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Surgical Neurology International

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SNI: Neuro-Oncology

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Case Report

Cranial vault lymphoma – A case report and characteristics contributing to a differential diagnosis

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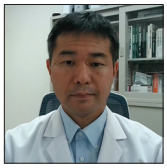

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Received : 15 November 2022
Accepted : 11 March 2023
Published : 24 March 2023

DOI
10.25259/SNI_1040_2022

Quick Response Code:

ABSTRACT

Background: Lymphomas of the cranial vault are rare and are often misdiagnosed preoperatively as presumptive meningioma with extracranial extension.

Case Description: A 58-year-old woman was referred and admitted to our department with a rapidly growing subcutaneous mass over the right frontal forehead of 2 months' duration. The mass was approximately 13 cm at its greatest diameter, elevated 3 cm above the contour of the peripheral scalp, and attached to the skull. Neurological examination showed no abnormalities. Skull X-rays and computed tomography showed preserved original skull contour despite the large extra and intracranial tumor components sandwiching the cranial vault. Digital subtraction angiography showed a partial tumor stain with a large avascular area. Our preoperative diagnostic hypothesis was meningioma. We performed a biopsy and histological findings were characteristic of a diffuse large B-cell lymphoma. A very high preoperative level of soluble interleukin-2 receptor (5390 U/mL; received postoperatively) also suggested lymphoma. The patient received chemotherapy but died of disease progression 10 months after the biopsy.

Conclusion: Several preoperative features of the present case are clues to the correct diagnostic hypothesis of cranial vault diffuse large B-cell lymphoma rather than meningioma, including a rapidly growing subcutaneous scalp mass, poor vascularization, and limited skull destruction relative to the size of the soft-tissue mass.

Keywords: Calvarial lymphoma, Calvarium, Cranial vault lymphoma, Skull

INTRODUCTION

Diffuse large B-cell lymphoma initially appearing in the calvarium is uncommon. Only about 40 cases have been reported, and when all histological types of lymphoma are included, only about 120 cases appearing in the calvarium have been reported.[14] Because the findings of cranial vault lymphoma on images are similar to those of meningioma, correct diagnosis is a challenge. However, there have been few reports studying how to differentiate lymphomas of the cranial vault from meningiomas. This article presents a case of cranial vault diffuse large B-cell lymphoma whose preoperative diagnostic hypothesis was meningioma with extracranial extension. By reviewing the literature, we specify characteristic features of cranial vault lymphoma in the present case that may be helpful for differentiating lymphomas from meningiomas.

CASE DESCRIPTION

A 58-year-old woman was referred and admitted to our department for surgical treatment with a rapidly growing subcutaneous mass and pain over the right frontal forehead of 2 months' duration. She presented with mild ptosis of her right eye associated with the mass. She had no history of head injury, serious illnesses, operations, or hospitalizations. The mass was approximately 13 cm at its greatest diameter, elevated 3 cm above the contour of the peripheral scalp, firm, nonpulsatile, mildly tender, and attached to the skull; the skin overlying the area was stretched and reddish. Neurological examination showed no abnormalities. She was afebrile. Laboratory tests, performed as routine preoperative testing and to detect other lesions, showed abnormally high levels of lactate dehydrogenase (13.58 μkat/L, normal range: 1.99–3.82 μkat/L), alkaline phosphatase (6.43 μkat/L, normal range: 1.92–5.98 μkat/L), amylase (3.07 μkat/L, normal range: 0.62–2.09 μkat/L), and lipase (12.75 μkat/L; normal range: 0.17–0.83 μkat/L). Beta-2-microglobulin, a marker of malignant lymphoma and obtained with other tumor markers to screen for the possibility of primary malignant tumors in other organs, was normal. The patient was not immunocompromised and tested negative for human immunodeficiency virus. Skull X-rays showed slight permeative deossification of the outer table and diploic space, sclerosis of the inner table, and preserved outline of the skull underlying the subcutaneous tumor [Figures 1a and b]. Digital subtraction angiography (DSA) showed a partial tumor stain from the bilateral middle meningeal arteries, left superficial temporal artery, and bilateral supraorbital arteries, with a large avascular area [Figures 1c and d]. Computed tomography (CT) of the head showed a hyperdense subcutaneous mass and mixed mildly hyper and hypodense subdural mass [Figure 2a]. Bone windows of CT showed mild periosteal reaction, permeative lytic changes of the outer and inner tables, smudgy interfaces between the diploe and the outer and inner tables, and preserved original skull contour despite the large tumor sandwiching the cranial vault [Figure 2b]. Contrast-enhanced (CE) CT of the head showed a diffuse and heterogeneously enhanced mass sandwiching the cranial vault, with hypodense edema in the right frontal lobe. On magnetic resonance imaging (MRI), the mass lesion was isointense on T1- and T2-weighted imaging (T1WI and T2WI, respectively) and heterogeneously enhanced with subarachnoid extension on CE-T1WI [Figures 2c-f]. Diffusion-weighted imaging showed a hyperintense mass (data not shown). Our first diagnostic hypothesis was a malignant meningioma with extracranial extension. We thought that a mesenchymal or a metastatic tumor with intracranial extension would cause more apparent skull destruction, and so would be the second or third differential diagnosis. We performed a biopsy in the marginal region of the frontal mass to obtain specimens of the pericranium. The mass was firm and moderately vascular; it was located under the pericranium and attached to the skull, suggesting that it originated from the skull. The skull under the subcutaneous mass had a rough surface with periosteal bone formation and with many ostia through which the tumor entered the skull. Histological findings were characteristic of a diffuse large B-cell lymphoma [Figure 3a]. Immunohistochemistry revealed that the tumor was positive for CD8, PAX5, Bcl-6, and CD19; weakly positive for CD4, CD10, and CD20; focally positive for Bcl-2 and c-Myc; and negative for CD3, CD5, CD7, CD30, CD56, CD79a, MUM-1, CCR4, granzyme B, p80 (ALK), and PD-1, suggestive of a B-cell lymphoma with aberrant expression of T-cell markers. Unfortunately, we did not receive the results of the preoperative level of soluble interleukin-2 receptor (sIL2R) until after the operation; it was 5390 U/mL, more than 8 times higher than normal (normal range: 121–613 U/mL). Postoperatively, a staging workup was completed. CE-CT of the abdomen,

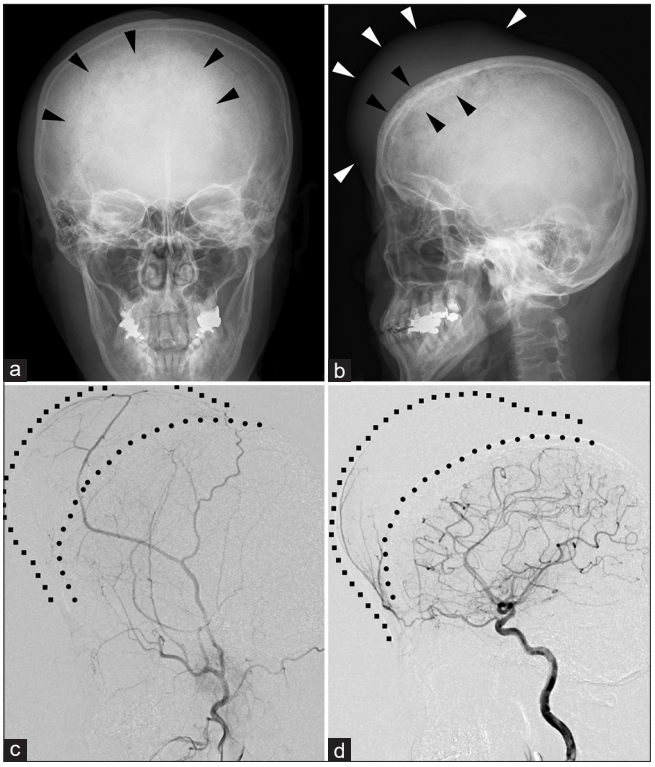

Figure 1: Preoperative X-ray and digital subtraction angiography. (a and b) Skull X-ray. Note mixture of permeative deossification and sclerosis with preserved outline of the skull (black arrowheads) underlying the subcutaneous tumor (white arrowheads). (c and d) Lateral digital subtraction angiography of the right external carotid artery (c) and right internal carotid artery (d). The angiograph shows poor vascularization of the extracranial and intracranial compartments of the tumor from both the external and internal carotid artery circulations. Line of circles: the outer table of the skull; line of squares: the contour of the skin.

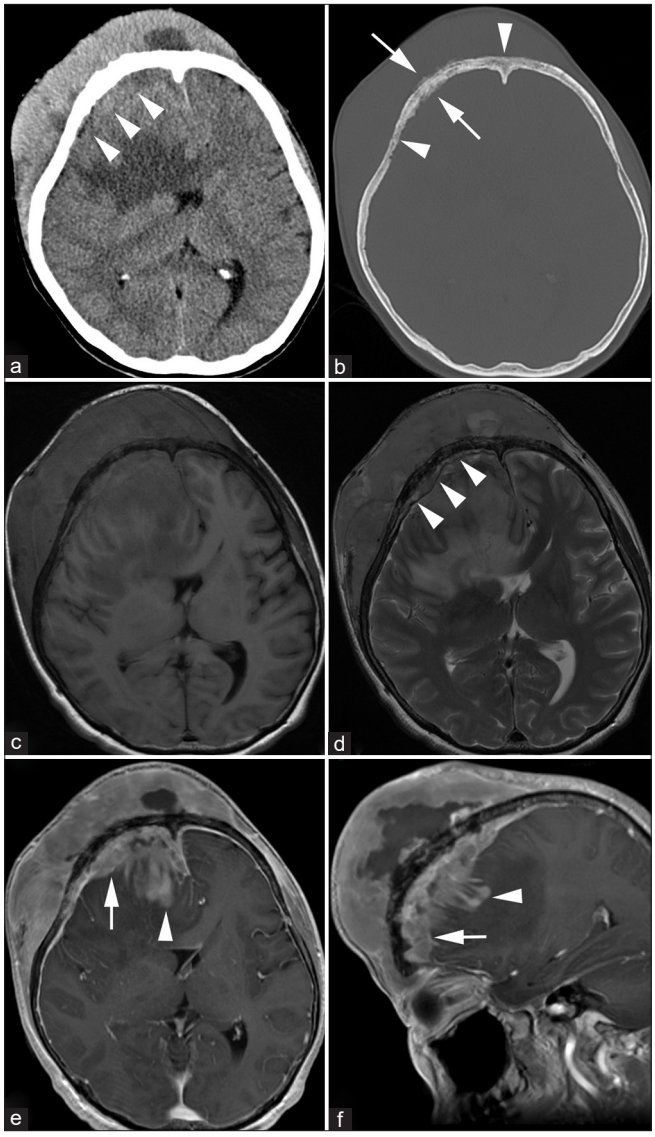

Figure 2: Preoperative computed tomography (CT) and magnetic resonance imaging. (a and b) Axial CT of the brain parenchyma window (a) and the bone window (b). The large extracranial component and relatively small intracranial component (arrowheads on [a]) sandwiched the cranial vault with permeative deossification (arrowheads on [b]) and periosteal reaction (arrows on [b]). (c-f) T1-weighted imaging (c), T2-weighted imaging (d), and post contrast T1-weighted imaging in the axial plane (e) and sagittal plane (f). The dura mater is raised from the cranial vault (arrowheads on [d]), and subdural extension (arrows on [e] and [f]) and brain invasion (arrowheads on [e] and [f]) are observed. Note that the cranial vault contour is preserved despite the large mass size in (b).

chest, and pelvis, as well as fluorodeoxyglucose F 18 positron emission tomography (FDG-PET), showed metastatic lesions in the lymph nodes of the head and neck, in the pancreas, and in the kidneys [Figures 3b-e]. This pancreatic lesion probably caused the slight increase of serum amylase and lipase. FDG-PET also showed a stronger signal in the cranial vault lymphoma than in the brain parenchyma [Figure 3c]. A bone marrow biopsy and ophthalmologic examination showed no lesions. This case was a malignant lymphoma initially appearing in the calvarium and, hence, we diagnosed it as a primary cranial vault lymphoma.

The patient received one course of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) and then one course of CHOP with rituximab (R-CHOP) in the hematology department of our hospital. The tumor, including the intracranial component, shrank markedly after the R-CHOP therapy. To treat the intracranial extension of the tumor, the patient received one course of intrathecal prednisolone, methotrexate, and cytarabine. She was well 2.5 months after the biopsy and was transferred to the hematology department of the hospital near her house to continue chemotherapy. She died of disease progression 10 months after the biopsy.

DISCUSSION

We have reported a case of cranial vault lymphoma. Its preoperative diagnostic hypothesis was meningioma, but the histological and immunohistochemical findings, as well as the sIL2R positivity, led us to diagnose it as diffuse large B-cell lymphoma. We conclude that when a subcutaneous tumor with intracranial extension is encountered, cranial vault lymphoma should be considered as a differential diagnosis.

The present case was a diffuse large B-cell lymphoma initially appearing in the calvarium. There is general agreement that cases with a solitary lesion arising in a bone should be considered as a primary bone lymphoma, whereas a lymphoma that has arisen in soft tissues, lymph nodes, or other organs and infiltrates an adjacent bone secondarily should be considered to be secondary bone lymphoma.[12] There is no consensus over the best categorization of cases with concomitant soft tissue, visceral, and/or lymph nodal infiltration like our case, and in such cases, a subjective judgment will be required about whether a case should be categorized as a primary bone lymphoma or lymphoma secondarily affecting the bone.[12] Although the present case was not "pure" primary cranial vault lymphoma,[12,15] we diagnosed it as a primary cranial vault lymphoma (that is, affecting the bone first) because the lesion in the cranial vault was largest and caused all of the symptoms, and lymphogenous metastasis was observed only in the vicinity of the cranial vault lesion, not in the vicinity of the pancreatic or kidney lesions.

We retrospectively analyzed the clinical and imaging characteristics of the present case to specify the features

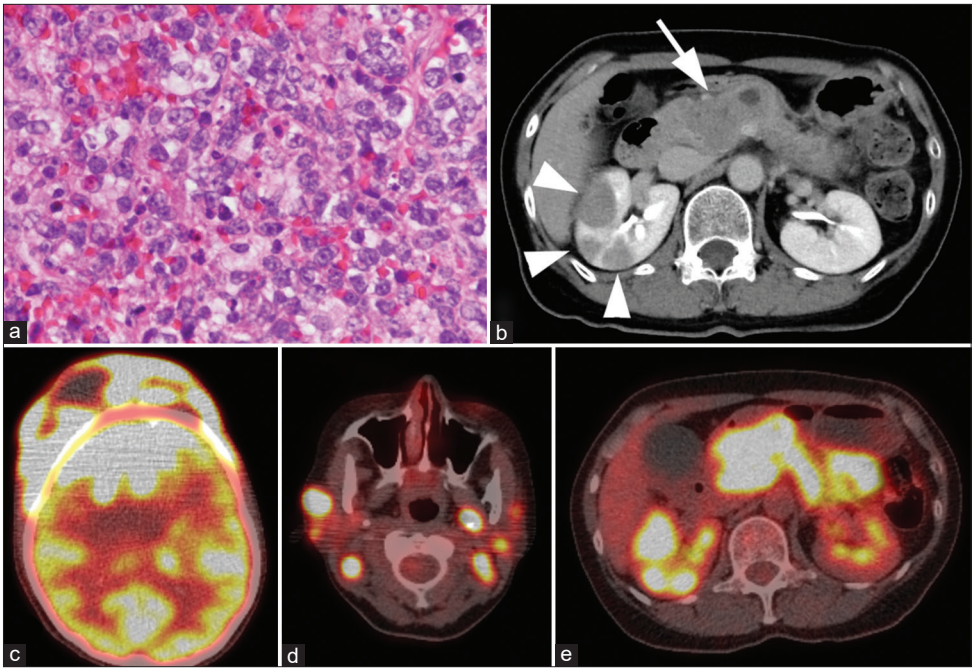

Figure 3: Histopathological features of the tumor and metastatic lesions. (a) Hematoxylin and eosin staining of the tumor at ×400 magnification, (b) post contrast axial computed tomography of the abdomen, and (c-e) fluorodeoxyglucose F 18 positron emission tomography (FDG-PET) of the head (c), neck (d), and abdomen (e). The cranial vault lymphoma shows a stronger signal on FDG-PET than does the brain (c). Note metastatic lesions in the lymph nodes of the neck (d) and in the pancreas (arrow on [b] and strong signal in [e]) and kidneys (arrowheads on [b] and strong signal in [e]).

helpful for differentiating lymphomas of the cranial vault from meningiomas. When a tumor with intra and extracranial extension sandwiching the skull is seen, meningioma with extracranial extension is often first suspected. We have experienced many cases of convexity meningioma, which is the most representative of the intracranial tumors that attach to the dura matter, and empirically, we know that in a few cases convexity meningiomas infiltrate the skull and extend into the extracranial subcutaneous space. Several of our findings from our case and the literature can be clues for the preoperative diagnosis of cranial vault lymphoma rather than meningioma with extracranial extension: (1) a rapidly growing subcutaneous scalp mass; (2) poor tumor vascularization; and (3) mild and disproportionately small skull destruction on images compared with the soft-tissue mass. The high preoperative level of sIL2R in laboratory tests and higher uptake of FDG than the brain parenchyma on FDG-PET is also suggestive of lymphoma rather than meningioma.[5,9,20]

In the case of extracranial extension of meningioma or intraosseous meningioma, the tumors tend to be slow-growing.[2,8,11,13,19] In the present case, a subcutaneous mass had grown very rapidly for only 2 months. In a previous review of cranial vault lymphoma, we found that the subcutaneous scalp mass also grew very rapidly before the patient presented for treatment, for a mean duration of 5.8 months.[14] From these previous reports, including our own, a rapidly growing subcutaneous mass with intracranial extension may be malignant lymphoma or another malignant mesenchymal tumor rather than meningioma.

Consistent with other reports,[14] DSA of our case showed poor tumor vascularization, which differs from the rich tumor vascularization from the external carotid artery circulation observed in many cases of meningioma.[19] CT or MRI findings on soft-tissue mass lesions of cranial vault lymphoma are unspecific and unlikely to clarify the diagnosis. Although a dural tail is observed in cases of meningiomas,[17] this finding is also observed in lymphomas, and thus is not a determinant.[21]

Lymphoma cells have been suggested to infiltrate the spaces within the diploe and to extend along the emissary veins to infiltrate the soft tissues on either side of the bone.[1,4,7,16] In cases of cranial vault lymphoma, mild osteolytic skull changes with permeative deossification with relatively preserved skull contour are frequently observed on CT and MRI.[14] Although the destruction of the cranial vault tends to be small, the extracranial and intracranial components of the tumor tend to be large.[14] Cranial vault intraosseous meningiomas tend to show sclerotic skull changes.[6,19] In

intracranial meningiomas with extracranial extension, some show skull destruction and others show hyperostosis of the skull.[2,3] The permeating growth pattern of a cranial vault tumor involving a large soft-tissue component and slight bony destruction, as observed in the present case, is also suggestive of lymphoma rather than meningioma.

Laboratory data are unremarkable in many cases.[14] In our case, sIL2R, a marker of lymphoproliferative neoplasms,[18] was more than 8 times the upper limit of normal, whereas beta-2-microglobulin, another marker of malignant lymphoma, was normal, suggesting that sIL2R is a more sensitive marker for lymphoma than beta-2-microglobulin. Kosugi *et al*.[10] also reported elevated sIL2R in a patient with cranial vault lymphoma, suggesting that elevated sIL2R associated with a cranial vault tumor might indicate lymphoma rather than meningioma. Unfortunately, it took a long time to get the sIL2R results in our institute, and we could not use the data preoperatively.

In our case, the tumor showed high uptake of FDG on FDG-PET [Figure 2], as previously reported for B-cell lymphoma.[9,20] Because meningiomas are mostly slow-growing tumors and their glucose metabolism might be only moderately elevated, the high physiological glucose uptake of the normal cerebral cortex leads to a low meningioma-to-background ratio.[5] Hence, a high tumor-to-background ratio may indicate a lymphoma and contributes to ruling out a meningioma. Unfortunately, FDG-PET is seldom used for preoperative evaluation of a cranial vault tumor, and we also obtained FDG-PET postoperatively.

CONCLUSION

Cranial vault lymphoma is a rare entity among skull tumors and its preoperative diagnostic hypothesis is often meningioma with extracranial extension. A rapidly growing subcutaneous scalp mass, poor vascularization on angiography, mild, and disproportionately small skull destruction despite the large size of the extracranial and/or intracranial component, as well as an increased level of sIL2R in laboratory tests and higher uptake of FDG than the brain parenchyma on FDG-PET, are suggestive of lymphoma rather than meningioma.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Aoyama S, Nitta N, Moritani S, Tsuji A. Cranial vault lymphoma – A case report and characteristics contributing to a differential diagnosis. Surg Neurol Int 2023;14:107.