Multimodal Treatment of Osteogenic Sarcoma of the Jaw

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ABSTRACT

Osteosarcomas (OSs) account for 40 to 60% of primary malignant bone tumors. About 10% occur in the head and neck region, frequently in the mandibula or maxilla. We treated a 30-year-old patient with 26-month history of right-sided facial pain and paresthesia. Investigation showed high-grade OS of the right mandibular coronoid process, affecting the mandibular nerve, middle cranial fossa, internal jugular vein, and internal carotid artery (ICA). True en bloc resection was performed after upfront adjuvant chemotherapy. The ICA was trap-ligated intradurally, whereafter the floor of the middle fossa, including the mandibular nerve and the glenoid fossa, was detached from the skull base in one piece. Subsequently, a hemimandibulectomy, total parotidectomy, ICA sacrifice, and removal of the pterygoid plates and muscles were performed, and the abovementioned structures were removed as a solitary specimen, including the facial nerve branches overlying the tumor. A sural nerve graft was interposed between five major facial nerve branches to reanimate the face. The patient had an uneventful recovery, is able to eat, and has a partial facial nerve palsy. He has no tumor recurrence 26 months after surgery. OS of the jaw should be treated with radical surgery as the primary modality.

KEYWORDS: Osteosarcoma, en bloc resection, tumor of the skull base, craniofacial surgery, jaw tumor

Osteosarcoma (OS) is a rare but highly malignant bone tumor. It is also the most common primary malignant lesion of bone in patients under 40 years, excluding multiple myeloma.¹⁻³ OS is a malignancy of mesenchymal cells that have the ability to produce osteoid or immature bone. The origin of these tumors is largely unknown. Head and neck OS are rare tumors, reported to represent only 10% of all OSs. Jaw OSs are even rarer, accounting for only 4% of all documented cases.⁴ In the jaw, the natural history of OS differs from that of tumors involving other skeletal bones. Also, the average age at onset of OS of the jaw is 10 to 20 years

later than that reported for skeletal lesions, and survival rates are higher.⁵⁻⁷ The most common signs and symptoms associated with OS of the jaw as reported in the literature are persistent pain, swelling, loose teeth, and paresthesia.^{8,9}

MANAGEMENT

Aggressive surgical resection and advanced reconstructive techniques have improved survival rates and decreased morbidity of patients undergoing resection of anterior cranial base malignancies. However, malignant

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Figure 1 Prechemotherapy, preoperative magnetic resonance imaging T1 with contrast. (A) Coronal section. (B) Axial section.

tumors involving the infratemporal fossa have previously been considered unresectable. Historically, tumor resection was avoided in this region because of the perceived biological aggressiveness of these tumors, difficulty in achieving negative histological margins, and the associated surgical morbidity and mortality.¹⁰

Modern operative techniques have made tumor resection feasible and safe in an en bloc fashion with negative histological margins. Surgery of OS of the jaw is likely to be curative when it is amenable to radical resection with clear margins^{11–17}; therefore, OS of the jaw should be treated with radical surgery as the primary modality.

Multimodal treatment of patients with OS in long bones is well established. In such patients, chemotherapy using multiple agents has been shown to improve survival.¹⁸ However, the role of chemotherapy in craniofacial OS is less clear, and results of meta-analyses are uncertain. If resectability with clear margins is questionable at diagnosis, preoperative chemotherapy is usually given to obtain tumor shrinkage.¹² Also, it does permit the potential advantages of early eradication of micrometastatic disease, delivery of chemotherapy into an intact blood supply, and assessment of the effectiveness of the preoperative chemotherapy regimen used.¹⁹

CASE REPORT

Clinical Presentation

A 30-year-old man was referred to the hospital with a 26-month history of pain and paresthesia on the right side of his maxilla and mandible. He also had trismus and was unable to open his mouth further than 2.5 cm. He presented with swelling over the zygomatic bone and the growth had expanded into the ramus of the mandible.

He was hospitalized and investigated by a multidisciplinary team, including head and neck surgeons, neurosurgeons, oncologists, radiologists, and pathologists. Magnetic resonance imaging (MRI)/computed tomography (CT) scan, skeletal scintigraphy, lung CT, and finally a biopsy of the right ramus mandibulae were

performed. The radiological investigations were consistent with a high-grade OS originating from the coronoid process of the mandible on the right-hand side (Fig. 1). No distant metastases were discovered. The tumor was growing up toward the skull base, affecting the mandibular nerve and the floor of the middle cranial fossa, encasing the internal carotid artery (ICA) and in close contact with the internal jugular vein.

Intervention and Technique

Based on the preoperative radiological evaluation of the patient, OS was suspected. Therefore, a biopsy of the right ramus mandibulae was performed under general anesthesia. This had to be done from an external access site so the biopsy canal could be excised during a subsequent operation. A biopsy with external access in this area carries a high risk for facial nerve damage, but it was deemed acceptable because the planned subsequent surgery carried the same risk. Histology of the biopsy specimen showed high-grade osteoblastic OS.

The patient was treated with preoperative chemotherapy according to the EURAMOS I trial (<http://www.ctu.mrc.ac.uk/euramos>). The regimen includes high-dose methotrexate, doxorubicin, and cisplatin. The scheduled duration of preoperative chemotherapy was 10 weeks. Surgery was performed 3 weeks after preoperative chemotherapy. Postoperatively, 12 cycles were given with the same drugs.

A clinical-radiological response was observed. There was less swelling, decrease of pain, and some reduction of the extraosseous soft tissue component on MRI after preoperative treatment. Lower signal and decreased contrast uptake were also seen (Fig. 2). CT showed increased ossification, indicating a therapeutic response. The planned surgical treatment involved ICA sacrifice, which required preoperative knowledge of the feasibility of permanent occlusion of the ICA. Conventional cerebral angiography with a balloon test occlusion was performed. Blood velocity in the ipsilateral middle cerebral artery (MCA) fell to 70% of the preocclusion value and increased to 100% during the subsequent minute, indicating that ICA sacrifice would be well

Figure 2 Postchemotherapy, preoperative magnetic resonance imaging T1 with contrast. (A) Coronal section. (B) Axial section.

tolerated.²⁰ Conventional angiography and magnetic resonance venography were used to evaluate the cerebral venous drainage, with special emphasis on the transverse sinuses bilaterally.

A multidisciplinary conference resulted in a detailed surgical plan, followed by a preoperative mock operation in the cadaver laboratory.

To navigate during the surgery, an image guidance system was used (BrainLAB, Bayern, Germany). The resection lines had been marked out on the preoperative CT images, thus facilitating their identification intraoperatively. Furthermore, the great vessels were also marked out on preoperative images, thus reducing the risk of accidental injury to the vessel (Fig. 3).

Figure 3 BrainLAB™ neuronavigation images illustrating tumor (green), internal carotid artery (red), internal jugular vein (blue), optic nerve/chiasm (yellow), eye bulb (lilac).

The operation was performed under general anesthesia with the patient's head placed in a Mayfield head holder in a neutral neck position. A modified Falconer incision was performed on the right side and carried preauricularly down to the tragus. The scalp flap was lifted and interfascial dissection over the temporal muscle was performed. Next, the skin incision was carried down along the sternocleidomastoid muscle toward the jugulum, and an extended dissection of the parotid region was performed, marking out the major facial nerve branches with the help of a nerve stimulator. The temporal muscle was divided transversely so that the cranial part was kept intact and attached to the superior temporal line, and the lower half was kept attached to the coronoid process. The temporal muscle was pulled caudally after a zygomatic arch osteotomy was performed.

A standard frontotemporal craniotomy was then carried down to the floor of the middle cranial fossa. An extradural anterior clinoidectomy *ad modum* Dolenc²¹ was performed. The middle meningeal artery was coagulated and cut, allowing cuts in the floor of the middle cranial fossa to be made from behind the glenoid fossa just anterior to the petrous ridge. The cut was made anteromedially to the foramen ovale, which defined the medial border of the craniotomy, and then anteriorly to the foramen rotundum, coming medial to the lateral pterygoid plate.

After the identification of the extradural carotid segment (C3), the dura mater was opened and the anterior part of the Sylvian fissure was split. The ipsilateral ICA, anterior choroidal artery, posterior communicating artery, and ophthalmic artery were identified, and ICA closure was performed with a Yasargil 720 clips (Gimmi GmbH, Tuttlingen, Germany) proximal to the

posterior communicating artery. The intradural closure of the ICA was a key step during this process to prevent backward blood flow from the brain down to the surgical field, thus preventing cerebral steal during surgery, as well as reducing the risk of thromboembolism from the ICA stump postoperatively.

The floor of the middle fossa, including the mandibular nerve, the glenoid fossa, and the overlying dura, was detached from the skull base. The mandible was exposed and cut between teeth 46 and 47, anterior to the attachments of the medial and lateral pterygoid muscles. The ICA was ligated just below the skull base and in the neck and subsequently sacrificed.

The specimen, including the tumor, the mandibular nerve, parts of middle fossa dura, large parts of the middle fossa floor, the medial and lateral pterygoid plates and muscles and part of the mandible with the caput and coronoid process, the zygomatic arch, and caudal half of the temporal muscle, as well as ipsilateral ICA and jugular vein, was removed as a solitary specimen (Fig. 4).

The dural defect was closed with the use of Tachosil (Nycomed AS, Asker, Norge). A vascularized pericranial graft was placed above the earlier dural incision down to the anterior clinoid process. The frontotemporal bone flap was repositioned and rigidly fixed (Fig. 5A, B). A reconstruction of the facial nerve was performed using a free saphenous nerve graft.

The patient was treated with antibiotics and high-dose steroids intra- and postoperatively. Because of the ICA sacrifice, he was kept sedated and on a ventilator for several days postoperatively with strict control of the mean arterial pressure and under surveillance with a transcranial Doppler (TCD). Baseline TCD readings in the various cerebral arteries were performed daily after the surgery. During these readings, the lower limit for

Figure 4 Schematic drawing of the craniotomy lines projected on a photograph of the skull. (A) Superior view. (B) Lateral view.

Figure 5 Postoperative images. Computed tomography with 3-D reconstruction: (A) front, (B) lateral view. Clinical photo: (C) front, (D) lateral view.

the ipsilateral MCA blood velocity was set to 80% of the preocclusion baseline value,²⁰ and this limit was never crossed. After extubation, the patient had no new neurological deficits apart from those related to the facial and mandibular nerves.

Histological examination of the tumor verified an osteogenic sarcoma of high-malignancy grade with osteoblastic and chondroblastic components. The amount of viable tumor cells in the resected specimen was greater than 10%, defined as poor histological response to chemotherapy (Euramos I). The resection margins were clear.

Postoperative chemotherapy was scheduled to commence 2 weeks after surgery. Moderate reductions

of glomerular filtration and cardiac output were registered, and therefore the treatment was postponed by another 2 weeks. Adjuvant chemotherapy was then completed without complications.

The patient had an uneventful recovery. He resumed his work as car mechanic after 3 months. He is in good health and has only minor difficulties with his jaw movement. He has no tumor recurrence or metastases 16 months after chemotherapy, 27 months after surgery (Fig. 5C, D).

Because he is considered to be a long-term survivor, we have planned a craniofacial reconstruction to improve his cosmesis and function. An artificial,

customized prosthesis that replaces his zygomatic arch, temporomandibular joint, and the mandibular ramus will be made.

DISCUSSION

Craniofacial OSs are rare tumors, reported to represent only 10% of all OSs.⁴ Similar to OS of the extremities, complete excision with a true en bloc resection with clear margins is a cornerstone in the treatment of OS in the head and neck region. However, due to the many critical nervous and vascular structures in this region, complete excision in an en bloc fashion is often extremely difficult and has been considered impossible in the past.

A multidisciplinary team, consisting of neurosurgeons, head and neck surgeons, plastic surgeons, oncologists, radiologists, and pathologists, may achieve more radical resections than a monodisciplinary approach. In selected patients, the use of preoperative chemotherapy may facilitate a complete excision. Furthermore, the use of advanced neuronavigation systems can support the safe planning and processing of the surgical treatment to achieve clear margins. Treatment of these tumors may involve therapeutic arterial sacrifice, where angiographic balloon test occlusion can provide the preoperative knowledge required of the feasibility of permanent occlusion of the ICA. Our case may serve to demonstrate the virtues of such a multidisciplinary approach, where meticulous presurgical planning, preoperative mock operation in the cadaver laboratory, and use of neuronavigation and intraoperative neurophysiology can help to make aggressive surgery feasible and safe.

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