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Meningiomas/Les méningiomes

Fractionated radiotherapy and radiosurgery of intracranial meningiomas

Radiochirurgie et radiothérapie fractionnée des méningiomes intracrâniens

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ABSTRACT

This review focuses on the role of radiosurgery and fractionated radiotherapy in the management of intracranial meningiomas, which are the most common benign intracranial tumors. Whenever feasible, surgery remains a cornerstone of treatment in effective health care treatment where modern radiotherapy plays an important role. Irradiation can be proposed as first-line treatment, as adjuvant treatment, or as a second-line treatment after recurrence. Stereotactic radiosurgery consists of delivering, a high-dose of radiation with high precision, to the tumor in a single-fraction with a minimal exposure of surrounding healthy tissue. Stereotactic radiosurgery, especially with the gamma knife technique, has reached a high level of success for the treatment of intracranial meningiomas with excellent local control and low morbidity. However, stereotactic radiosurgery is limited by tumor size, < 3–4 cm, and location, i.e. reasonable distance from the organs at risk. Fractionated radiation therapy is an interesting alternative (5 to 6 weeks treatment time) for large inoperable tumors. The results of fractionated radiation therapy seem encouraging as regards both local control and morbidity although long-term prospective studies are still needed.

Mots clés :
Radiothérapie
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RÉSUMÉ

Cette revue fait le point sur le rôle de la radiochirurgie et de la radiothérapie fractionnée dans la prise en charge des méningiomes intracrâniens, qui sont les tumeurs bénignes intracrâniennes les plus fréquentes. La chirurgie reste, quand elle est possible, une des pierres angulaires du traitement des méningiomes où la radiothérapie moderne joue un rôle important. La radiothérapie peut être proposée comme le traitement de première ligne, après chirurgie ou au moment de la récidive. La radiochirurgie stéréotaxique consiste à délivrer une fraction unique de forte dose dans la tumeur, avec un minimum de dose dans les tissus sains environnants. La radiochirurgie, en particulier avec le Gamma Knife, a atteint un niveau de preuve élevé avec d'excellents taux de contrôle local et peu de morbidité. Cependant, la radiochirurgie est limitée par la taille de la tumeur (< 3–4 cm), et la localisation avec une distance suffisante des organes à risque. La radiothérapie fractionnée peut être une alternative pour les méningiomes de taille élevée et/ou avoisinant les organes à risque. Les résultats de la radiothérapie fractionnée semblent encourageants tant en terme de contrôle local et de morbidité mais des études prospectives sont nécessaires.

1. Introduction

Meningiomas are the most common primary intracranial tumor, accounting for about 35–44% of cases [1,2]. The fifteen subtypes of meningothelial cell tumors fall into three grades: benign or grade I, uncertain behavior or atypical meningioma or grade II, and malignant or anaplastic meningioma or grade III [3]. The conditions for

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tumor discovery vary considerably from intracranial hypertension to an incidental finding. Surgery remains a cornerstone of meningioma treatment, which aims to minimize functional risks [4], although this treatment will vary according to tumor location, size, growth rate and grading, as well as patient expectations and medical facilities. In 1957, Simpson showed that the extent of surgical resection is an important predictor of recurrence and progression [5]. In most cases, gross total resection (GTR) of I, II and III Simpson grades, basically depends on tumor location and extent [6].

As an alternative to surgical resection, stereotactic radiosurgery (SRS) has been used for more than 30 years to treat patients with intracranial meningioma. Local control rate is excellent, generally > 90% at 5–10 years with low morbidity (Table 1) [7–15]. However, SRS is limited by tumor size, < 3–4 cm, and location, i.e. reasonable distance from critical structures, such as chiasma and optic nerves. When SRS is not suitable, i.e. large growing tumor causing significant symptoms, or special locations, such as involvement of critical structures such as the cavernous sinus or the optic nerve, or close contact with critical structures, external beam fractionated radiotherapy (FRT) remains an alternative. Numerous studies have reported that FRT decreases tumor recurrence and improves survival, after partial tumor resection or as primary treatment for unresectable meningiomas, such as optic nerve sheath and cavernous sinus meningioma (Table 1) [16–24]. However, most series report uni- or multicenter retrospective experience. Two ongoing prospective studies from the European Organization for Research and Treatment Cancer (EORTC 22042-26042) and Radiation Therapy Oncology Group (RTOG 0539) should provide interesting data regarding FRT for meningioma. FRT requires 5 to 6 weeks of treatment time whereas SRS requires only a single-fraction.

Advances in imaging, treatment planning and radiation delivery techniques have dramatically changed irradiation of meningiomas. Irradiation is considered as primary therapy, adjuvant treatment following surgery or treatment after recurrence. Irradiation is proposed depending on tumor size, location, histopronostic grade (WHO grading: types I, II and III), extent of resection (Simpson grading: types I, II, III, IV and V), general condition and the patient's expectations. In this review, we have extensively analyzed the literature regarding intracranial meningioma SRS and FRT using selected articles retrieved from the PubMed literature over a period of 15 years to report results using only modern irradiation techniques.

2. Indications and outcomes

2.1. Primary radiotherapy

SRS or FRT in cases where SRS is not possible are a first-line of treatment when significant surgical resection is not achievable, usually due to the meningioma lines or it involves critical structures, or that patients are inoperable (age, comorbidities, etc.). SRS is generally considered more suitable for lesions of less than 3 to 4 cm in diameter, and at a reasonable distance from critical structures, such as chiasm and optic nerves, allowing to deliver a high-dose to the target volume and low-dose to healthy critical structures [25].

Outcomes after primary SRS of meningiomas are impressive, with large cohorts being reported (Table 2) [7,15,26–28]. Santacroce et al. [28] reported a 5-year and 10-year PFS of 95.2 and 88.6% respectively, in more than 4500 patients treated with gamma knife SRS, with very low morbidity. As regards FRT, at 5 and 10 years respectively, 93–95% and 86–88% of patients with grade I meningioma are free of progression [16,23]. Morbidity may be higher but FRT is usually used to treat larger meningiomas and/or involving critical structures. FRT is the first-line treatment of choice for optic nerve sheath meningioma (ONSM) because of high risk of blindness after surgery, even on biopsy [29]. ONSM either remains stable or reduces in size after FRT in 95–100% of cases (Table 3), and visual symptoms are stable or improve in 80–90% [30–40].

However, tumor growth kinetics before SRS or FRT treatment are not always available. The indication of treatment should be limited to symptomatic patients or proven growth tumors. Moreover, selected asymptomatic patients with a significant meningioma volume could benefit by SRS, assuming that the likelihood of progression is high, and the smaller the volume, the better the prescribed dose, therefore increasing safety-efficacy ratio. Usually the tumor size does not significantly reduce after FRT, whereas it is often reported after SRS in 22 to 79% of cases (Table 2). It has been observed that patients improve without any significant change in tumor size. When the tumor is symptomatic, RT should not be delayed, and if symptoms are severe "debulking" surgery followed by RT may be more appropriate [41,42].

2.2. Adjuvant radiotherapy following surgery

GTR resection of grade I meningiomas does not require any adjuvant treatment. Nevertheless, imaging follow-up is still performed because malignancy cannot be excluded [43]. Subtotal resection (STR) seems to reduce the percentage of patients with grade I meningioma benefiting from long PFS [44]. STR followed by RT could be as effective as GTR based on percentages of patients benefiting from long progression-free survival (PFS) [45]. SRS could be an alternative to FRT, as adjuvant therapy to surgery; percentages of patients benefiting from long PFS being comparable [46]. Nevertheless, no difference has been reported in overall survival among patients with grade I meningioma treated with STR followed by RT after recurrence, versus STR with routine upfront RT, suggesting it may be safe to delay RT until progression [45].

As regards malignant meningiomas, the benefit of routine adjuvant radiotherapy has been demonstrated after STR or GTR, where local control increases from 15–35% to 80% [47,48]. This is less clear for atypical meningioma. Adjuvant RT for grade II meningiomas significantly increased PFS for patients treated with STR, but not for patients with GTR [49,50]. However, Komotar et al. [51] reported that routine adjuvant RT of grade II meningiomas after GTR decreased recurrences from 41% to 8% with a median follow-up of 44 months. Current practice tends to propose routine adjuvant RT, either for malignant and atypical meningiomas, especially after STR. The RT technique is usually FRT [52], although some groups support SRS in this setting [49].

2.3. Radiotherapy after recurrence

Recurrent meningiomas after the first surgery exhibit a more aggressive course than newly diagnosed meningiomas [53]. As several studies show improved salvage control rates with surgery plus RT, or radiation alone versus surgery alone [44,54], the National Comprehensive Cancer Network (NCCN) has advised that recurrent a meningioma should be resected if possible, and an adjuvant RT should be delivered [53]. Non-surgical patients should receive RT alone, chemotherapy being reserved for meningioma progressing after RT [55]. For patients with tumor progression after RT, the safety and efficacy of a second course of RT has not been evaluated; only a retrospective analysis of a small series has been reported [56,57]. Wojcieszynski et al. [56] concluded that only patients with grade I meningioma achieved an extended PFS following reirradiation and therefore should be offered this type of treatment. Data regarding toxicities remain lacking.

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