Neoadjuvant Chemotherapy to Reduce Morbidity and Improve Surgical Resection in a Skull Base Ewing’s Sarcoma: case report

Quimioterapia Neoadjuvante para Redução de Morbidade e Melhora de Ressecção Cirúrgica em Sarcoma de Ewing de Base de Crânio: relato de caso

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ABSTRACT

Ewing’s Sarcoma (ES) affects skull base in 1-6% of the cases. Involvement of orbit, optic nerve and the brain may preclude complete surgical resection without severe morbidity. Neo-adjuvant chemotherapy is part of the standard care in extracranial ES. Imaging suggesting a different, more common diagnosis or urgent need to decompression of neural structures are commonly reasons by which neoadjuvant chemotherapy is not used in skull base ES. We present a case of a 3-year-old patient presenting a skull base ES where in spite of the fast progressing visual decline, neoadjuvant chemotherapy had demonstrated to be a valuable tool to symptoms improvement and reduce surgical morbidity without compromising radical surgery.

Keywords: Ewing; Sarcoma; Skull base; Tumor

RESUMO

O Sarcoma de Ewing (SE) afeta a base do crânio em 1-6% dos casos. O envolvimento da órbita, do nervo óptico e do cérebro pode impedir a ressecção cirúrgica completa sem morbidade grave. A quimioterapia neoadjuvante faz parte do cuidado padrão no SE extracraniano. Exames de imagem sugerindo um diagnóstico diferente, mais comum ou sob necessidade urgente de decompressão de estruturas neurais são comumente as razões pelas quais a quimioterapia neoadjuvante não é usada em SE da base de crânio. Apresentamos um caso de um paciente de 3 anos com SE da base de crânio onde, apesar do rápido declínio visual, a quimioterapia neoadjuvante demonstrou ser uma ferramenta valiosa para melhora dos sintomas e redução de morbidade cirúrgica sem comprometer a cirurgia radical.

Palavras-chave: Ewing; Sarcoma; Base de crânio; Tumor

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INTRODUCTION

The Ewing’s sarcoma family of tumors (ESFT) is an entity that encompasses 3 highly aggressive forms of childhood cancer: Ewing’s sarcoma, Askin tumor, and peripheral primitive neuroectodermal tumor\(^1\). While Ewing’s sarcoma is most commonly found in pelvis, chest, femur, tibia, vertebrae and humerus; skull base involvement is extremely uncommon\(^2\). Therefore, management is usually extrapolated from other locations. Surgical resection is the initial treatment in most cases, as imaging usually suggest a different, more common diagnosis, or due to the need of decompression of neural structures\(^4\). We present a case of an extensive Ewing’s sarcoma of the anterior skull base in a pediatric patient that was treated with neoadjuvant chemotherapy followed by surgery.

CASE PRESENTATION

A 3-year-old girl was presented with a history of fifteen days of progressing proptosis in the left eye associated with visual impairment and anosmia. She had unremarkable past medical history. MRI showed a contrast-enhancing mass in the anterior skull base, centered in the ethmoid sinus with intracranial extension and extending into the left orbit (Figure 1). The patient underwent an endonasal endoscopic biopsy due to the uncertainty of the diagnosis, with frozen section compatible with a small blue round cell tumor, and definitive pathology consistent with Ewing’s sarcoma. Immunohistochemistry was positive for CD99, S100 and EMA, and fluorescent in-situ hybridization was positive for ESR1 rearrangement of the chromosome 22q1, confirming ES. PET Scan and whole body MRI excluded metastatic disease.

The patient underwent induction chemotherapy with vincristine, doxorubicin and cyclophosphamide, alternating with ifosfamide and etoposide (VDC-IE protocol). Follow-up MRI after 8 weeks showed significant reduction of the contrast-enhancing mass, with residual lesion in the ethmoid bone (Figure 2). Due to the patient’s age, surgery of the remaining mass was preferred over radiation therapy.

A combined approach (transcranial and endonasal) was chosen to effectively decompress the infero-medial wall of the optic canal as well as medial wall of the orbits. Reconstruction is also more effectively harvesting pericranium plus bilateral temporal facia graft superiorly and a nasal septum flap or lateral wall, allowing a three-plane reconstruction.

Through a bifrontal craniotomy, the anterior cranial base was exposed extradurally, with transection of the olfactory fibres. The tumor was seen at the level of planum sphenoidale and left orbital roof. The bulk of the tumor was resected, as well as the cribriform plate and planum. The left optic canal was unroofed along with the orbit, and the periorbit was also resected. Adjacent dura mater and both olfactory bulbs were also removed. Endonasally, both middle and superior turbinates were removed bilaterally along with the remaining ethmoid cells and lamina papyracea. Decompression of the left optic canal was achieved in a 360-degree fashion by removing the medial and inferior walls. Frozen section confirmed negative surgical margins (Figure 3).

Reconstruction of the skull base was performed with a large pericranial plus temporal muscle fascia flap, titanium mesh and nasal septum flap. Postoperative MRI demonstrate a complete surgical resection (Figure 4).

The early postoperative period was unremarkable, however, on postoperative day 5, the patient developed paraparesis due to symptomatic vasospasm on the anterior cerebral arteries, that was managed with intra-arterial milrinone followed by intravenous milrinone for 48 hours, with complete relieve of the symptoms. The patient was discharged on postoperative day 10.

Afterwards, the patient received 9 cycles of the VDC-IE protocol starting fourteen days after discharge. At one year follow-up the patient is in complete remission.

DISCUSSION

Ewing’s sarcoma is thought to involve the skull in 1-6% of cases\(^6\), and due to the rapid growth, most patients present with compressive neurological symptoms, or sinonasal complaints such as nasal obstruction, rhinorrhea and epistaxis. In particular, patients with periorbital extension may present with proptosis, periorbital edema and decreased visual acuity\(^8\).
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Figure 1. Axial and sagittal T1WI post gadolinium MRI demonstrating an enhancing tumor mass extending from upper clivus to anterior cranial fossa centered at the cribriform plate, ethmoid and sphenoid bone extending into right and left orbital cavity, compressing the optic nerve (white arrow) and invading the periorbit (black arrow). A proptosis is seen in the left eye.

Figure 2. Comparative T1WI post gadolinium MRI (A. pre adjuvant chemotherapy; B. post adjuvant chemotherapy after 8 weeks of adjuvant chemotherapy) demonstrating a significant reduction in the tumor mass, absence of periorbit involvement and resolution of the proptosis in the left eye.
Current treatment for Ewing’s sarcoma relies on multi-drug chemotherapy\(^{10,11}\), which has improved overall survival from 10 to 75% for localized disease\(^1\). Chemotherapy may be associated with surgery and/or radiation therapy for local control. Neoadjuvant chemotherapy has been increasingly used for, but no report on its use for skull base disease has been reported\(^12\).

Ewing’s sarcoma involving the skull base possesses a unique challenge, as location, size, extension, and effect on neurological structures dictate the need of urgent volume reduction. Moreover, imaging is usually non-diagnostic, and may suggest a primary lesion such as meningioma. Therefore, the need of surgical resection must be weighted toward the possibility of achieve negative surgical margins, which has been shown to reduce local recurrence rates\(^1\). Induction chemotherapy in this setting provides an interesting opportunity to optimize both goals, as in responding cases, cytoreduction is rapidly achieved, potentially sparing structures that would otherwise be resected, such as the optic pathway. Moreover, by controlling microscopic disease adjacent to the bulk of the tumor, we believe that also improves the rate of negative margins achieved by surgery, which is exemplified by our case, where induction chemotherapy achieved rapid improvement of visual acuity, mass reduction, and allowed us to achieve negative margins without the need of orbit exanteration, which would have been probably needed otherwise.

Figure 3. Comparative images. A. preoperative T1WI post gadolinium MRI.; B. postoperative T1WI post gadolinium with subtraction MRI demonstrating complete surgical resection of the residual tumor. An adequate decompression of the orbit as well as the optic canal can be seen.
CONCLUSION

In conclusion, induction chemotherapy is a feasible approach to manage Ewing’s sarcoma of the skull base, possibly improving the rate of negative margins after surgery.

REFERENCES

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