CASE REPORT

Malignant Granular Cell Tumor of the Skull Base

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ABSTRACT

Objective and Importance: Malignant granular cell tumors (MGCTs) are extremely rare, high-grade sarcomas of Schwann cell origin. They often metastasize and are associated with short survival. We describe a patient with a large MGCT arising from the suboccipital nerve that eroded the posterior skull base, invaded the perifocal neck muscles, demonstrated perineural extension, and metastasized to regional lymph nodes. **Clinical Presentation:** A 60-year-old woman with several years' history of neck pain noticed a right-sided suboccipital swelling 4 months prior to seeking medical attention. Magnetic resonance imaging (MRI) showed a 5-cm bone-eroding suboccipital tumor and a second tumor, antero-caudal to this, 4 cm in diameter. **Intervention:** The patient underwent surgery. A 4-cm multinodular tumor was removed, freeing it from the internal jugular vein. A 5-cm suboccipital tumor infiltrated the trapezius, semispinalis capitis, and longissimus capitis muscles. The major and minor rectus capitis muscles were completely engulfed by tumor and their attachments to the occipital bone completely eroded. The oblique capitis muscle was infiltrated at its attachment to the C1 transverse process. These muscles were resected with a free margin to remove all tumor tissue. We then removed tumor encasing the right vertebral artery, the medial mastoid process up to the transverse sinus and anteriorly to the stylomastoid foramen, and lastly, the posterior third of the occipital condyle, achieving a gross total removal and no visible residual on postoperative contrast-enhanced MRI. **Conclusion:** This case represents the first report of resected primary MGCT involving the posterior fossa and arising from the suboccipital nerve.

KEYWORDS: Granular cell tumor, malignant, skull base, surgery

Granular cell tumors (GCTs) are uncommon lesions. They were first described in 1926 by

Abrikossoff¹ who postulated a myogenic origin and coined the term "granular-cell myoblastoma."

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Later, histochemical, immunohistochemical, and electron microscopic studies suggested a Schwann cell origin.²⁻⁵

A 2:1 female to male ratio has been noted.⁵ The lesion is typically diagnosed between the ages of 30 and 60, but it can arise at any age. As many as 15% of patients will have GCTs at multiple anatomic sites.⁵

These neoplasms arise in different parts of the body, in particular the tongue (in more than 40% of cases), subcutaneous tissue, and breast. The head and neck site likely to be involved is the larynx.⁶ Other sites such as urogenital, gastrointestinal, and respiratory tract have also been described.⁵ GCTs of the central nervous system are very rare, but cases with tumor occurrence in the pituitary gland,^{7,8} within the brain,⁹⁻¹¹ and in the leptomeninges,¹² and sporadic cases of cranial nerve involvement have been described.¹³⁻¹⁸ GCTs are also encountered in the peripheral nervous system and well-documented cases have been published showing involvement of the radial,¹⁹ median,²⁰ sciatic,^{21,22} and recurrent laryngeal nerves.²³

These tumors are usually benign, slowly growing tumors, clinically silent, and mostly incidentally found at autopsy. Fewer than 2% of all GCTs are malignant.²⁴ Malignant granular cell tumors (MGCTs), first described by Ravich et al in 1945,²⁵ are extremely rare, high-grade sarcomas with a high rate of metastases and short survival.²⁶

With respect to treatment, operation is the first choice. Unfortunately, total microsurgical removal is not always achieved, especially when extensive surgery would produce unacceptable morbidity. The role of adjuvant radiotherapy of malignant GCTs is controversial: generally they are considered to be radioresistant. However, these observations appear largely in older literature. Dose, fractionation, and technique are generally not specified in sufficient detail to draw any firm conclusion. Rosenthal et al²⁷ suggest that in those cases where the GCT demonstrates high-risk features such as large size, positive margins of resections, the presence of mitosis, or a history of recurrence, clinicians should consider the use of adjuvant radiotherapy. In

a recent paper, Aksoy et al²⁸ present a case report in which radiotherapy was given for palliative purpose. Sixty Gy of external radiotherapy was administered to a pulmonary lesion. Palliation of hemoptysis was obtained without any change in size of the lung lesion. The authors also identified 52 previously reported cases of metastatic GCT. Almost all the patients had been treated surgically at diagnosis. Seven underwent adjuvant radiotherapy and 5 received adjuvant chemotherapy. They concluded that neither radiotherapy nor chemotherapy appeared particularly effective and that chemotherapy should be reserved only for selected patients.

We report a case of an MGCT destroying the posterior skull base and metastasizing to regional lymph nodes.

CASE REPORT

Clinical Presentation

The patient is a 60-year-old female with a past medical history of coronary heart disease, hypertension, and type 2 diabetes. She also has several years' history of neck pain. She noticed a suboccipital swelling on the righthand side 4 months prior to seeking medical attention. She went on to develop increasing lethargy alongside an increasing suboccipital swelling. She was eventually seen by ENT and had a computed tomography (CT) scan showing a large bone-destroying suboccipital tumor 5 cm in diameter and a second tumor slightly antero-caudal to this 3 cm in diameter. She underwent a fine-needle aspiration cytology (FNAC) that demonstrated atypical granular cells consistent with either a GCT or an oncocytic tumor. A subsequent open biopsy confirmed a GCT with areas of necrosis and vesicular nuclei with prominent nucleoli, whereas a biopsy from epipharynx did not reveal pathology.

The patient was referred to our clinic for further surgery. On admittance she was alert and well with no cranial nerve deficits, in particular not the accessory nerve.

Figure 1 Preoperative MRI shows a brightly contrast-enhancing lesion.

Radiologic Findings

A full radiologic work-up was performed, including contrast-enhanced magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) to visualize the vertebral artery (VA) and magnetic resonance venography (MRV) to visualize the internal jugular vein. The scans showed the above-mentioned suboccipital lesion eroding the lateral skull base medial to the mastoid cells and around the jugular foramen with some enhancement of the dura (Fig. 1). The jugular vein and the ipsilateral transverse sinus were compressed by the tumor. The caudal lesion is seen to be separate from the main lesion, indicating lymph node metastases. A three-dimensional CT scan was performed to visualize the skull base erosions (Fig. 2).

Intervention and Technique

The patient underwent surgery, in park bench position, with the head fixed in a Mayfield headrest,

and the table tilted toward the surgeon. Perioperative facial nerve monitoring was performed. A lazy-S-shaped incision was made two fingerbreadths from the auricle at the level of the lambdoid suture and carried down along the sternocleidomastoid muscle. A 3.5 × 4.0-cm multinodular tumor was removed, representing the caudal metastases of the superficial and the superior, deep cervical lymph nodes, freeing the latter from a medial attachment to the internal jugular vein. Thereafter, a more medial approach was taken to remove the superficial portions of the rostral tumor. The deep part of the trapezius muscle was densely infiltrated by tumor from about C3 level all along to its suboccipital attachment. Both the semispinalis capitis and the longissimus capitis muscles were affected, but to a lesser extent than the trapezius (Fig. 1). They were all partially resected with a margin to remove all tumor tissue. The major and minor rectus capitis muscles were completely engulfed by tumor (Fig. 1) and their attachment sites to the occipital bone completely eroded (Fig. 2). The oblique capitis muscle was infiltrated at its attachment to the C1 transverse process and hence

Figure 2 Preoperative CT shows bone destruction of the posterior skull base.

resected. We then resected tumor along the right VA and performed a hemilaminectomy of a partially eroded lamina C1 to better visualize the artery. During the dissection along the superior margin of the VA, a brisk bleeding occurred. Prefitted vessel loops on the VA were used to rapidly control the bleeding, allowing the identification of a lacerated posterior meningeal artery and meticulous electrocoagulation of the latter. The dura was found to be thickened and tumor infiltrated clinically. However, due to fear of postoperative cerebrospinal leak and infection, tumor was radically shaved off from the dura with an ultrasonic aspirator, rather than excising the dura. The dissection was then carried anteriorly. The medial parts of the mastoid process were removed up to the level of the transverse sinus and anteriorly to the stylomastoid foramen, keeping the facial nerve under close electrophysiologic surveillance. Likewise, the posterior third of the occi-

pital condyle was partly removed due to tumor infiltration (Figs. 1 and 2). In the end, a very small piece of tumor was left in the jugular tuberculum for fear of damaging the nerves of the jugular foramen, as well as a thin sleeve of tumor along the VA at its perforation of the dura. Fat from the thigh was used to fill the cavity and the wound was closed in multiple layers.

Histological Examination

Histological examination demonstrated gross infiltration of tumor into muscles and adipose tissues. Microscopically the tumor consisted of polygonal cells with abundant eosinophilic granular cytoplasm. The cells showed an increased nuclear to cytoplasmic ratio and vesicular nuclei with prominent nucleoli (Fig. 3A). Furthermore, there were

Figure 3 (A) Histopathological appearance of the tumor cells with granular eosinophilic cytoplasm, nuclear pleomorphism, and one mitosis (hematoxylin and eosin [H & E], $\times 400$). (B) Spindling of tumor cells (H & E, $\times 400$). (C) Immunohistochemical staining for S-100 protein. Strong immunoreactivity for perineural tumor cells ($\times 400$).

Table 1 Histopathological Criteria for Malignancy in Granular Cell Tumor,²⁶ Present or Not Present in the Discussed Case

Necrosis	Present
Spindling of cells	Present
Vesicular nuclei with large nucleoli	Present
More than two mitoses/10 HPF ($\times 200$)	Not present
High nuclear to cytoplasmic ratio	Present
Pleomorphism	Present

Three or more fulfilled criteria classify as malignant granular cell tumor.
One to two criteria present are regarded as atypical granular cell tumor.
HPF, high-power field.

areas of spindling of the tumor cells and necrosis (Fig. 3B). Therefore the tumor fulfilled five out of six criteria for malignant GCT (Table 1).⁵ In addition, perineural infiltration in several small peripheral nerves was detected (Fig. 3C). Immunohistochemically there was a strong immunoreactivity for S-100-protein, vimentin, and NSE (neuron specific enolase). Ki67 showed a low proliferation rate with fewer than 1 to 5% positive cells.

FURTHER TREATMENT

The patient made an uneventful recovery. When the swelling subsided, a weakness of the trapezius muscle was noted, as expected. A contrast-enhanced MRI immediately after surgery showed no apparent residual tumor (Fig. 4). She underwent adjuvant image-modulated radiotherapy (IMRT) starting 4 weeks after surgery. Patient immobilization and adequate reproducibility was reached by an individualized thermoplastic mask encompassing the shoulders. The gross target volume (GTV), the clinical target volume (CTV), and spinal cord and other structures were outlined on CT treatment planning scans. The GTV included the area medial to the mastoid process and the CTV included GTV and the surrounding tissues at risk for microscopic disease (operation cavity and neck muscles). The CTV was expanded 3 mm to obtain the planning target volume (PTV). IMRT plans were generated using five equally spaced coplanar axial 10MeV beams for a multileaf

Figure 4 Postoperative MRI demonstrating no contrast-enhancing residual with an autologous fat graft in the excision cavity.

collimator-equipped linear accelerator (Siemens Oncor, Siemens AG). The IMRT plan was developed using Oncentra MasterPlan 1.4 Service Pack 4 (Nucletron BV, Veenendaal, The Netherlands), using gradient-based optimization of the cost function. Dose distribution calculation included the effects of inhomogeneities such as air and bone. Treatment was delivered using a schedule consisting of 1.8 Gy fractions once a day to 59.4 Gy. Maximum dose to the spinal cord was 51.5 Gy.

DISCUSSION

In the head and neck region, MGCTs are usually found in the oral cavity, but case reports have described tumors arising from the recurrent laryngeal nerve,²³ the cervical sympathetic nerve trunk,²⁹ the retrotracheal space,³⁰ and in the infratemporal fossa.³¹ Furthermore, a case presenting with Eagle syndrome, that is, elicitation of pain on swallowing, turning the head, or extending the tongue caused by irritation of the glossopharyngeal nerve, has been described.³²

Perineural extension of head and neck tumors is well known and most commonly seen in squamous cell carcinomas and adenoid cystic carcinomas.^{33,34} However, this pattern of spreading is also seen in GCTs,³⁵ desmoplastic fibromas,³⁶ malignant melanomas,³⁷ and nasopharyngeal carcinomas.³⁸ In most cases, the tumor spreads directly in the perineural or the endoneural tissue planes along the path of least resistance.³⁵

In our case, the suboccipital nerve was the nerve of origin. The posterior division of the first cervical or suboccipital nerve emerges above the posterior arch of the atlas and beneath the VA.³⁹ It enters the suboccipital triangle and supplies the muscles that bound this triangle, that is, the rectus capitis posterior major and the obliqui superior and inferior. It gives branches also to the rectus capitis posterior minor and the semispinalis capitis. The nerve occasionally gives off a cutaneous branch which accompanies the occipital artery to the scalp

and communicates with the greater and lesser occipital nerves.³⁹ In our case, it was very evident that the MGCT extended via a perineural mechanism along the posterior ramus of the suboccipital nerve, invading the perifocal muscles of the neck (Fig. 1).

The anterior division of the suboccipital nerve issues from the vertebral canal above the posterior arch of the atlas and runs forward around the lateral aspect of its superior articular process, medial to the vertebral artery.³⁹ In most cases it descends medial to and in front of the rectus capitis lateralis, but occasionally it pierces the muscle. It then unites with the anterior divisions of the other upper four cervical nerves to form the cervical plexus.³⁹ In our case, the antero-caudal lesion represented tumor extension along the anterior branch of the first cervical nerve (Fig. 1), as well as a metastasis to a regional lymph node.

CONCLUSION

In conclusion, this case represents the first report of resected primary MGCT involving the posterior fossa and arising from the suboccipital nerve.

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