Cancer/Radiothérapie 21 (2017) 55–59

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Case report

Visceral and bone metastases of a WHO grade 2 meningioma: A case report and review of the literature

Méningiome de grade 2 de l'OMS métastatique viscérale et osseux : cas clinique et revue de la littérature

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ARTICLE INFO

Article history:
Received 22 November 2015
Received in revised form
11 September 2016
Accepted 16 September 2016

Keywords:
Meningioma
Metastasis
Radiotherapy
Targeted treatment

ABSTRACT

Meningiomas represent the most common tumours of the central nervous system in adults. Risk factors include ionizing radiation, female hormones exposure, head trauma, cell phone use, breast cancer and family history of meningioma. Despite complete surgical resection, natural history of meningiomas often includes local recurrence but very few metastatic meningiomas have been reported. Here, we report the case of a metastatic meningioma. A 43-year-old woman was firstly treated for a symptomatic parietal meningioma WHO grade II by surgical resection followed by an irradiation of the surgical bed. After surgical resection and irradiation, the patient recovered incompletely. Two months after the end of the radiation treatment, the patient presented at the emergency unit for sciatic pain revealing bone metastases that has been histologically confirmed. Moreover, imaging led to the diagnosis of liver and lungs metastasis. Despite lack of guidelines for metastatic meningioma, few treatments have been used and published for recurrent and multiple meningioma management. In case studies, some partial responses have been seen with mifepristone and improved progression-free survival rates have been obtained with hydroxyurea and sunitinib. Metastasis in meningioma is very uncommon and no specific management has been described. Hydroxyurea, sunitinib and mifepristone could be options if no clinical trial data is available.

Mots clés :
Méningiome
Métastase
Radiothérapie
Thérapie ciblée

RÉSUMÉ

Les méningiomes sont les tumeurs intracrâniennes les plus fréquentes. Les facteurs de risque de méningiome incluent l'exposition aux radiations ionisantes, l'exposition aux hormones féminines, les traumatismes cérébraux, l'utilisation de téléphone portable, l'association avec le cancer du sein et des antécédents familiaux de méningiomes. En dépit d'une résection chirurgicale complète, les méningiomes récidivent fréquemment localement mais très peu de méningiomes métastatiques ont été décrits. Nous rapportons ici le cas d'une patiente atteinte de méningiome métastatique. Une femme de 43 ans prise en charge pour un méningiome pariétal de grade 2 selon l'Organisation mondiale de la santé (OMS) par résection chirurgicale suivie d'une irradiation du lit opératoire. La patiente a récupéré une partie de ses fonctions après la chirurgie et la radiothérapie. Deux mois après la fin de la radiothérapie, la patiente s'est présentée aux urgences avec un tableau de lombosciatique révélant des métastases osseuses, confirmées histologiquement. En outre, le bilan d'extension a mis en évidence des métastases hépatiques et pulmonaires du méningiome. Malgré l'absence de recommandation sur la prise en charge des méningiomes métastatiques, quelques études ont décrit la prise en charge de méningiomes récurrents et multiples. Dans une série de cas, la mifépristone a montré des réponses partielles et des améliorations des taux

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http://dx.doi.org/10.1016/j.canrad.2016.09.012
1278-3218/

de survie sans progression ont été rapportées chez des patients traités par hydroxyurée ou sunitinib. Les métastases de méningiomes sont très rares et aucune prise en charge spécifique n'a été décrite. L'hydroxyurée, le sunitinib et la mifépristone peuvent être des options de traitement en l'absence d'essai clinique disponible.

1. Introduction

Meningiomas are tumours derived from meningothelial cells. They represent 36% of intracranial neoplasms in the US. Risk factors include ionizing radiation, female hormones exposure, head trauma, cell phone use, breast cancer and family history of meningioma [1]. According to the WHO classification of tumours of the central nervous system, meningiomas can be classified into three grades: I – benign meningiomas, II – atypical meningiomas, and III – anaplastic/malignant meningiomas [2,3]. Most meningiomas are grade I (90%); grade II represents 5–7% of all meningiomas and grade III constitutes 1–3% [4,5]. Surgical resection aims to remove as much tumor burden as possible while minimizing neurologic deficits. However, while meningiomas may show local recurrence after gross total resection, very few distant meningiomas metastasis have been described. We report the case of a patient at our clinic with a meningioma distant metastasis.

2. Case presentation

A 43-year-old woman presented with a recent history of slowly progressive mental confusion, memory impairment, dysgraphia, mental arithmetic trouble, right arm paresis and abnormal gait. The patient was not treated with hormonal therapy. Brain MRI showed a right parietal mass measuring 54 × 42 × 28 mm with surrounding oedema (Fig. 1). The patient underwent a subtotal surgery removal of the mass, which revealed a meningioma WHO grade II with a minority rhabdoid and papillary contingent. Mitotic index was 5/1.6 mm^2 and Ki67 proliferative index ranged from 5 to 10%. Immunohistochemical analysis demonstrated a low expression of EMA, SSTR2, and CD34, and a significant labelling of Stat 6, desmin, cytokeratin AE1–AE3 and Bcl2. After presentation of the case in multidisciplinary board, a postoperative surgical bed irradiation was performed. A 5-point thermoplastic mask immobilized the patient. Clinical target volume (CTV) was defined as the surgical bed. Planning target volume (PTV) was generated with a CTV expansion of 2 mm in all directions. The patient underwent an intensity-modulated radiotherapy of the surgical bed for a total dose of 60 Gy delivered in 30 daily fractions of 2 Gy, 5 days a week. Intensity-modulated and image-guided radiotherapy was performed on a Novalis Tx® (Varian Medical System) (Fig. 2). The patient recovered incompletely with partial relief of dyslexia, dysgraphia and walking instability. Two months after the end of radiation therapy, the patient was referred to the emergency unit of the hospital with sciatica pain. CT scan showed osteolysis of the 8th and 10th thoracic vertebrae, 1st and 4th lumbar vertebrae, 8th right rib and coccyx. It also revealed multiple bilateral lungs nodules and liver nodules. (^{18}F)-FDG PET-CT was performed and showed hypermetabolic lesions corresponding to the osteolytic lesions and lung and pulmonary nodules observed on CT scan (Fig. 3). The coccygeal lesion was biopsied and pathologic analysis revealed meningioma metastasis with morphological likeness and the same immunohistochemical profile as the rhabdoid contingent found in the primary meningioma. Moreover, despite S100 expression, no other melanotic marker was found and Ki67 ranged from 15 to 20% with a mitotic index of 13/17.5 mm^2. A medullar MRI was performed and revealed spinal cord compression in front of the 8th thoracic vertebrae. The patient underwent an osteosynthesis from the 6th to the 10th thoracic vertebrae. An external irradiation was performed; the clinical target volume included the 7th, 8th and 9th thoracic vertebrae, and a total dose of 30 Gy in 10 daily fractions of 3 Gy was delivered. Treatment was well tolerated with a fatigue grade 2 and a dysphagia grade 2 (Common Terminology Criteria for Adverse Events v4.0). According to the recommendations of a multidisciplinary staff, an oral treatment of sunitinib 50 mg/day was started. Sunitinib was well tolerated with only grade 2 fatigue reported. Two months after sunitinib was started, the CT scan showed a stabilization of pulmonary metastasis and a progression of hepatic and bone metastasis.

3. Discussion

A review confirmed that reference treatment of meningioma consists of surgical removal of the tumour, followed by radiation therapy of the surgical bed for tumours that are WHO grade 2 or higher or where there is incomplete removal of the meningioma [6]. However, for malignant meningiomas, recurrence rate ranges from 65 to 100%, despite irradiation [6,7].

A recent review of the literature reported that 115 cases of metastatic meningiomas have been reported since 1990, with a men:women sex ratio of 1:1, and a median age of 52 years. Meningioma WHO grade did not seem to be a prognostic factor. Metastatic sites included the lungs (37%), bones (16.5%), intraspinal (15.2%), liver (9.2%) and miscellaneous (21.9%) [8].

To our knowledge, no consensus guidelines for metastatic meningioma treatment have been published. Few studies reported results of chemotherapy agents in recurrent meningiomas treatment (Table 1). As reviewed by Whittle et al., 57 to 67% of meningiomas express progesterone receptors [4]. Based on that observation, several studies evaluated antiprogestogen. A recent review analysed seven preclinical and six clinical studies evaluating 200 mg daily of mifepristone in recurrent meningiomas. Results were conflictive; most of the studies reported outcomes in favour of mifepristone with partial response ranging from 28.6% to 38.5%, and stable disease rates between 25 and 58% [9].

Whittle et al. reported that 70 to 100% of meningiomas express somatostatin receptor. This observation led to study administration of somatostatin analogue in recurrent meningiomas. Chamberlain et al., in a non-randomized prospective study, evaluated the intramuscular administration of 30 mg of somatostatin once every 28 days in 16 patients whom the presence of somatostatin receptors was available to evaluate response with the (^{111}In)-octreotide SPECT-CT. Four partial responses were observed and 6-month progression-free survival rate was 44% [10]. Johnson et al., in a non-randomized prospective study, evaluated the outcomes of subcutaneous injection of octreotide 500 μg, three times a day, in 12 patients with recurrent meningiomas. No complete or partial response was observed but stable disease was observed in 42% of patients and median time to progression was 17 weeks [11].

Two studies evaluated daily administration of 1000 mg/m^2 of hydroxyurea in recurrent meningiomas. Chamberlain et al. reported the results of a non-randomized prospective study