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Clinical Study

Malignant giant cell tumor of the skull base originating from clivus and sphenoid bone

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Key words: giant cell, radiotherapy, skull base

Summary

We present a case report of a giant cell tumor located in the skull base orginating from clivus and sphenoid bone treated by surgery and external beam radiotherapy (EBRT).

Introduction

Primary giant cell tumors (GCTs) mainly originate in the metaphyseal region of long bones in the appendicular skeleton [1]. Several GCTs are as well reported to arise in paranasal region [2–15]; while sphenoidal locations are exceedingly rare with only a few reports in the literature considering the management [12,15]. When they do occur in the base of the skull, surgical treatment is frequently difficult and therefore, the use of adjuvant therapy is important in no optimal management regimen era for these GCTs. We present a case report of a GCT located in paranasal sinuses invading the skull base treated by surgery and external beam radiotherapy (EBRT).

Clinical observation

The patient was a 14-year-old girl, with no known allergies and no smoking or drinking habits, who had a clear medical history. She was admitted to the hospital because of progressive frontal headache, and double vision in the last 2.5 months in December 2002. The physical examination revealed a good general state of health. She had no apparent craniofacial dysmorphism, but a minimal left sided sinus and facial tenderness. The motor and sensory neurological examinations including cerebellar tests were normal with full cooperation and orientation. Cranial nerves (CN) were intact in examination from CN II to CN XII. Visual examination revealed double vision, but complete fields in confrontation with normal range of eye motion and isochoric pupils; papilledema was negative. Endoscopic nasal examination showed an erythematous left nasal mass filling the entire nasal cavity.

Laboratory tests carried out on admission to hospital, including blood biochemistry, complete blood count, thyroid function tests and tumor markers, were in normal range.

The chest X-ray was negative for a suspicious lung mass. Cranial magnetic resonance imaging (MRI) demonstrated a lytic expansive mass lesion (Figure 1) originating primarily from left sphenoid sinus and clivus with a soft tissue component of $6 \times 4 \times 3.5$ cm expanding into prepontine cistern. The mass was eroding through the lamina paprycea and filling the sphenoid sinus anteriorly, protruding into the sella and pushing the pituitary gland superiorly while compressing on the chiasm and bilateral optic nerves. The lesion was also invading bilateral ethmoid sinuses, most pronounced on the left, and blocking the nasal meata. Although the mass lesion approaches the parapharyngeal structures in the nasopharynx, it did not seem to originate from nasopharynx, while the parapharyngeal soft tissue and clival cortex border was intact and well defined.

The patient underwent neuro-navigation guided transsphenoidal surgery on December 2002 and lesion was resected subtotally with no post-operative neurological complications. Histopathological examination of the surgically resected specimen revealed GCT, demonstrating well vascularized tissues uniformly comprised of plump, spindly or ovoid undifferentiated stromal cells, with numerous large multinucleated giant cells.

On follow-up in February 2003, cranial MRI demonstrated a recurrent expansive mass lesion (Figure 2) measuring $3 \times 4 \times 3$ cm expanding into nasal cavity and left orbital cavity. Subsequently the patient was treated by EBRT to the recurrent mass. Treatment was delivered with three field technique in 6MV photons by 2 Gy/fraction/day in 30 fractions to 60 Gy (Figure 3).

Further post- EBRT MRI follow-up in May and September 2003 revealed stable mass with no clinical complaints of progression; however she was admitted to hospital in April 2004 – 1 year after EBRT – with epistaxis and headache. MRI defined a progressive increase in size of the mass lesion invading the nasal cavity, sella turcica, sphenoid sinus and clivus; as extending through the cribriform plate to the intracranial compartment. The expanding mass invaded the sphenoid sinuses, clivus, bilateral cavernous sinuses, right Meckel cave and right medial temporal lobe. Endoscopic nasal evaluation showed a fragile nasal mass in the nasal cavity with bloody discharge and a

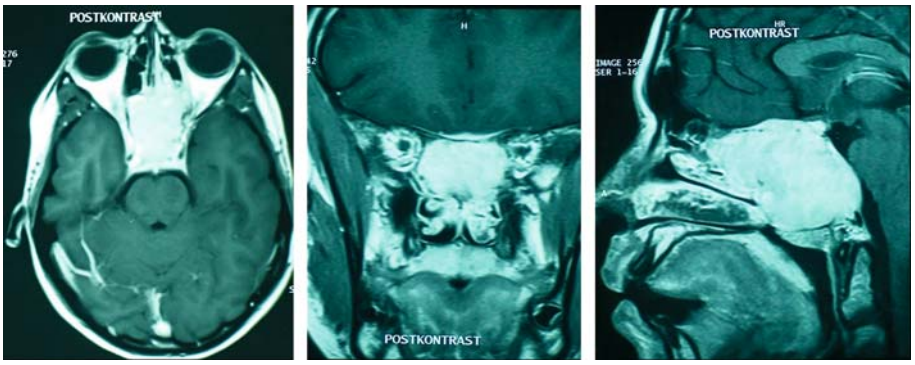

Figure 1. Initial cranial magnetic resonance imaging demonstrated a lytic expansive mass lesion originating primarily from left sphenoid sinus and clivus in December 2002.

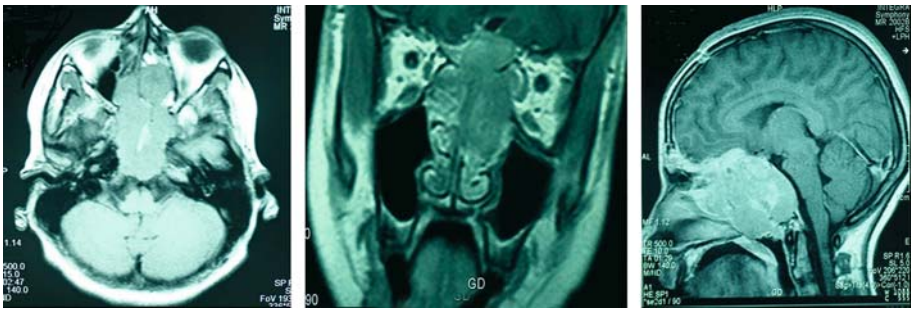

Figure 2. Cranial MRI before external beam radiotherapy in demonstrating a recurrent expansive mass in February 2003.

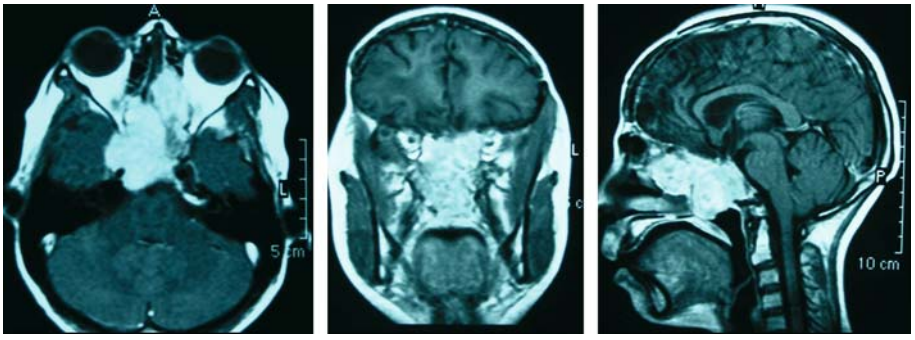

Figure 3. Cranial MRI following external beam radiotherapy in demonstrating a recurrent expansive mass in April 2004.

limited resection of intranasal mass was performed to relieve the symptoms.

Discussion

Being uncommon, GCTs comprise of 3–7% of all primary bone tumors [16]. They are rarely seen before the closure of the epiphyseal plate and mostly occur in the epiphyseal–metaphyseal regions of long bones, especially around knee joint [16–18]. Although it is infrequent, cranial GCTs has a tendency to involve the skull [19,20] and if situated over the skull base, most commonly involve the sphenoid bone [6,13,21,22], followed by the petrous temporal bone [23–27]. GCTs have a female preponderance and young adult prevalence with a peak incidence between 20 and 30 years of age [17,18]. GCTs of the craniospinal axis are rare and present with lytic localized bone lesions [17,18]; where cranial lesions preferably arise from the skull base rather than the vault [19,20]. Here we present our EBRT experience of a young girl with uncommon GCT located in paranasal sinuses invading the skull base.

Typical physical findings depend on the site of the involved bone; mainly pain or neurological deficits [28–30]. In patients with skull base lesions, pain, swelling and neurological symptomatologies are the most common initial complaints [28]. Frontal headaches, diplopia, proptosis, and visual disturbances are frequent symptoms with sphenoid involvement which were also mostly observed in our case as well. A 'typical presentation' of patients with GCTs involving the skull base has previously been defined by Watkins et al. [13]: a woman in her 20s or 30s having headaches, ocular palsy and visual loss with erosion of the body of sphenoid, but with normal endocrine function. This typical appearance is in concordance with our female young adolescent case.

Table 1. Clinical presentation and outcome of cases reported as giant cell tumors of the sphenoid in the English literature

Author	Patient #, Age, Gender	Location	Initial therapy	Histology	Tumor recurrence	Patient Status (Follow-up in years)
Martins et al. [99]	1 Patient, 20 years old, Male	Sphenoid	Biopsy; radiotherapy (50 Gy)	Benign GCT	Malignant transformation	DWD (3 years)
Pau et al. [10]	1 Patient, years old, Female	Sphenoid	Debulking and post-operative radiotherapy	GCT	No	ANED (44 years)
Kishima et al. [8]	1 Patient, 12 years old, Female	Sphenoid	Debulking twice and radiotherapy (50 Gy) on recurrence	GCT	Recurrent after debulking, but stable after radiotherapy for 5 years	AWD (5 years)
Wolfe et al. [14]	9 patients, 16–35 years old, 4F & 5M	Sphenoid	Subtotal excision (1 patient only biopsy) and radiotherapy (dose not specified)	GCT	Recurrent in 2 cases (one had no resection except biopsy)	7 patients ANED, 1 AWD at 5 years and 1 DWD at 1 year (0.5–21 years)
Doshi et al. [22]	2 patients, 18 and 21 years old, both female	Sphenoid	Decompressive surgery & post-operative radiotherapy (31 Gy) Subtotal resection and post-operative radiotherapy (34 Gy)	GCT	None	ANED (4 years)
Present case	1 Patient, 14 years old, Female	Sphenoid, clivus	Debulking and radiotherapy (60 Gy)	GCT	Recurrent both after debulking and after radiotherapy	AWD (2 years)

Abbreviations: GCT: giant cell tumor; ANED: alive with no evidence of disease; DWD: dead with disease; AWD: alive with disease.

Due to the insufficient follow-up of the majority and scarce number of skull base GCT cases, the precise role of the extent of surgery (total versus partial resection, biopsy) and adjuvant therapies (irradiation and chemotherapy) remains undefined yet in emerging literature [10,28,31–33]. In general, a wide local excision is preferred at first step whenever feasible to expect a complete clinical cure [17,18]; as simple curettage is known to have a relatively high local recurrence rate, in a range of 24–40%, decreasing with adjuvant treatment delivered to the tumor site [10,29,31–35]. However, surgical extent for skull base lesions seems to be limited with compromises whether to cause esthetic or neurologic sacrifices. Therefore, subtotal excisions were possible in our case which required adjuvant local additive treatment, irradiation. It is increasingly being realized that adjuvant radiotherapy is of paramount importance in surgically untreatable or incompletely excised lesions. We treated our patient with post-operative radiotherapy after second subtotal resection in order to prevent further progress of the tumor which is close to chiasm and left optic nerve. Overall carefully planned and delivered super voltage irradiation is safe and effective as noted previous pertinent literature [10,31–33]. Besides GCT is not a radio-resistant tumor as once believed (Table 1), and complications seen with modern mega-voltage irradiation therapy are minor and tolerable [8–10,14,22]. On this background, we have applied therapeutic irradiation of 60 Gy to the gross tumor; however an obvious radiological regression could not be achieved as expected due to previous encouraging reports and we observed our patient being mostly stabile radiologically at 1 year follow-up.

Chemotherapy, on the other hand, has not been largely evaluated in the skull base GCTs. Yamamoto et al. reported two cases of cranial base GCT that responded well to chemotherapy on periodic CT scans with regression [31] where adriamycin was used after partial tumor excisions. We have awaited a possible apparent progression of the tumor before administration of chemotherapeutic agents and therefore have not applied any yet.

Conclusion

The adjuvant radiotherapy does not seem to offer a clear local control benefit in our case with skull base GCT after incomplete excision and local recurrence; however long terms follow-up is required in this case to conclude for the final outcome.

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