Characteristics of Bone Destruction in Cranial Vault Lymphoma Compared with Other Skull Tumors

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Abstract: Cranial vault lymphomas are rare and challenging to diagnose. We present herein two cases of cranial vault lymphoma. The first patient was a 72-year-old woman who presented with a large mass in the parietal bone found incidentally following a head injury. The second patient was a 63-year-old man who presented with an occipital subcutaneous mass associated with visual disturbance and occipital headaches. The diagnosis of a malignant tumor in the second patient was straightforward due to his symptoms and considerable bone destruction, but the first patient was more difficult to diagnose due to a lack of symptoms and only slight bone destruction detected by computed tomography (CT). Both were histopathologically diagnosed with diffuse large B cell lymphoma (DLBCL) in the cranial vault. We also investigated the clinical features, including initial symptoms and patterns of bone destruction, in 23 patients with other types of skull tumors. This comparison showed that cranial vault lymphomas cause large masses on the scalp and lead to characteristic incomplete bone destruction, indicating that cranial bone is destroyed very slowly despite the expanding subcutaneous mass. This feature is unique compared with other benign and malignant skull tumors. In addition, cranial vault lymphoma can be confirmed via bone window CT.

Keywords: lymphoma, DLBCL, cranial vault, bone destruction, computed tomography.

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Introduction

Primary diffuse large B-cell lymphomas (DLBCLs) often arise in the midline or paraventricular regions of the central nervous system. DLBCLs that arise primarily in the cranial bone, by contrast, are rare, and some are difficult to diagnose. The clinical features of cranial vault lymphomas include development of a large, indolent scalp mass, with most patients not experiencing any neurological deficits initially [1-4]. No studies to date have investigated the clinical differences between cranial vault lymphomas and other skull tumors, including metastatic skull tumors and meningiomas. This study retrospectively compared clinical findings and features of two patients with cranial vault lymphoma and 23 other types of skull tumor treated at our hospital. The local ethics committee provided approval for the use of the collected data.

Case Report

Patient 1

A 72-year-old woman with a mass growing subcutaneously in the left parietal region was admitted to our
facility. The patient noticed the mass following a head injury. She had a history of hypertension and chronic renal failure, and required dialysis three days a week. Initial evaluation revealed slight fever and a painless, subcutaneous 10 cm mass. Lymphadenopathy was not observed, and all other physical findings were normal. Her laboratory results showed abnormal concentrations of serum creatinine (5.02 mg/dl) and hemoglobin (7.9 g/dl), as well as abnormal estimated glomerular filtration rate (7.19 ml/min/1.7 m²), findings that are consistent with renal anemia. Computed tomography (CT) scans showed a hyperdense mass in the intra- and extracranial space (Fig. 1A). Bone window CT showed a slight bony change in the left parietal bone (Fig. 1B). Magnetic resonance imaging (MRI) showed that the mass was isointense on both T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI) (Fig. 1C, D). Contrast enhanced T1-weighted imaging (CE-T1WI) was not performed owing to renal failure. Because she was admitted following a head injury, she had been initially diagnosed with a subcutaneous and subdural hematoma, and the slight bony change was initially missed. A linear skin incision in the left parietal region revealed a hypovascular, rubbery and white-colored mass. The portion of the skull under the mass had been slightly eroded (Fig. 1E), and the dura mater had been invaded by the tumor (Fig. 1F). She was promptly diagnosed with lymphoma and underwent surgery. Immunohistochemistry showed that the atypical lymphocytes were positive for CD20, with some positive for CD3 and B-cell lymphoma 2 (BCL2). None of the lymphocytes were positive for CD30 or epithelial membrane antigen. These histological findings confirmed a diagnosis of DLBCL. Assessment of the portion of removed cranium showed that the vessels in the cranial bone were filled with tumor cells, as was the subcutaneous mass (Fig. 1G, H). It was not possible to administer chemotherapy because of renal failure, but whole brain radiation therapy (45 Gy) and corticosteroids were administered. The left parietal tumor disappeared, and the patient was discharged without neurological deficits.

Fig. 1. Clinical evaluation of Patient 1, diagnosed with a cranial vault lymphoma in the left parietal bone. A: Computed tomography (CT) scan of the brain parenchyma window showing a large left parietal mass. B: CT scan of the bone window showing slight changes in bone. C: Axial T1-weighted magnetic resonance imaging (MRI) scan showing an isointense subcutaneous mass. D: T2-weighted MRI scan showing a similar isointense structure. E, F: Intraoperative photographs of the subcutaneous tumor. White arrow heads in panel E show the white, rubbery, subcutaneous mass. The white arrow in F indicates the burr hole through which the invaded dura was exposed. G: Pathology of the removed bone and subcutaneous mass. Vessels in the bone had been invaded by tumor cells, although some normal bone structures remained. H: Pathologic examination, showing that the subcutaneous mass was filled with tumor cells.
Patient 2

A previously healthy 63-year-old man felt a subcutaneous mass in the occipital region of his skull. A month later, he experienced visual disturbance and consulted a clinic, where he was diagnosed with optic neuritis and administered corticosteroids. After transient improvement, the visual disturbance worsened and the subcutaneous mass became enlarged within 2 months. On his initial visit to our facility, he presented with occipital headaches, bilateral papilledema, visual disturbance, and a 4.0 cm painless occipital mass; laboratory results were normal. Notably, he did not have any fever or lymphadenopathy.

CT scans showed a subcutaneous occipital mass, with invasion into the intra-cranial space (Fig. 2A). Bone window CT showed destruction of the internal and external tables of the cranium (Fig. 2B). MRI showed that the mass was hypointense on T1WI (Fig. 2C), slightly hyperintense on T2WI (Fig. 2D), and homogeneously enhanced on contrast-enhanced-T1WI (Fig. 2E). MRI also demonstrated invasion of the transverse sinus. The potential diagnoses based

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**Fig. 2. Clinical evaluation of Patient 2, diagnosed with a cranial vault lymphoma in the occipital bone.** A: Computed tomography (CT) scan of the brain parenchyma window showing a large occipital mass. B: CT scan of the bone window showing bone destruction. C: Axial T1-weighted (T1WI) magnetic resonance imaging (MRI) scan, showing that the subcutaneous mass in the occipital region was isointense. D: T2-weighted MRI scan, showing that the mass was slightly isointense. E: Contrast-enhanced (CE)-T1WI scan, showing that the mass was homogeneously enhanced. MRI also showed tumor invasion of the transverse sinus and intradural space. F: Intraoperative photograph showing absence of the occipital bone and invasion of the transverse sinus (white arrow heads). G: Pathology of the removed bone, with bone marrow replaced by tumor cells. The white arrow indicates remaining normal bone structure.
on these findings were metastatic tumor of unknown origin, malignant lymphoma or osteosarcoma. For definitive diagnosis and decompression, a U-shaped skin incision was made in the occipital area, exposing the occipital bone and tumor. The hypovascular, rubbery, yellow tumor had caused bone destruction, with invasion of the subcutaneous tissue, periosteum and inner tables of the skull bone. An occipital craniectomy was performed, with partial tumor excision. The dura mater and transverse sinus had been invaded by the tumor (Fig. 2F). Resection was performed. A diagnosis of DLBCL was confirmed histologically, with diffuse proliferation of lymphoma cells staining positively for CD20; however, the cells were negative for CD3, CD10, BCL2, and CD30. A portion of the resected occipital bone revealed almost complete replacement of the bone marrow by tumor cells, with very little bone structure remaining (Fig. 2G).

Chemotherapy with high-dose methotrexate was initiated because of the intradural invasion, but was not effective. The chemotherapy regimen was changed to rituximab, cyclophosphamide, cytarabine, etoposide, and dexamethasone (CHASER regimen). The visual disturbance and headache improved rapidly, and the patient was discharged without neurological deficits.

**Other types of skull tumors**

We analysed 23 Japanese patients, including 10 men and 13 women (mean age: 41.7 years), who had been admitted to our hospital between January 2007 and December 2014. Six (26.1%) had metastatic skull tumors, seven (30.4%) had Langerhans cell histiocytosis (LCH), and 10 (43.5%) had other skull tumors (intraosseous meningioma, dermoid cyst, epidermoid cyst, fibrous dysplasia, endolymphatic sac tumor, hemangioma, cavernous hemangioma, osteoma and malignant myeloma). Table 1 shows their initial symptoms, symptoms, and pathology.

| Case | Age/Sex | Initial symptom       | Bone CT     | Pathology                                |
|------|---------|-----------------------|-------------|------------------------------------------|
| 1    | 64/M    | exophthalmos          | completely eroded | metastatic tumor (adenocarcinoma)       |
| 2    | 17/F    | visual loss           | completely eroded | metastatic tumor (non-keratinizing carcinoma) |
| 3    | 69/F    | visual loss           | completely eroded | metastatic tumor (invasive ductal carcinoma) |
| 4    | 66/M    | headache              | completely eroded | metastatic tumor (adenocarcinoma)       |
| 5    | 84/F    | headache              | completely eroded | metastatic tumor (clear cell carcinoma)  |
| 6    | 81/F    | frontal mass          | completely eroded | metastatic tumor (squamous cell carcinoma) |
| 7    | 52/F    | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 8    | 14/F    | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 9    | 9/F     | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 10   | 6/F     | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 11   | 57/F    | tumor pain, hearing loss | completely eroded | Langerhans cell histiocytosis            |
| 12   | 9/M     | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 13   | 9/M     | tumor pain            | completely eroded | Langerhans cell histiocytosis            |
| 14   | 52/M    | hearing loss           | completely eroded | endolymphatic sac tumor                  |
| 15   | 49/F    | limited eye movement  | completely eroded | malignant myeloma                        |
| 16   | 37/F    | orbital mass          | partially eroded | dermoid cyst                             |
| 17   | 0/M     | frontal mass          | partially eroded | epidermoid cyst                          |
| 18   | 11/M    | parietal mass         | partially eroded | fibrous dysplasia                         |
| 19   | 18/M    | double vision         | osteohypertrophy | fibrous dysplasia                         |
| 20   | 63/M    | double vision         | partially eroded | hemangioma                               |
| 21   | 61/M    | temporal mass         | partially eroded | cavernous hemangioma                     |
| 22   | 65/F    | tumor pain            | ossification   | osteoma                                  |
| 23   | 65/F    | frontal mass          | osteohypertrophy | meningioma                               |

CT: computed tomography
CT features and other clinical characteristics.

Of these 23 patients, 15 (65.2%) had malignant tumors, including metastatic skull tumors, LCH, endolymphatic sac tumor, and malignant myeloma, whereas the other eight (34.8%) had benign tumors, including dermoid cyst, epidermoid cyst, fibrous dysplasia, hemangioma, cavernous hemangioma, osteoma, and intraosseous meningioma. Malignant skull tumors sometimes induce neurological deficits by invasion through the cranial bone. Such tumors destroy the cranial bone completely and subsequently invade the brain and cranial nerves. Table 1 shows all the malignant skull tumors that had completely eroded the bone. For example, a bone window CT scan of Patient 5, diagnosed with a metastatic parietal skull tumor that induced headache, showed that the invaded bone had eroded completely (Fig. 3A). In contrast, Patient 19, with fibrous dysplasia, experienced double vision caused by compression of the eyeball, suggesting that the symptoms of benign skull tumors may have been due to compression, rather than destruction, of normal tissue. Bone window CT (Fig. 3B) showed osteohypertrophy. Patient 20 had a hemangioma and also experienced double vision caused by skull tumor compression of the left eyeball. Bone window CT showed partial destruction without internal and external tables (Fig. 3C).

The malignant skull tumors in our series always show complete bone destruction and sometimes neurological deficits caused by invasion. On the other hand, benign skull tumor shows partial bone destruction or osteohypertrophy, which causes neurological deficits by compression of surrounding tissues rather than invasion.

**Discussion**

Symptoms of cranial vault lymphoma have been reported to include a painless scalp mass and focal neurological deficits secondary to infiltration of the cerebral cortex [1, 4–12]. Primary cranial vault lymphoma is rarely different from typical metastatic bone lymphomas, and it is defined as solitary mass lesion without any evidence of disease at another site and no systemic dissemination within 6 months of tumor detection [13]. Intracranial symptoms, such as seizures and hemiplegia, have also been observed [14–16]. Cranial vault lymphoma involves cranial bone destruction. Although bone change is initially minimal, these tumors can ultimately infiltrate the skull and destroy it completely [11].

In our cases, both patients showed the same pattern. Patient 1 had a large subcutaneous mass without neurological deficits. Patient 2 had an occipital mass first, and later experienced visual loss caused by increased intracranial pressure, ultimately owing to sinus invasion. The bone destruction in Patient 1 was minimal on bone window CT (Fig. 1B), whereas the destruction in Patient 2 was considerable (Fig. 2B).

In the other 23 skull tumors, we found that all other

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**Fig. 3. Clinical evaluation of other patients.** A: Bone window computed tomography (CT) of patient 5, diagnosed with a metastatic bone tumor, showing that invaded bone was completely eroded. B: Bone window CT of patient 19, diagnosed with fibrous dysplasia; the white arrow indicates osteohypertrophy. C: Bone window CT of patient 20, diagnosed with hemangioma; the white arrow indicates bone destruction without external and internal table.
types of malignant skull tumor completely destroy bone and all intracranial tissues, with most patients experiencing neurological deficits from the initial stages. Thus, symptoms in patients with malignant skull tumors are induced by invasion of the cortical lesion into the cranial nerves. Actually, there were malignant bone tumors with sclerotic change [17], and our cases were limited in number, but most metastatic skull tumors have eroded bone like our series [18]. Patients with benign skull tumors sometimes have neurological deficits induced by tumor compression rather than invasion; bone destruction by benign skull tumors only occurs in part. This means that external and internal tables remain in bone window CT (Fig. 3C). In benign skull tumors, the occurrence of neurological deficits relates to tumor location. Patients with parietal skull tumors do not experience neurological deficits.

Cranial vault lymphomas are very different from malignant and other benign skull tumors. These tumors are characterized by an infiltrative growth pattern and large soft-tissue component, although destruction of cortical bone may be limited [2, 19–21]. The pattern of bone destruction is different from other skull tumors. Fig. 1B and Fig. 2B show that bone change occurs diffusely and includes internal and external tables, and that this change develops slowly. This infiltrative slow destruction is not observed in other benign and malignant skull tumors.

We investigated why this bone change occurred by examining the pathology in two cases. The pathology of Patient 1 showed that vessels in the bone (Fig. 1G) and the subcutaneous mass itself (Fig. 1H) were filled with tumor cells, although normal bone structures remained. The pathology of patient 2 showed bone invasion, with tumor cells almost completely destroying the bone; however, they still had normal bone structures (Fig. 2G). These findings suggest that tumor cells may easily permeate and accumulate within subcutaneous tissues, expanding the initial subcutaneous mass. Cranial bone is destroyed very slowly as the lymphoma cells permeate the intradiploic space by extending along the diploic veins, but without destroying the overall bone structure. Tashiro et al also reported this pathological feature [22]. Thus, infiltrative destruction is observed in cranial vault lymphoma and is different from the destruction observed in other skull tumors.

This mechanism limits the bone changes.

The prognosis for patients with cranial vault lymphoma is relatively good, with 5-year overall survival rates of 40–60% [2, 11, 23]. Survival is enhanced by accurate diagnosis and treatment.

Bone window CT findings are important, as this technique clearly demonstrates the growth pattern of cranial vault lymphoma. A large subcutaneous mass with infiltrative bone destruction is the most characteristic feature of cranial vault lymphoma.

**Conclusion**

Cranial vault lymphomas are rare tumors that are difficult to diagnose. We encountered two patients with these rare tumors and showed that the most important diagnostic feature of cranial vault lymphoma is a large, subcutaneous mass with infiltrative bone destruction on bone window CT. This feature is specific to cranial vault lymphomas and may be better understood by comparing their features with those of other skull tumors.

**Conflict of Interest**

The authors declare no conflict of interest associated with this manuscript.

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頭蓋骨悪性リンパ腫における他の頭蓋骨腫瘍と比較した特徴的骨破壊像

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要 旨: 頭蓋骨悪性リンパ腫は稀な腫瘍であり, 初期診断に苦慮することがある。我々は, 2症例の頭蓋骨悪性リンパ腫を経験したため報告する。最初の症例は72歳の女性であり, 頭部外傷後に頭頂部の大きな腫瘍を指摘された。次の症例は63歳の男性であり, 視力障害と後頭部痛に伴う後頭部皮下腫瘍を指摘された。2症例目では, 悪性腫瘍の診断は症状と骨破壊の状態から容易であった。しかしながら, 最初の症例においては, 症状を認めず, 頭部CTにおける骨破壊もわずかであったため診断が困難であった。病理診断では, 両方の症例は頭蓋骨に発症したびまん性B細胞性リンパ腫であった。我々は, 23症例の異なる頭蓋骨腫瘍について初期症状, 骨破壊像を調査した。これらの症例と比較により, 頭蓋骨リンパ腫の特徴は頭蓋骨に大きな腫瘍を認めること, 不完全な骨破壊像を伴っていることと考えられた。この特徴は腫瘍による頭蓋骨の破壊が皮下腫瘍と比べゆっくりであるためと考えられた。この特徴は, 良性, 悪性の頭蓋骨腫瘍と比較しても特異的であり, 頭蓋骨リンパ腫は骨条件CTにて確定診断し得ると考えられた。

キーワード: リンパ腫, びまん性大細胞型B細胞リンパ腫, 頭蓋骨, 骨破壊, CT.

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