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Original Article

Proton Therapy for Craniopharyngioma — An Early Report from a Single European Centre

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Abstract

Aims: Proton beam therapy (PBT) is being increasingly used for craniopharyngioma. We describe our early outcome of patients treated with PBT.
Materials and methods: Between August 2013 and July 2016, 18 patients with craniopharyngiomas were treated with 54 Cobalt Gray Equivalent (CGE) in 30 fractions over 6 weeks at our centre. The early outcome of 16 patients included in a registry study was analysed. Radiological response was assessed by RECIST criteria and the disease- and treatment-related toxicities were scored according to the CTCAE 4.0.
Results: All patients are alive at a median follow-up of 32.6 months (range 9.2–70.6 months) from initial diagnosis. The median age at PBT was 10.2 years (range 5.4–46.9 years). One patient progressed 8.7 months after PBT and subsequently had complete resection of the tumour. At a median follow-up of 18.4 months after PBT, five patients remained in complete remission, four in partial remission and seven with stable disease. The most common adverse effects during PBT were grade 1 (cutaneous in seven patients and fatigue in six patients). There were no treatment-related grade 3 toxicities.
Conclusions: Our early results are encouraging and comparable with the limited literature on PBT for craniopharyngioma.

Key words: Craniopharyngioma; proton therapy; toxicity

Introduction

Craniopharyngiomas are benign slow-growing tumours of the sellar and parasellar region that can infiltrate neighbouring structures and cause significant morbidity and mortality. Although gross total resection (GTR), or maximal debulking of the tumour to relieve pressure effects on the optic pathways and/or to re-establish the cerebrospinal fluid (CSF) pathways, remains the treatment of choice, a risk-adapted multimodality treatment strategy is evolving [1]. Previous studies show that attempts of GTR in patients with tumours invading the hypothalamus can result in significant morbidity in terms of hypothalamic dysfunction and altered neurophysiological profile [2]. A preoperative radiological grading system has therefore been developed in paediatric patients to guide a risk-adapted strategy to avoid significant morbidity [3]. Using this grading, GTR should be attempted in type 0 (no hypothalamic involvement on magnetic resonance imaging [MRI] scan) and type 1 tumours (distorts or elevates the hypothalamus, but it is still visible) [4]. The surgical approach in type 2 tumours (hypothalamus is not visible) is a subtotal resection (STR) leaving the hypothalamic component [3,5,6]. Studies show that about 18–84% of patients have a GTR and on follow-up 0–26% of tumours will recur [3]. After incomplete surgery, tumours recur in 50–91% of patients and, therefore, patients may be considered for postoperative radiotherapy, particularly if further surgery for recurrence is not feasible [7]. A systematic review suggests that STR followed by radiotherapy in paediatric craniopharyngiomas leads to similar 5 year control as

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that of GTR [8]. A recent SEER analysis also suggests that the overall survival is not different with GTR, STR with radiotherapy and definitive radiotherapy [9]. However, in paediatric craniopharyngioma, the role of adjuvant radiotherapy continues to be controversial. Craniopharyngiomas after GTR or with small residual disease after STR may be managed with serial imaging, with consideration for further surgery on progression. In cases of significant residual tumour after STR, the exact timing for radiotherapy is not known and is currently being addressed in the German Craniopharyngioma 2007 study randomising children with residual disease at age over 5 years to receive either immediate postoperative radiotherapy or radiotherapy at the time of progression [10]. In clinical practice, some authors recommend early radiotherapy to avoid recurrence and its associated tumour-related morbidity [11]. After postoperative radiotherapy up to 20% of tumours may recur [3,12]. The reported 10 year progression-free survival (PFS) after surgery followed by postoperative radiotherapy ranges from 56 to 95% and 10 year overall survival from 65 to 96% [9,13–18].

A number of radiotherapy techniques are being used in the postoperative management of craniopharyngiomas. Conventional radiotherapy and stereotactic fractionated radiotherapy yield a 10 year overall survival of >80% [19]. Gamma knife radiosurgery has been used in the past for selected patients whose tumour is well away from the optic apparatus. However, a systematic analysis of the reported studies shows that radiosurgery leads to inferior 5 year survival compared with fractionated radiotherapy (Ajithkumar and Brada, personal communication, 2017).

Proton beam therapy (PBT) is being increasingly used for the treatment of craniopharyngioma. Treatment planning studies have shown that PBT may result in lower doses to critical organs and thereby minimise the risk of neurocognitive, vascular and optic nerve complications and of second cancers [20–22]. Early clinical results of PBT in craniopharyngioma are encouraging [23–26].

We report our experience of PBT for craniopharyngioma patients treated at the West German Proton Therapy Centre Essen (WPE).

Materials and Methods

Since August 2013, all patients with craniopharyngioma were enrolled in the standardised registry study either for children under the age of 18 years (KiProReg) or for adults (ProReg) in order to prospectively collect data on patients, diagnosis, treatment, early and late toxicities and tumour control. Patients with extensive cystic tumour parts were generally not accepted at WPE for PBT in order to exclude uncertainties due to cyst growth. Patients were treated in a supine position, lying on a vacuum bag with a facemask and knee rest. Planning computed tomography scans were taken at 1 mm and 2 mm slices, which was co-registered with a planning MRI scan as well as a preoperative MRI scan. The tumour bed was delineated according to the Craniopharyngioma 2007 guidelines. The clinical target volume (CTV) was defined as the postoperative tumour including the tumour bed with a margin of 5 mm individually adapted to anatomical barriers and the planning target volume (PTV) was derived by adding a 3–5 mm margin to the CTV depending on technical uncertainties and patient set-up. The clinical dose goals for treatment planning were as follows: temporal lobe D30 < 25 Gy and D60 < 20 Gy, hippocampus D30 < 30 Gy, D60 < 25 Gy and mean dose < 20 Gy, cochlea mean dose < 36 Gy and supratentorial brain D92 < 25 Gy, D70 < 30 Gy, D53 < 40 Gy, D34 < 45 Gy, D24 < 50 Gy and D16 < 55 Gy. The maximum dose to the optical apparatus and brainstem should not exceed 7% of the prescribed dose. Compromising CTV coverage was not allowed, but PTV coverage was considered acceptable at 95% isodose in order to achieve sparing of important organs at risk.

Treatment was planned using the RayStation- or XiO-system, using uniform scanning (for patients treated before April 2014) or pencil beam with spot scanning. Typically three to four fields were used.

All patients were treated to a dose of 54 CGE in 30 fractions treating five fractions per week. Patient treatment fields were verified daily using stereoscopic kV imaging. kV imaging was compared with digitally reconstructed radiography (DRR)s using Verisuite 1.6. Daily treatment corrections were applied if needed using the 6D couch according to the departmental protocol. Patients also had a verification scan. Patients with a cystic component in the residual tumour underwent a biweekly verification MRI scan. Testing of endocrine function was carried out and treatment toxicities were recorded using Common Terminology Criteria for Adverse Events (CTCAE) V4.0.

Patients were followed-up 3 months after treatment and then annually. Follow-up investigations included a clinical examination, including endocrine and ophthalmology assessment and a MRI scan. Patients who were unable to travel to WPE for a follow-up examination were asked to complete a standardised questionnaire on side-effects and tumour control and treating centres were contacted for follow-up information.

Results

Patient Characteristics

Between August 2013 and July 2016, 18 patients completed PBT for craniopharyngioma at WPE. The outcome of 16 patients who have consented to be included in our registry study was analysed for this report (Table 1). Five patients were men and 11 were women. The median age was 10.2 years (range 5.4–46.9 years) and 13 patients were less than 18 years. The median interval between primary diagnosis and PBT was 0.9 years (range 0.4–4.6 years). Fifteen patients received PBT for progressive disease a median period of 1 year (range 0.4–4.5 years) after surgery and one received treatment as immediate postoperative treatment. In 14 patients, tumours did not only consist of solid, but also cystic components. Some cysts were completely

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