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Case Report OMICS International

Primary Bone Burkitt's like Lymphoma of the Skull Mimicking Meningioma - Case Report and Review of Literature

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Abstract

Primary Bone Lymphoma of the skull is extremely rare and has a variable clinical course and prognosis. We are describing a case of a 26 year old woman who presented with a 2 year history of intermittent scalp swelling and skull pain. Brain MRI showed thickening of the bilateral frontal bones and band thickening of the underlying meninges suggestive of band meningiomatosis. Patient was presumably diagnosed with a meningioma based on radiological findings and underwent resection; however, pathology was consistent with a B-cell lymphoma with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma. A PET CT scan showed sacral bone hypermetabolic lesion which was biopsied and consistent with same lymphoma features. She received chemotherapy with Rituximab and Hyper-CVAD protocol (Table 1) and had a sustained ongoing complete remission 19 months after her initial diagnosis. Several cases of primary lymphoma of the skull or cranial vault have been described in the literature, but only one other case with the same pathology of Burkitt- like lymphoma was found.

Keywords: Lymphoma; Burkitt lymphoma; Pathology

Introduction

Primary bone lymphoma is an extremely rare form of extranodal lymphoma, originally described in 1928 by Oberling, which is limited to the bone or bone marrow without any systemic involvement [1]. It represents around 7% of all primary malignant bone tumors and less than 1% of malignant lymphomas [1]. It usually emerges from the medulla, presents as a localized, single lesion and can involve any part of the skeletal body. PBL has variable cell subtype, molecular features, and diagnosing criteria. It has high cure rates and different treatment plan compared to other primary bone tumors, and thus it is very important to differentiate between them [2].

Schedule A: Cycles 1,3,5,7	Schedule B: Cycles 2,4,6,8
Cyclophosphamide Vincristine Doxorubicin Dexamethasone	Methotrexate Cytarabine
Hyper: Hyperfractionated, C: Cyclophosohamide, V: Vincrisine, A: Adriamycin (Doxorubicin), D: Dexamethasone, alternating with Methotrexate and Cytarabine	

Table 1: HyperCVAD Protocol.

The PubMed database of the National Library of Medicine and National Institutes of Health, Google Scholar, and Science Direct databases were used to search for published cases meeting the definition of PBL of the skull. The following terms were searched, "primary non-Hodgkin's lymphomas of the skull","Primary skull lymphoma", "Primary lymphoma of the cranial vault", and "Primary non-Hodgkin's lymphoma of the cranial bone", "lymphoma mimicking meningioma". In this article, we report a case that received a different treatment strategy from those previously reported and provide a literature review of this disease.

Case Report

A 26 year old lady presented to our Hematology Oncology Clinics in April 2015. She had a 2 year history of intermittent scalp swelling and mild scalp pain. At that time, patient underwent several imaging studies including a CT scan brain and MRI brain.

CT scan was suggestive of hyperostosis meningioma en plaque and showed multifocal dural enhancing thickening/masses mostly seen along the right cerebral hemisphere extending from the frontal into the parietal regions with a small focus along the left frontal region associated hyperostosis involving both sides more so on the right with areas of sclerosis and lysis. Lesion appeared to be infiltrating the dura at multiple areas with invasion of the overlying bone and soft tissue (Figure 1).

Brain MRI showed thickening of the bilateral frontal bones symmetrically with a symmetrical and benign looking overgrowth of the inner table of the frontal bones bilaterally along with band thickening of underlying meninges especially on the right side. Lytic enhancing lesion in the left frontal bone with mixed sclerotic and lytic changes and intraosseous enhancement of the lesions were also seen (Figure 2).

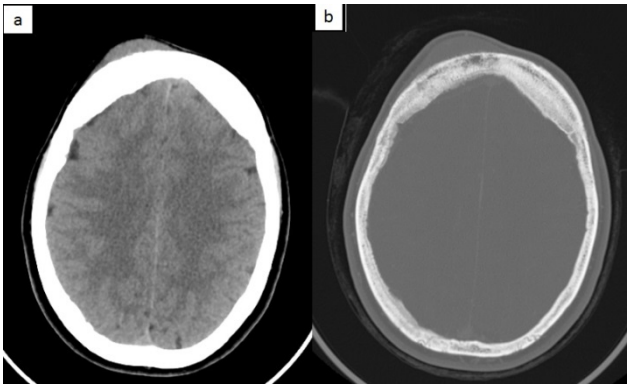

Figure 1: Brain CT scan suggestive of hyperostosis meningioma en plaque: multifocal dural enhancing thickening /masses mostly along the right cerebral hemisphere from the frontal to the parietal regions associated with hyperostosis of the skull infiltrating the dura and adjacent bone and soft tissue.

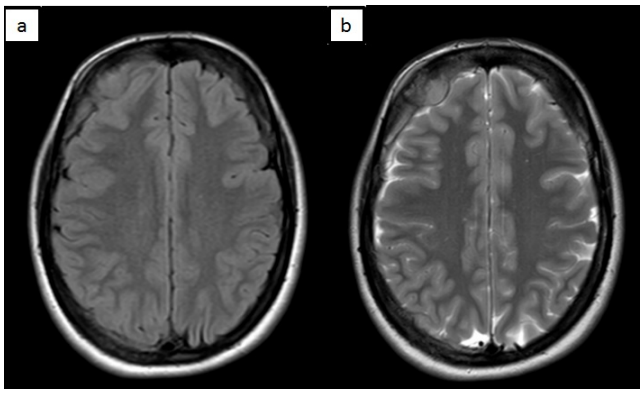

Figure 2: Brain MRI showing irregular dural thickening at the right frontal lobe having a band-like appearance with a nodular component associated to an overlying mild hyperostosis and a minimal overlying soft tissue thickening having an intermediate to high T2/Flair signal intensity. 2a: Flair, 2b: T2.

This was very suggestive of hyperostosis frontalis interna or band meningiomatosis. A craniotomy and tumor resection was done under the consideration that the patient most likely had a meningioma. Pathology examination showed that both the dura and bone were involved by a diffuse infiltrate of large atypical lymphocytes displaying irregular nuclear contours, prominent nucleoli, conspicuous mitoses, and numerous tingible-bodymacrophages (Figure 3). Immunohistochemistry of atypical lymphocytes was positive for CD20, CD10, and Bcl-6 and negative for CD3, CD5, TdT, and CD34. Index of proliferation by Ki-67 was greater than 90%. EMA was negative for meningioma (Figure 4). These findings were consistent with a high grade B Cell Lymphoma.

Cytogenetics by FISH studies were done which were positive for MYC/IGL fusion (90% of nuclei), 3 copies of IGK (45% of nuclei), and 3 copies of IGH (40% of nuclei) but negative for BCL2 gene rearrangement and BCL6 gene rearrangement. Absence of translocations BCL2 or BCL6 excludes the possibility of "double-hit lymphoma."

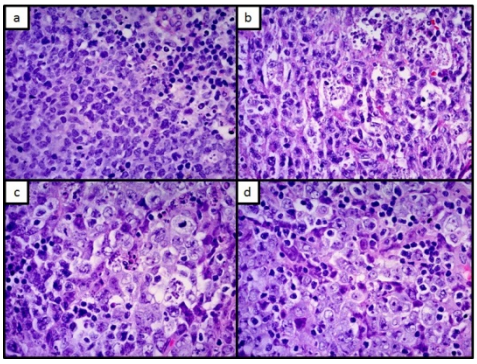

Figure 3: High grade lymphoma showing features intermediate between DLBCL and Burkitt lymphoma (H&E 400X). 3a: Intermediate sized neoplastic lymphocytes with non-neoplastic small lymphocytes (upper right corner) 3b: Intermediate sized neoplastic lymphocytes with numerous tingible body macrophages resembling the "starry sky" appearance seen in Burkitt lymphoma. 3c & 3d: Large size neoplastic lymphocytes resembling diffuse large B cell lymphoma.

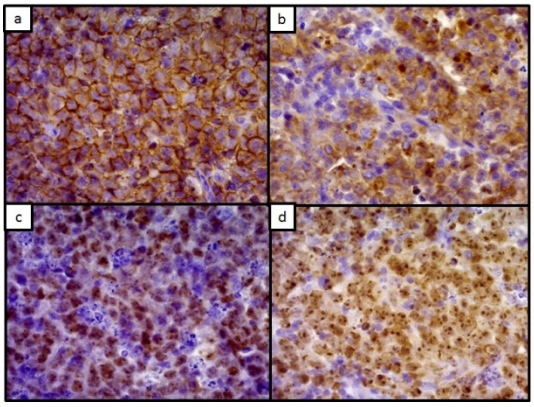

Figure 4: High grade lymphoma (H&E 400X). 4a: CD20 positive neoplastic lymphocytes. 4b: CD10 positive neoplastic lymphocytes. 4c: BCL6 positive neoplastic lymphocytes. 4d: Ki-67 is positive in over 90% of the neoplastic lymphocytes.

This lymphoma was best classified as B-cell lymphoma with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma at the time of diagnosis according to the 2008 WHO Classification of lymphomas. But currently it would be best classified as High Grade B cell lymphoma, NOS.

Pet CT scan was also done and was positive in the S1 vertebra which was biopsied and showed the same pathology. Bone Marrow biopsy and aspirate were negative. HIV and Hepatitis B testing were negative.

Our patient had a primary bone lymphoma of the skull invading the dura with another lesion in the vertebra with a pathology classified as B-cell lymphoma with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma. Therefore, due to the aggressive

nature of Burkitt lymphoma, we decided to start the patient on a high intensity chemotherapy regimen, Hyper-CVAD (Table1) with Rituximab. She received 8 cycles of Rituximab and HyperCVAD, and had a complete remission. Follow up for 19 months post diagnosis by brain MRI's and PET-CT's scan showed no recurrence of the tumor.

Discussion

Primary bone lymphoma is characterized as a lymphoma of the bone or bone marrow without proof of any simultaneous systemic involvement [1]. The diagnosis of PBL follows the criteria originally proposed by Coley in 1950 with slight modifications and are as follows: "Lymphoma presenting in an osseous site with no evidence of disease elsewhere for at least six months after diagnosis. The presence of regional lymph node involvement does not exclude a diagnosis of PBL, but a histological examination of the lymph node is necessary [3].

These criteria suggested that only a solitary bone was involved, so in 1987, Ostrowski et al reclassified bone lymphomas into 4 subgroups: "Group 1 consists of solitary primary bone lymphoma, Group 2 includes cases in which more than one bone is affected but no nodal or visceral disease is present. Group 3 includes cases with distant nodal disease and Group 4 with visceral disease.

According to the 2002 World Health Organization classification of tumors of soft tissue and bone, the criteria for a diagnosis of PBL are [1] a single skeletal tumor with or without regional lymph node involvement, and [2] multiple bone lesions without visceral or lymph node involvement [1,4].

According to all those criteria mentioned above, our patient was diagnosed with a primary bone lymphoma with 2 bone lesions (skull and spine) that was invading the dura.

And according to the Ann Arbor staging system [5], she was evaluated as stage IVe due to the distant vertebral lesion.

It's occurrence in the skull is actually the rarest to find and is seen in only 1% of primary bone lymphoma, while the femur (50%) and pelvis (15-25)% are the two most common sites, and others include the tibia/fibula, humerus, spine and scapula [1,2]. Our patient was diagnosed at the age of 26, much younger than the median age of this population which was 48 years in 19 similar cases of primary bone lymphoma of the skull which we reviewed [3-22].

The clinical presentation was the most commonly seen with skull lymphoma, where most cases reviewed also presented with a scalp lump or swelling [6-13], [15,21,22].

Other presentations included headache [9,10,13,14,18,20] focal neurological deficits such as loss of vision [10] , behavioral changes [10] , double vision [14] , facial nerve palsy 14, and seizures [19,22] . Four of the cases were also confused with a meningioma [13,17-20] and one case with osteomyelitis [16].

The pathology in our case was B-cell lymphoma with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma, however, only one case of primary skull lymphoma of the same pathology was found in the literature 6 . In the different case series and reviews of literature, it was observed that most primary bone lymphomas seen were diffuse large B-cell lymphomas, other lymphomas with fewer occurrence were follicular, marginal zone, anaplastic large cell, Hodgkin, and T-cell lymphomas [1]. There are also only three reported cases of Burkitt lymphoma involving skull bones [11].

Most of the cases reviewed were treated with a low intensity chemotherapy regimen similar to CHOP or CEOP with or without Rituximab [7-20] and one case was treated with high dose methotrexate [17].

DLBCL with mutations of c-myc and intermediate B-cell lymphoma have shown poor results with standard DLBCL treatment like R-CHOP [23,24] .

For B-UCL (B cell lymphoma, unclassifiable with features intermediate between DLBCL and Burkit lymphoma) patients with MYC rearrangement who were treated with R-CHOP had a significantly shorter overall survival than those treated with intensive regimens such as R-hyperCVAD [25].

And for these reasons, we decided to treat our patient with an intensive regiment, R-HyperCVAD, and according to our knowledge, no other cases of primary bone lymphoma treated with this regimen have been reported in the literature. Follow up 19 months later, patient is still in complete remission by brain MRI's and PET-CT scans. In general, primary bone lymphomas have a 5-year overall survival of 61% with 46% of patients progression free at 5 years [26] and most of the cases in our review of literature had no recurrence at follow up.

Conclusion

To date, no optimal treatment for cranial vault malignant lymphoma has been established due to the low incidence and challenging diagnosis of this entity. Therefore, collaborative research is necessary to improve the treatment of cranial vault lymphoma treatment and its prognosis. The fact that this particular case initially underwent surgical resection and R- HyperCVAD treatment made our approach to this rare presentation of lymphoma even more unusual. Consideration of a primary bone lymphoma in a case of scalp swelling is important for proper treatment planning and possibly avoiding surgery.

References

1. Bhagavathi S, Fu K (2009) Primary Bone Lymphoma. Archives of Pathology & Laboratory Medicine. 133: 1868-1871.
2. Zhou HY, Gao F, Bu B, Fu Z, Sun XJ, et al. (2014). Primary bone lymphoma: A case report and review of the literature. Oncology Letters. 8: 1551-1556.
3. Rahmat K, Wastie M, Abdullah B (2007) Primary bone lymphoma: report of a case with multifocal skeletal involvement. Biomedical Imaging and Intervention Journal. 3.
4. Unni KK, Hogendoorn PCW (2002) Malignant lymphoma. In: Fletcher CDM, Unni KK, Mertens F. eds. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon, France: IARC Press. World Health Organization Classification of Tumours.
5. Armitage JO (2005) Staging Non-Hodgkin Lymphoma. CA: A Cancer Journal for Clinicians. 55: 368-376.
6. Tanimura A, Adachi Y, Tanda M, Yuasa H, Ishii Y, et al. (2005) Primary Peripheral B Cell Lymphoma, Burkitt-Like, of the Cranial Vault. Acta Haematol. 113: 258-261.
7. Fadoukhair Z, Lalya I, Amzerin M, Elkhanoussi B, Sbitti Y, et al. (2011) Successful management of primary non Hodgkins lymphoma of the cranial vault. Pan African Medical Journal. 8 .
8. Fukushima Y, Oka H, Utsuki S, Nakahara K, Fujii K, et al. (2007) Primary malignant lymphoma of the cranial vault. Acta Neurochir (Wien) Acta Neurochirurgica. 149: 601-604.

9. Galarza M, Gazzeri R, Elfeky HA, Johnson RR (2006) Primary diffuse large B-cell lymphoma of the dura mater and cranial vault. Neurosurgical FOCUS. 21: 1-4.
10. Ghosh S, Kumar P, Varshney R, Das D (2014) Primary diffuse large B-cell non-Hodgkin lymphoma of the cranial vault. Neuroimmunology and Neuroinflammation Neuroimmunol Neuroinflammation. 1: 98.
11. Palled S (2006) Primary Burkitt's Lymphoma of Frontal Bone: A Rare Presentation. Journal of Clinical Oncology. 24: 4521-4522.
12. Rasouli J, Patel SA, Skovrlj B (2014) Primary extranodal marginal zone lymphoma involving the skull. Journal of Clinical Neuroscience.21: 351-353.
13. Rezaei-Kalantari K, Samimi K, Jafari M, Karimi M, Ansari K, et al. (2012) Primary Diffuse Large B Cell Lymphoma of the Cranial Vault. Iranian Journal of Radiology 9: 88-92.
14. Scuotto A, Rotondo M, Conforti R, Conforti R, Nastro A, et al.(2008) Primary lymphoma of the skull base. European Journal of Radiology Extra. 66: 81-83.
15. Senapati S, Dhir M, Das S, Burma S, Mishra S, et al. (2013) A case of primary skull lymphoma: Review of literature. Neurology India. 61: 334.
16. Senthilvel E, Subbiah S, Jain V, Seidman M (2011) Primary diffuse large B-cell lymphoma of the skull mimicking osteomyelitis. Ear Nose Throat Journal.
17. Wang L, Lin S, Zhang J, Wang C (2013) Primary non-Hodgkin's lymphoma of the skull base: A case report and literature review. Clinical Neurology and Neurosurgery.115: 237-240.
18. Parekh HC, Sharma RR, Keogh AJ, Prabhu SS (1993) Primary malignant non-Hodgkin's lymphoma of cranial vault: A case report. Surgical Neurology. 39: 286-289.
19. Isla A, Alvarez F, Gutierrez M, Gamallo C, Garcea-Blezquez M (1996) Primary cranial vault lymphoma mimicking meningioma. Neuroradiology. 38: 211-213.
20. Muin IA, Saffari HM, Hasimah YN, Path M (1997) Primary Non-Hodgkin's Lymphoma of the cranial vault mimicking a meningioma: A case Report. Medical journal of Malaysia. 52.
21. Jaiswal M, Gandhi A, Purohit D, Singhvi S, Mittal R, et al. (2016) Primary non-Hodgkins lymphoma of the skull with extra and intracranial extension presenting with bulky scalp mass lesion. Asian Journal of Neurosurgery.11: 444.
22. El Asri AC, Akhaddar A, Baallal H (2012) Primary lymphoma of the cranial vault: case report and a systematic review of the literature. Acta Neurochirurgica.154: 257-265.
23. Savage KJ, Johnson NA, Ben-Neriah S (2009) MYC gene rearrangements are associated with a poor prognosis in diffuse large B-cell lymphoma patients treated with R-CHOP chemotherapy. Blood. 114: 3533-3537.
24. Perry AM, Crockett D, Dave BJ (2013) B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and burkitt lymphoma: study of 39 cases. British Journal of Haematology Br J Haematol.162: 40-49.
25. Lin P, Dickason TJ, Fayad LE (2011) Prognostic value of MYC rearrangement in cases of B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma. Cancer. 118: 1566-1573.
26. Heyning F, Hogendoorn P, Kramer M (1999) Primary non-Hodgkin's lymphoma of bone: a clinicopathological investigation of 60 cases. Leukemia.13: 2094-2098.