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Original article

Meningioma of the skull base: Long-term outcome after image-guided stereotactic radiotherapy

Méningiomes de la base du crâne : résultats à long terme de la radiothérapie stéréotaxique guidée par l'image

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ABSTRACT

Purpose. – The purpose of this study was to analyse the feasibility, safety, and long-term efficacy of linear accelerator-based fractionated stereotactic radiotherapy for meningiomas of the skull base. We evaluated the long-term clinical outcome of patients and identified prognostic factors after fractionated stereotactic radiotherapy.
Patients and methods. – Between 10/1995 and 03/2009, 136 patients with a median age of 57 years with skull base meningioma received fractionated stereotactic radiotherapy. A total of 34 patients had a grade I meningioma, in 102 cases no histology was obtained (grade 0). Fractionated stereotactic radiotherapy was delivered as primary treatment for 57 patients and postoperatively for 79. The patients received a mean total dose of 56.95 (min/max 32.4/63) Gy.
Results. – Median follow-up was 44.9 months. Overall progression-free survival was 96.9% after 3 years, 93.8% after 5 years, and 91.5% after 10 years. Patients with unknown histology showed progression-free survival rates of 100%, 98.7%, and 93.5% at 3, 5, and 10 years and patients with biopsy-proven grade I meningioma showed rates of 100% after 3 years, 91.7% after 5 years and 85.9% after 10 years. Patients with adjuvant radiotherapy showed significantly worse progression-free survival rates than patients who had been treated with primary radiotherapy ($P = 0.043$), progression-free survival rates were independent of tumour size. The most common acute grade I symptoms were headache, fatigue, and local alopecia. The most common chronic grade I symptoms were fatigue and headache.
Conclusions. – This large study showed that fractionated stereotactic radiotherapy is an effective and safe treatment modality with high progression-free survival rates for intracranial meningioma. We identified "prior surgery" as significant poor prognostic factor.

Mots clés :
Méningiome
Base du crâne
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Radiothérapie guidée par l'image
Contrôle local

RÉSUMÉ

Objectif de l'étude. – L'objectif de l'étude était d'analyser la faisabilité, l'innocuité et l'efficacité à long terme de la radiothérapie stéréotaxique fractionnée de méningiomes de la base du crâne. Nous avons évalué les résultats à long terme et identifié les facteurs pronostiques.
Patients et méthodes. – Entre octobre 1995 et mars 2009, 136 patients d'âge médian 57 ans ont été traités par irradiation stéréotaxique fractionnée pour un méningiome de la base du crâne. Trente-quatre patients étaient atteints d'un méningiome de grade I, tandis que pour les 102 autres patients l'histologie n'était pas disponible (grade 0). Sur ces 136 patients, l'irradiation était de première intention pour 57 et elle était postopératoire pour 79. Les patients ont reçu une dose totale moyenne de 56,95 Gy (32,4 Gy–63 Gy).
Résultats. – Le suivi médian était de 44,9 mois. La probabilité de survie sans progression était de 96,9 % à 3 ans, 93,8 % à 5 ans et 91,5 % à 10 ans. Elle était en cas d'histologie indisponible, respectivement de 100 %,

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98,7 %, et 93,5 % et en cas de méningiome de grade I, prouvé par biopsie, de 100 %, 91,7 % et 85,9 %. Si la radiothérapie était adjuvante, elle était significativement inférieure ($p = 0{,}043$), et elle était indépendante de la taille de la tumeur. Les symptômes aigus de grade I les plus courants étaient des céphalées, la fatigue, et l'alopécie locale, les symptômes chroniques de grade I les plus courants la fatigue et des céphalées.
Conclusion. – Cette grande étude montre que la radiothérapie stéréotaxique fractionnée est un traitement efficace et sans danger pour les méningiomes de la base du crâne, avec des probabilités élevées de survie sans progression. De plus, nous avons mis en évidence que la chirurgie associée à la radiothérapie représente un facteur pronostique défavorable.

1. Introduction

There has been a long lasting debate about the optimal management of meningioma of the skull base. Surgery, stereotactic radiotherapy, and radiosurgery are all therapies used to treat meningiomas. Typically, meningiomas exhibit a benign behaviour, growing slowly. Cases of meningiomas with an intricate anatomic invasion of the skull base have specific related symptoms.

Meningiomas invading anatomically intricate structures include lesions of the sphenoid wing, olfactory groove, and the suprasellar and posterior fossa. Meningiomas of the sphenoid wing may be invasive and extend to the dura of the orbital and sphenoidal regions. They also invade the wall of the cavernous sinus, anteriorly into the orbit, and laterally into the temporal bone. Tumours in this location can involve critical structures (e.g. cavernous sinus, or carotid arteries), and, therefore, may make total tumour resection difficult. Invasion of cranial nerves within the cavernous sinus results in the dysfunction of oculomotor, trochlear, trigeminal, or abducent nerves, causing related symptoms. Olfactory groove lesions may deteriorate the sense of smell and cause persistent headaches and changes in personality and behaviour. Lesions that are located in the posterior fossa are considered the most critical due to the limited space and the potential involvement of critical neural structures. These lesions may cause dysfunction of the facial or vestibular nerves. They may also induce cranial nerve deficits by compressing the brain stem or the cerebellum causing the loss of motor functions. This array of symptoms for individual patients indicates the necessity of research to aid in enhancing the optimal clinical management of meningiomas of the skull base. Traditionally, surgery has been considered as the standard of care in the vast majority of skull base meningioma cases [7]. Arguments for using a surgical approach to treatment include removal of the lesion, mass reduction, and the opportunity to obtain clear pathology. Advances in skull base surgery in the recent decade have led to a refinement of surgical approaches [5,7,8]. Surgery is optimal when lesions are relatively avascular and occur on the cortical convexity; however, when highly vascularized meningiomas arise deep in the base of the skull, surgery is a formidable challenge. Interdisciplinary cooperation between neurosurgeons and otorhinolaryngologists is necessary to tackle skull base lesions [19–21]. A better anatomical understanding of skull base meningiomas due to advances in imaging technologies, dedicated narcosis techniques, neuromonitoring, microsurgical techniques, and instruments has increased the success of skull base surgery [3,11,17,26].

In addition to surgical intervention, another therapy used to treat meningiomas is radiotherapy. Radiotherapy technology has fundamentally evolved over the last two decades [7]. Dedicated image-guided high precision technologies such as the stereotactic radiotherapies, fractionated stereotactic radiotherapy, and stereotactic radiosurgery have emerged. Aside from efficacy, an important feature of these new stereotactic techniques is their safety. This safety is derived from delivering highly precise radiation using a stereotactic frame with judicious dose selection and image guidance systems [1,14,23]. Large data sets have been generated demonstrating the feasibility, safety, and efficacy of stereotactic radiosurgery and fractionated stereotactic radiotherapy for meningioma [2,4,6,10,18,22,24]. These data sets include the use of different machines, typically Gamma Knife or linear accelerators, and different techniques and anatomic locations. However, valid data on fractionated stereotactic radiotherapy delivered by using dedicated linear accelerators to the skull base is limited [6,9,10,13,15,16,23,25].

The purpose of this study was to analyse the feasibility, safety, and long-term efficacy of linear accelerator-based fractionated stereotactic radiotherapy for patients with meningiomas of the skull base. We evaluated the long-term clinical outcome of patients and identified prognostic factors after linear accelerator-based fractionated stereotactic radiotherapy.

2. Methods

2.1. Patient selection and dose regimen

We performed a retrospective analysis of 136 patients who underwent fractionated stereotactic radiotherapy of skull base meningiomas between October of 1995 and March of 2009. Our local ethics committee approved this study. The research complied with the Helsinki Declaration. In our institution, treatment decisions are made by an interdisciplinary tumour board. Symptomatic grade I meningiomas are treated with adjuvant radiotherapy after incomplete resection or if there is a recurrence of meningioma after total resection. Inoperable symptomatic grade I tumours were treated using primary fractionated stereotactic radiotherapy. The dose regimen encompassed a single dose of 1,8–2 Gy, delivered in 30–33 fractions.

2.2. Grouping and follow-up

We distinguished groups of patients between those receiving primary radiation treatment and those receiving postoperative radiotherapy. Acute toxicity in the first 90 days after fractionated stereotactic radiotherapy was graded using a modified version of the Common Terminology Criteria of Adverse Events (CTCAE v4.0). Patient data were analysed according to grading, predicted perioperative risk/operability, tumour size, and sequence of therapy. Follow-up examinations, including MRI and clinical and neurologic examinations were performed at 6 weeks, 3 months, 9 months, and 15 months after treatment and continued annually. Tumour control was defined as the absence of radiological progression.

2.3. Technical set-up

From 1995 to 2003, meningioma patients underwent "sharp" fixation using a stereotactic head ring and an oral bite plate. A 6 MV Linac (Varian® USA) with an add-on micro-multileaf collimator