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Craniopharyngioma with malignant transformation: A case report

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ABSTRACT

Introduction: Craniopharyngiomas are usually slow growing, benign epithelial tumors, arising from cell remnants of Rathke's pouch with its ultimate site of origin being the embryologic stomadeum. Although considered WHO grade I tumors, they are often locally aggressive. However, malignant transformation is extremely rare. Until now, 42 cases of malignant craniopharyngioma have been reported. In this article, the interdisciplinary, i.e. neurosurgical and maxillofacial, approach to a case of secondary malignant craniopharyngioma with multiple recurrences is discussed.

Case report A 73-year-old woman with a history of recurrent, extracranially expanding craniopharyngioma was referred to the department of Neurosurgery following the MRI finding of a 7th tumor recurrence, located at the level of the right lateral orbital wall. Previously, the patient had already undergone five surgical resections and three radiotherapeutic treatments elsewhere. Histopathological examination revealed an adamantinomatous craniopharyngioma with sites of malignant transformation. Tumor resection with exenteration of the right eye was performed with an immediate reconstruction using a PEEK-PSI (Patient Specific Implant) and anterolateral thigh flap. Histopathological examination confirmed the diagnosis of craniopharyngioma with malignant transformation.

Conclusions: Malignant transformation in a craniopharyngioma is uncommon but has a poor prognosis. The assumed correlation between radiotherapy and malignant transformation is not yet clearly established. Therefore, radiotherapy remains a good choice to reduce recurrence of a benign cranopharyngioma. PEEK implantation seems a safe option for allogenic reconstruction in patients with large maxillofacial defects. In complex cases the benefit of a multidisciplinary approach should not be underestimated.

1. Introduction

Craniopharyngiomas are slow growing, benign epithelial tumors, arising from cell remnants of Rathke's pouch [1–3].They can be divided in two different subtypes, the adamantinomatous and the papillary squamous type, each with distinct histopathological characteristics [2–4].

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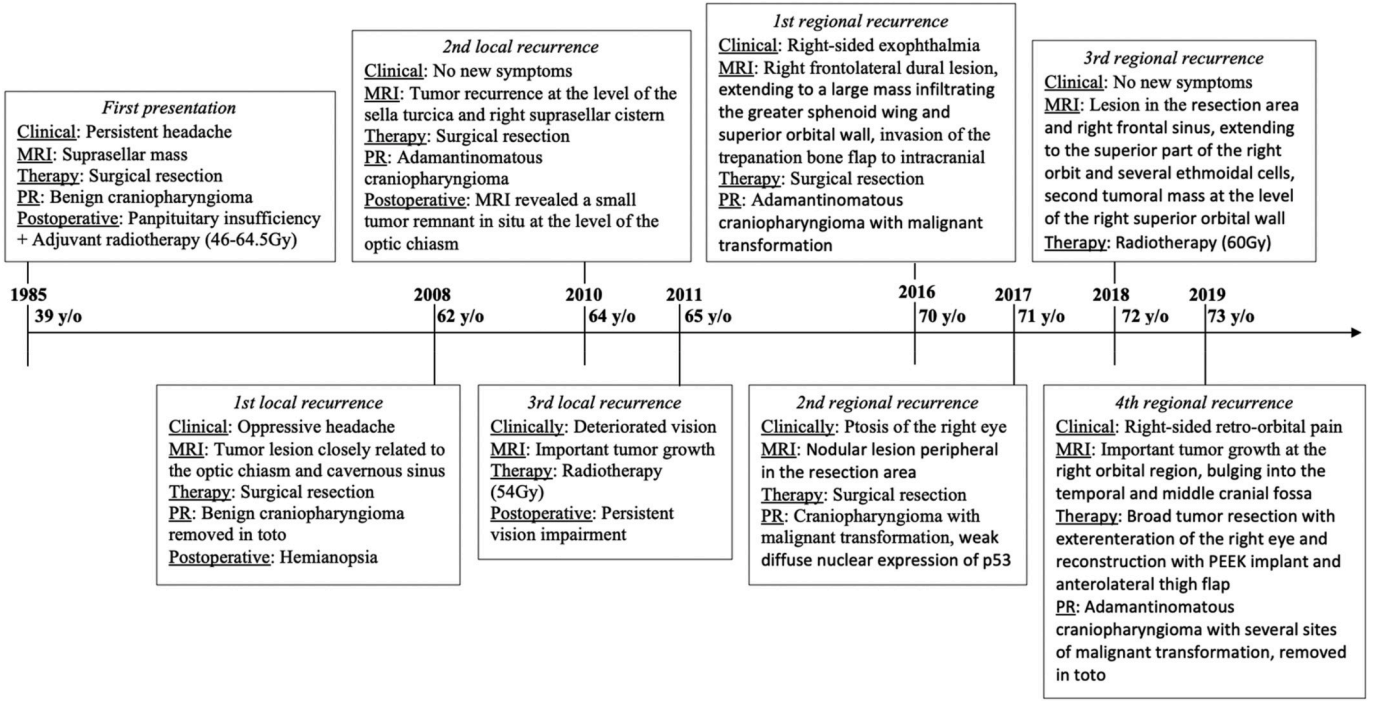

Fig. 1. Timeline of oncological history. PR, Pathology report.

Although craniopharyngiomas are considered WHO grade I tumors, they often show aggressive local behavior like hypothalamic brain invasion and multiple recurrences, with the vast majority being confined to the intracranial compartments [2,5]. Malignant transformation in a craniopharyngioma is extremely rare and limited to the adamantinomatous subtype [2]. It was first reported in 1973 by Salyer et al. [6]. Since then, 42 cases of malignant craniopharyngioma have been described [7,8]. Radiotherapy has been suggested as an inducing factor [2,4].

In this article, a case of secondary malignant craniopharyngioma with multiple recurrences and extracranial expansion is discussed. We will focus on the interdisciplinary, i.e. neurosurgical and maxillofacial, approach to the 7th tumor recurrence, occurring at the level of the right orbit, the greater sphenoid wing and the dura of the anterior temporal pole. A broad tumor resection with exenteration of the right eye, removal of the affected dura over the anterior temporal base and reconstruction with a PEEK-PSI and anterolateral thigh flap was performed by a team of maxillofacial- and neurosurgeons.

1.1. Case report

A 73-year-old woman with a history of recurrent craniopharyngioma was referred to the department of Neurosurgery following the MRI finding of a 7th tumor recurrence. The lesion was located in the right lateral orbital wall, invading the greater sphenoid wing and bulging into the temporal base and middle cranial fossa. The complete oncological history is displayed in Fig. 1.

The patient presented with right retro-orbital pain. Clinically, there were no eye movement disturbances, nor signs of exophthalmia. Due to previous radiotherapy, vision was almost completely lost in the right eye. MRI showed an increased volume of a tumor remnant in the right lateral orbital wall, extending into the lateral part of the orbit. Anterior, the mass reached to the eyeball, posterior to 4–5mm before the superior orbital fissure. Tumor growth through the posterolateral orbital wall was seen, bulging into the middle cranial fossa with presumably meningeal invasion. The greater sphenoid wing was invaded up to the inferior orbital fissure. Furthermore, there was limited intradural bulging of the mass into the temporal fossa. Dimensions of the tumor were estimated at 42 × 26 × 30mm (Fig. 2).

Further staging with a CT of the orbits, thorax and abdomen was performed without evidence of metastatic disease. The case was discussed multidisciplinary and despite the potential meningeal involvement, the lesion was considered resectable. A combined

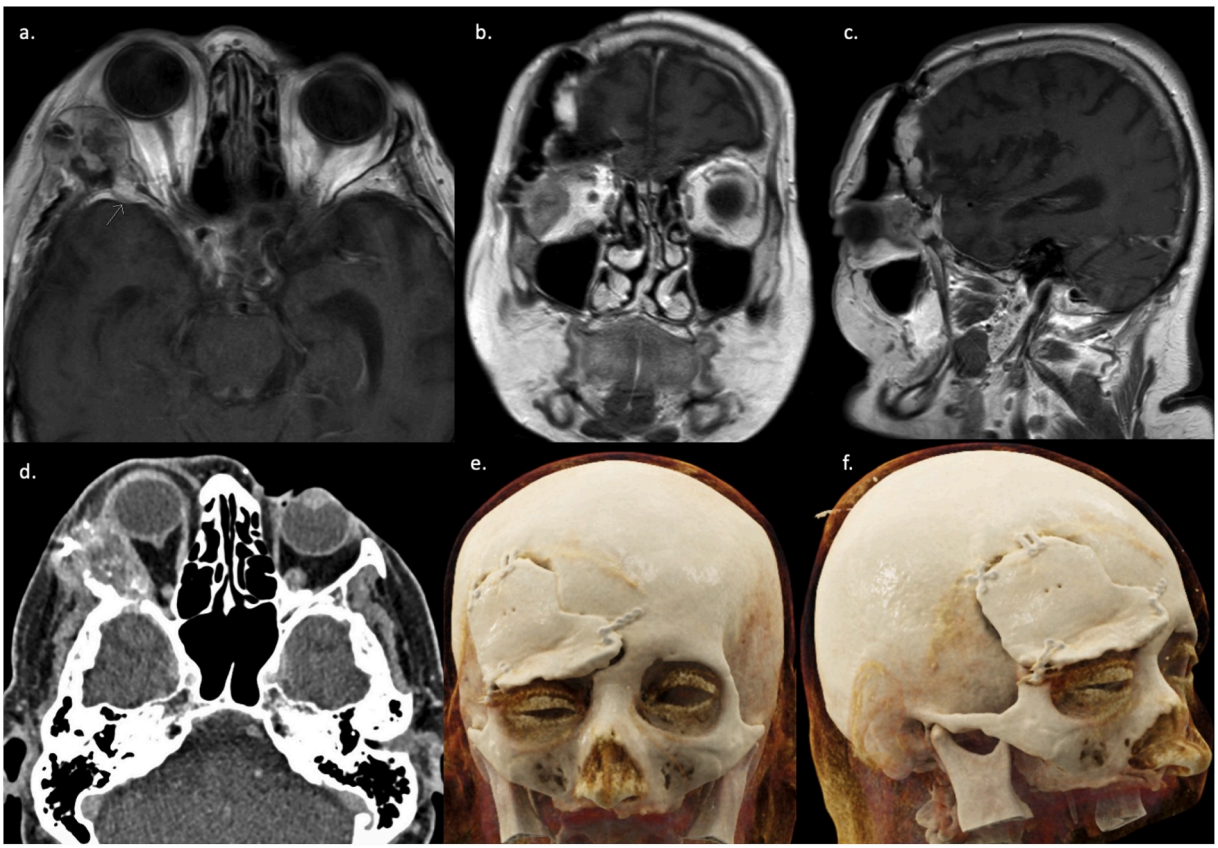

Fig. 2. Preoperative imaging. (a–c) MRI imaging (T1-weighted) showing a tumor lesion at the level of the right lateral orbital wall, extending into the lateral part of the orbit. Anterior, reaching to the eyeball, posterior to 4–5mm before the superior orbital fissure. Estimated dimensions: 42 × 26 × 30mm. (d) CT imaging confirmed the presence of a lobulated tumor recurrence at the right lateral orbital wall with secondary exophthalmia. (e–f) 3D-reconstructed CT images.

neurosurgical and maxillofacial surgical intervention was planned with resection of the former temporal craniotomy bone flap, the right lateral and superior orbital wall, the posterior orbital floor, a part of the zygomatic body, the lateral wall of the maxillary sinus and the skull base from sphenoid till orbital fissure, along with the right eyeball. This trajectory was simulated using 3D-models (Fig. 3). Furthermore, a PEEK-PSI was designed based on the CT data of the surgical plan.

For surgical access, the pre-existent right-sided hemicoronal approach was used. The old craniotomy bone flap was removed and the zygomatic arch till the orbit and the greater sphenoid wing were exposed. Craniotomy of the squamous part of the temporal bone was performed. At the site of intracranial tumor growth, invasion of the dura was confirmed for which resection from temporal base to 2mm before the superior orbital fissure dura was performed. A right vitrectomy with afterwards, an osteotomy of the lateral orbital wall and posterior floor was done. For the osteotomy of the zygomatic body a 3D cutting guide was used successfully keeping the maxillary sinus mucosa intact. The optic, oculomotor, trochlear and abducens nerves were dissected posteriorly in the orbit. Finally, an osteotomy of the skull base from sphenoid till orbital fissure was done. The tumor was removed en bloc with the eye (Fig. 4).

Reconstruction of the bony defect was performed with a PEEK-PSI, fixated using 1.5 and 2.0 KLS systems (Fig. 5). Watertight dural closure was obtained using local temporal fascia and Tachosil. To provide additional soft tissue reconstruction, an anterolateral thigh flap of the left leg was used. The muscular bulk of the vastus lateralis muscle was inserted on the inside of the orbit while the skin paddle of the flap was used to cover the PSI. After an ischemia time of 1h15min, arterial and venous end-to-end anastomosis was performed on the right superficial temporal artery and vein, respectively.

Postoperative histopathological examination of the resection specimen confirmed the adamantinomatous craniopharyngioma with sites of malignant transformation. Surgical margins were negative with a minimal tumor-free margin of 1 mm on the lateral side. Multidisciplinary team decision was for careful follow-up without further adjuvant therapy.

Immediate postoperative course and recovery were uneventful. MRI follow-up at 3 months showed no evidence of tumor remnant or recurrence.

2. Discussion

Craniopharyngioma is a well-recognized benign tumor of the central nervous system, arising from cell remnants of Rathke's pouch [1,3]. Often, patients present with visual disturbances, anterior pituitary hormone deficiency, hydrocephalus or non-specific symptoms of an elevated intracranial pressure [9]. Malignant transformation is extremely rare [5]. The first case was reported in 1973 by Salyer et al. [6]. Since then, a total of 42 cases of malignant craniopharyngioma have been described, including the present case [7,8].

In 11 patients (26%) the malignancy originated de novo, whereas in 31 patients (74%) there was malignant transformation of a benign craniopharyngioma. The mean age at diagnosis of a benign craniopharyngioma was 17.7y (range 3–58y). However, the mean age at diagnosis of a malignant craniopharyngioma, both primary and secondary types, was 30.5y (range 2.5–70y). Consequently, the mean time to malignant transformation was 13.2y (range 2–55y). The overall male/female ratio was 1:1.2.

The mechanism for malignant transformation in craniopharyngiomas is still unknown. Most common characteristics of patients presenting with malignant transformation are numerous tumor recurrences, multiple surgical resections and adjuvant radiotherapy [7].

As in our case, benign craniopharyngioma recurrence is very frequent. Recurrence rates after complete tumor resection are approximately 20–30%, while partially resected tumors have recurrence rates up to 60–70% [1,10]. Adjuvant radiotherapy appeared to decrease the risk of benign tumor recurrence in incomplete surgical resections to 5–30% [1,10,11].

Among 31 cases of secondary malignant craniopharyngioma reported in literature, 24 patients (77%) received radiotherapy before the malignant transformation, whereas 7 (23%) did not. Accordingly, several authors presumed that radiotherapy plays an important role in inducing malignant transformation of a craniopharyngioma [1,12,13]. Radiation-induced DNA damage may cause carcinogenesis but the precise mechanism is not yet fully understood [14]. Nevertheless, following Gao et al. there have to be some other factors contributing to the malignant transformation of a craniopharyngioma, because the vast majority of cases in which the patients

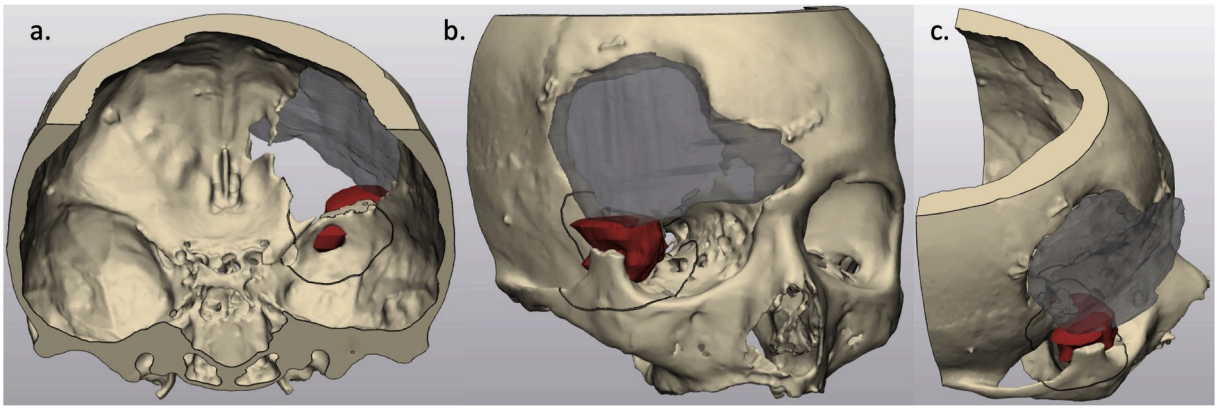

Fig. 3. Preoperative 3D-planning with tumor segmentation. (a) Posterior view. (b) Quarter view. (c) Superior view.

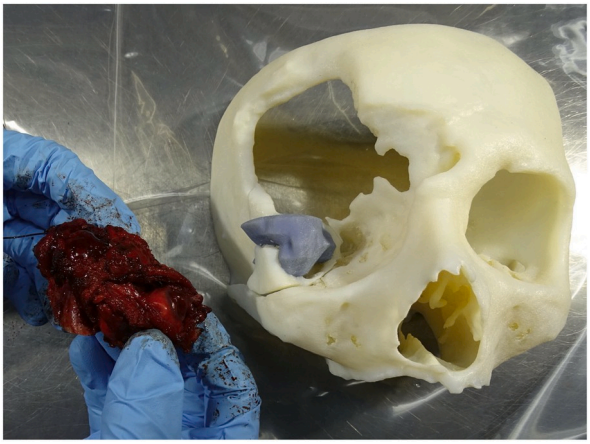

Fig. 4. Resection specimen.

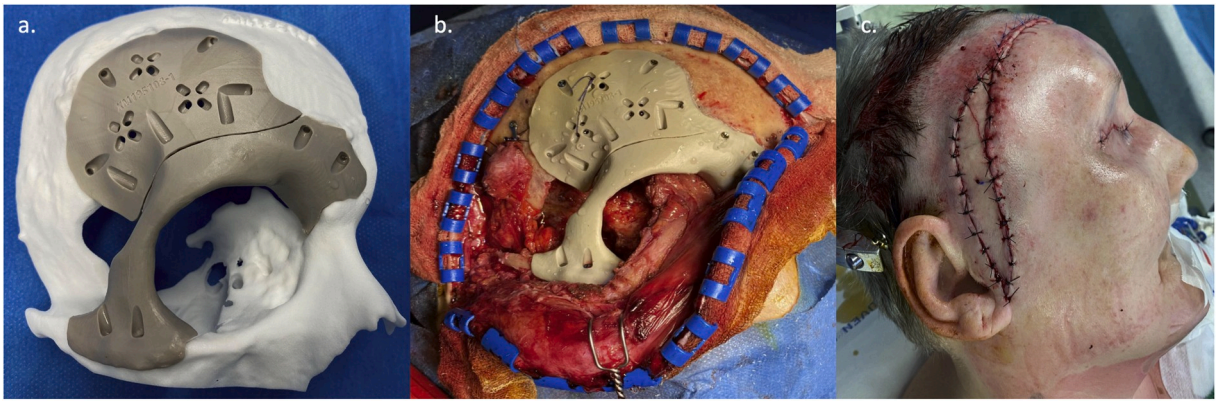

Fig. 5. (a) Patient-specific PEEK implant. (b) Inset of the PEEK implant. (c) After closure.

received radiotherapy have not resulted in malignant transformation and in some cases of malignant craniopharyngioma no prior radiotherapy was administered [5]. Still, patients receiving adjuvant radiotherapy should be carefully selected and the indication assessed individually. The benefits, i.e. significant reduction of recurrence, and risks, including rare malignant transformation, should always be discussed with the patient [1,7,11].

In addition, several investigators reported an overexpression of the tumor suppressor protein p53 in the malignant tumor component [1,2,14,15]. In the present case, p53 staining after diagnosis of malignant transformation showed a weak diffuse nuclear expression in the atypical regions. P53 gene mutation has well-known effects involved in carcinogenesis, e.g. loss of cell cycle control, genomic instability and neoplastic growth [1,14]. According to Wang et al. these findings could suggest the involvement of p53 mutations in the development of a malignant craniopharyngioma [15].

Malignant craniopharyngioma has a very poor prognosis. In 22 of the reported cases (56%), the patient died within one year after diagnosis of the malignant craniopharyngioma. The mean time of death was after 7.5 months (range 2w–3y). Yin et al. reported the longest survival in literature, namely 13 years. This concerned a female patient with a de novo malignant craniopharyngioma, diagnosed on the age of 31 [16]. In the case discussed here, the patient was still alive 4 years after diagnosis of the malignant transformation. Remarkably, in most of the reported cases death was due to local tumor progression rather than metastatic disease [3].

As seen in this case, a multidisciplinary treatment approach can play an important role in optimizing the quality of life and survival of patients. The effectuation of multiple surgical interventions for local and regional tumor recurrences turns the presence of a craniopharyngioma into a complex pathology. In the rather rare cases in which a craniopharyngioma is not contained to the intracranial department, not only a neurosurgical advice but also a maxillofacial, ophthalmological or other surgical opinion can be useful in treatment planning. Such a combined expertise can benefit the patient especially in cases where tumor expansion is beyond an individual surgeon's most common field of expertise.

In our case, reconstruction of the orbital region was performed with a patient-specific polyetheretherketone implant (PEEK-PSI). PEEK is a semicrystalline polyaromatic linear polymer exhibiting an excellent combination of biocompatibility, mechanical strength, stiffness and radiographic translucency [17,18]. Marbacher et al. reported an exceptional clinical and cosmetic 5-year outcome without any postoperative complications after patient-specific PEEK implantation for temporo-orbital reconstruction [19]. In the study

described by Alonso-Rodriguez et al. there were five patients (35.7%) with postoperative complications, i.e. a seroma, cerebrospinal fluid leak, implant exposure and infection, after craniofacial defect reconstruction with a PEEK-PSI [17]. Recently, Morselli et al. compared the complications rates of cranioplasty with titanium, PEEK, PMMA and hydroxyapatite implants after decompressive craniectomy [20]. For all these allogenic reconstruction materials, similar complication rates of around 20% were found. They concluded that the choice of material should be based on individual patient characteristics, e.g. craniectomy size [20]. PEEK-PSI seems a good choice for allogenic reconstruction when autologous bone is not available or in patients with large maxillofacial defects [17]. However, further investigation of the long-term results remains necessary.

3. Conclusion

Although malignant transformation of a craniopharyngioma is uncommon, awareness of its occurrence is important because of a poor prognosis. The correlation between radiotherapy and malignant transformation is not yet clearly established, but caution is advised. Nevertheless, due to the greatly reduced risk of tumor recurrence in partial resections, the administration of radiotherapy remains a good choice in carefully selected patients. Because of limited postoperative complications, PEEK-PSI appears a safe option for allogenic reconstruction in patients with large maxillofacial defects. The benefit of a multidisciplinary approach in certain complex cases should not be underestimated.

Ethical approval

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Informed consent

Acquired.

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Declaration of competing interest

None.

CRediT authorship contribution statement

Janssens E: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing - original draft. **Verhelst PJ:** Conceptualization, Methodology, Software, Visualization, Writing - review & editing. **De Vleeschouwer S:** Validation, Writing - review & editing. **Van Calenbergh F:** Validation, Writing - review & editing. **Hauben E:** Validation, Writing - review & editing. **Politis C:** Supervision, Validation, Project administration, Writing - review & editing. **Bila M:** Supervision, Validation, Project administration, Resources, Writing - review & editing.

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