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Case report

Brain dose-sparing radiotherapy techniques for localized intracranial germinoma: Case report and literature review of modern irradiation

Radiothérapie conformationnelle avec modulation d'intensité avec épargne du cerveau pour des germinomes intracrâniens localisés : à propos d'un cas et analyse de la littérature moderne

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ABSTRACT

We examined the effects of intensity-modulated radiation therapy with dose-sparing and avoidance technique on a pediatric patient with localized intracranial germinoma. We also reviewed the literature regarding modern irradiation techniques in relation to late neurocognitive sequelae. A patient with a localized intracranial germinoma in the third ventricle anterior to the pineal gland received a dose-sparing intensity-modulated radiation therapy. The planning was compared to the radiation oncologist's guide of organs at risk and dose constraints for dosimetric analyses. The patient received radiation therapy alone. The total dose was 54 Gy delivered in 2.0 Gy fractions to the primary tumour and 37 Gy in 1.4 Gy fractions to whole ventricles using a dose-sculpting plan. Dosimetry analyses showed that dose-sparing intensity-modulated radiation therapy delivered reduced doses to the whole brain, temporal lobes, hippocampi, cochleae, and optic nerves. With a follow-up of 22 months, failure-free survival was 100% for the patient and no adverse events during radiation treatment process. Intensity-modulated radiation therapy with dose sparing and avoidance technique can spare the limbic circuit, central nervous system, and hippocampus for pineal germ cell tumours. This technique reduces the integral dose delivered to the uninvolved normal brain tissues and may reduce late neurocognitive sequelae caused by cranial radiotherapy.

Mots clés :
Germinome du système nerveux central localisé
Radiothérapie
Organes à risque

RÉSUMÉ

Nous avons examiné les effets de la radiothérapie avec modulation d'intensité (RCMI) avec économie de dose et épargne de structures chez un enfant atteint de germinome intracrânien localisé. Nous avons aussi revu la littérature sur les séquelles neurocognitives de l'irradiation moderne. Un patient atteint de germinome localisé entre l'avant du troisième ventricule et la glande pinéale a reçu ce type de radiothérapie. La planification a été comparée au guide de la radiothérapie oncologique et des contraintes de dose dans les organes à risque pour les analyses dosimétriques. La radiothérapie était exclusive et a délivré une dose totale de 54 Gy par fractions de 2 Gy dans la tumeur primitive et 37 Gy par fractions de 1,4 Gy dans la totalité des ventricules. L'analyse dosimétrique a montré une diminution de la dose dans tout le cerveau, les lobes temporaux, les hippocampes, les cochlées et les nerfs optiques. Avec un suivi de 22 mois, il n'a été observé aucun échec et aucun événement indésirable n'a non plus été constaté pendant le traitement. La RCMI pour tumeur germinale pinéale peut épargner le circuit

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limbique, l'encéphale et les hippocampes. Elle permet de réduire la dose dans le cerveau sain, ce qui peut réduire les séquelles tardives neurocognitives de la radiothérapie crânienne.

1. Introduction

Intracranial germinomas are rare primary central nervous system germ cell tumours that account for 2.5% to 4.4% of all paediatric central nervous system (CNS) tumours in Western countries [1–3]. In Asia, germ cell tumours of the central nervous system in children are common, representing 15 to 18% of all childhood CNS tumours [4,5]. The reported incidence rate at the largest hospital in Taipei was approximately 14%. The mean age of onset was approximately 10- to 12-year-old [6]. There are two main types of germ cell tumours: germinomas and non-germinomatous germ-cell tumours. Non-germinomatous germ cell tumours are more common in younger children and pure germinomas are more common among older patients. Treatment outcome of non-germinomatous germ cell tumours are worse than intracranial germinomas [7]. Radiotherapy is curative for pure germinoma. The standard dose is 45 to 50 Gy to the primary tumour, in combination with about 24 Gy of whole ventricular irradiation, the 5-year control rate was 88% [8].

The long-term radiotherapy-induced brain injury is raising significant concerns due to the high curability of many germ cell tumours and the large treatment volumes often used in these young patients [9,10]. Therefore, there are ongoing efforts to explore the feasibility of delivering reduced radiotherapy doses to patients with germ cell tumours and spare brain structure from irradiation. Standard intensity-modulated radiation therapy (IMRT) for whole ventricular irradiation has already been shown to spare a significant amount of normal central nervous tissue for patients with localized germ cell tumours as compared to whole brain irradiation using opposed lateral beams [11,12]. Whole brain irradiation can be associated with subacute and late decline in memory and other cognitive functions, which is likely to be caused by the damage to the neural stem cell compartment, limbic circuit and hippocampus [9,13,14]. Therefore, its use in different primary paediatric intracranial tumours has been limited [15,16]. In reducing the incidence and severity of late adverse cognitive effects, the idea of sparing of these critical structures using intensity-modulated radiation therapy with dose sculpting was suggested: the technique escalates the dose to the tumour and spares normal tissues. It has not been well studied in paediatric patients with intracranial tumour [17]. We thus examined the case of a patient with pineal germinoma treated with dose-sparing intensity-modulated radiation therapy and avoidance techniques in our institution and reviewed the literature regarding modern irradiation for localized germ cell tumours and the adverse events of neurocognitive dysfunction.

2. Clinical case

After approval by the institutional review committee, the medical records of patients with a CNS germ cell tumour treated at our institution over a 2-year period were examined. A patient who received intensity-modulated radiotherapy with dose-sparing and avoidance techniques was identified and selected for study.

The patient, age 16, had a pineal tumour in the third ventricle anterior to the pineal gland and marked dilation of the ventricle with obstructive hydrocephalus. Magnetic resonance (MR) imaging of the brain showed a 6 × 6 cm isointense pineal gland lesion on T1 and T2 with bright enhancement on contrast studies (Fig. 1). An infratentorial supracerebellar approach was performed to remove the lesion.

The patient received intensity-modulated radiotherapy (IMRT) in our department 1 week after surgery. The radiation oncologist used dose-sparing techniques with four phases of treatment planning via the dynamic IMRT to spare the limbic circuit, hippocampus, and neural stem cell compartment. The treatment planning target volume was contoured and varied by diagnosis using computed tomography simulation with a custom-made immobilization device. The planning target volume was generally consisted of the gross tumour as it was identified on imaging. For the primary tumour, the gross tumour volume was defined as the extent of disease at diagnosis. The clinical target volume was designed to allow 0.8 cm margin beyond the gross tumour volume to obtain the planning target volume in phase 1, and 1.2 cm margin beyond the residual tumour in phases 3 and 4 to obtain the planning target volume. For whole ventricular irradiation, the clinical target volume comprised bilateral ventricles with a 0.5-cm expansion to obtain the planning target volume. In this case, 6 MV photons were used. The planning objectives were delivered non-uniform dose to different target volume with minimizing the dose to critical organs at risk. The treatment delivery was on Clinac® iX linear accelerator (Varian).

After four phases of radiotherapy, the follow-up MRI imaging revealed that the patient's lesion was decreased from 5.17 cm to 2 cm (Fig. 2). The patient's neurological symptoms remained stable; no optic neuropathy appeared throughout the radiation treatment courses. Unfortunately, he developed impaired recent memory 3 months after radiotherapy; as a result, he refused to receive a boost dose. The follow-up MRI imaging after 6 months revealed a dramatic reduction in the size of the germinoma (Fig. 3). The patient did not receive chemotherapy due to the diagnosis of a localized tumour and excellent response to radiotherapy. At 22 months follow-up, MRI imaging revealed no progression of the disease and the patient's condition remained stable upon clinical evaluation.

The calculation of ventricles dose was based on the patient's neuroanatomy and required superimposing the radiation therapy isodose lines over the average anatomy. The total dose was 54 Gy delivered in 2.0 Gy fractions to the primary tumour and 37 Gy in 1.4 Gy fractions to whole ventricles using dose-sparing and avoidance techniques. The dose distribution is shown on Fig. 4.

The germinoma located in the third ventricle was treated with multileaf dose-sparing intensity-modulated radiation therapy only. Table 1 compares the total dose constraints (standard

Table 1
Whole ventricular radiotherapy of central nervous system germinoma: organs at risk dose constraints for sparing plans.
Radiothérapie crânienne avec épargne de dose pour un germinome intracrânien : contraintes de dose dans les organes à risque.

Standard organs at risk	Literature data	Current study
Eyes	*D*mean < 25 Gy [18]	*D*mean = 10.2 Gy
Lenses	*D*max < 6 Gy [19]	*D*max = 5.02 Gy
Optic nerves	*D*max < 54 Gy [20]	*D*max = 52 Gy
Optic chiasms	*D*max < 55 Gy [20]	*D*max = 50 Gy
Cochleae	*D*mean < 35 Gy [21]	*D*mean = 19.6 Gy
Brainstem	*D*max < 54 Gy [22]	*D*max = 50.6 Gy
Temporary lobe	*D*max < 30 Gy [23]	*D*max = 30 Gy
Hippocampus	*D*mean < 30 Gy [24]	*D*mean = 50 Gy