other sources report similar survival rates of 85-95% for Stage I and II NHL, better survival rates for Stage III and IV BL-75-85%, and similar rates for Stage III and IV lymphoblastic NHL-65-75% [10,11,12].

Table 1. Published literature on skull base primary lymphoma published in adult population. Abbreviations: N.A.: not available, SB: sphenoid bone, ES: ethmoid sinus, CS: cavernous sinus, RP: retropharyngeal space, MF: middle fossa, PF: posterior fossa, Bx: biopsy, PR: partial resection, GTR: gross total resection, RT: radiotherapy, CT: chemotherapy, iv: intravenous, it: intrathecal

	Age	Sex	Symptom Interval	Pathology	Involvement Site	Surgery	Treatment	Outcome	Follow Up
Oyama <i>et al.</i> 1992 [9]	62	M	4 months	B cell lymphoma	SB, CS	PR	RT, CT	Alive (R)	5 months
Jaiswal <i>et al.</i> 2000 [8]	40	M	6 months	B cell lymphoma	PF, CS	PR	CT, RT	Alive	3 months
Dare <i>et al.</i> 2001 [1]	64	F	3 months	B cell lymphoma	SB, ES, CS, MF	Bx	RT, CT (it, iv)	Alive	1 year
Tsai <i>et al.</i> 2002 [3]	60	F	2 months	B cell lymphoma	SB	PR	CT	N.A.	N.A.
Jung <i>et al.</i> 2004 [5]	56	F	2 months	B cell lymphoma	SB, CS	Bx	CT (iv, it)	N.A.	N.A.
Hans <i>et al.</i> 2005 [4]	64	M	9 months	B cell lymphoma	SB, ES	Bx	CT (iv), RT	Alive	1 year
Teo <i>et al.</i> 2013 [2]	49	M	3 weeks	B cell lymphoma	SB, ES, MF, RP	GTR	CT (iv, it)	Died	16 years

4. Conclusion

Non-Hodgkin lymphoma involving the skull base is a very rare tumor. With an increasing incidence of CNS lymphoma, more atypical presentations are reported. It is, therefore, important to include lymphoma in the differential diagnosis of skull base lesions. Early diagnosis and treatment of this rare pathological entity are necessary for clinicians who may encounter similar presentations, as prompt management is crucial for both a visual and vital prognosis.

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