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Radiation-associated grade 2 meningiomas: A nine patient-series and review of the literature

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ABSTRACT

Introduction: Radiation-associated meningiomas (RAM) remain rare but recognized to harbor a high potential of aggressiveness. Only few studies focused on grade 2 histological variants.
Objective: Our study aims to report the natural history of patients with radiation-associated grade 2 meningiomas followed in a single institution.
Materials and methods: This retrospective study included all patients with grade 2 RAM operated in our institution between 1994 and 2011. We used the WHO 2007 classification for histological grading. The degree of resection was evaluated using Simpson Classification. The tumor was considered radiation-associated, if the patient had a medical history of cranial irradiation for another medical condition (1 year before at least). Patients benefited from a post-operative close clinical and radiological (cranial MRI) follow-up every 4 months during 2 years and annually thereafter, to detect any tumor progression. Adjuvant therapy and/or monitoring were systematically decided during a multidisciplinary team meeting.
Results: Nine patients (6 men and 3 women) were included in the study. The mean age at diagnosis was 34 years old (range 20–55 years). The mean follow-up was 77 months (range 31–180 months). The mean delay between initial cranial radiation therapy and the diagnosis of grade 2 RAM was 23 years (range 16–33 years). Among all patients, 4 harbored a meningiomatosis, while 5 patients harbored a single tumor. Post-operative local tumor progression was noted in 4 patients. Progression free survival (PFS) after the first surgery in these 4 patients was 15, 23, 35, and 47 months. In these 4 progressive patients, 7 surgical resections, 3 GKS and 1 fractionated radiation therapy have been performed. Post-operative tumor progression was noted at distance from the operated meningioma in 1 patient with meningiomatosis. At final control, 2 patients had severe oculomotor palsy and 1 patient needed palliative cares related to progressive meningiomatosis with anorexia and swallowing disturbance.
Conclusion: Grade 2 RAM is a severe radiation-associated disease occurring preferentially in younger male patients. Although, surgery remains the mainstay treatment, the high potential of tumor progression often requires adjuvant therapeutic tools. Thus, new radiation therapy should be discussed in some cases and the role of radio surgery is still to be better defined.

1. Introduction

The side effects of cerebral radiation therapy are well studied in the literature. Neurocognitive disorders and radionecrosis are the most frequently described complications [10,29]. Even if less commonly reported, radio-associated tumors are important concerns as they can be life-threatening. Radiation-associated meningiomas (RAM) and gliomas are the most frequent histological types [7]. Fortunately, the recent improvement of radiation therapy techniques is likely to reduce the occurrence of these adverse events [6,19]. Radiation-associated tumors often occur after an interval of several years [28], and some predisposing factors have been identified (neurofibromatosis) [14]. Some authors suggest that RAM are more aggressive and require looking for any history of whole brain radiation therapy (WBRT) [21,37], as this is

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Table 1
Summary of main demographical data.

Patient	Age at diagnosis (years)	Initial irradiated disease	Delay between radiotherapy and diagnosis of grade 2 meningioma (years)	Meningiomatosis	Location	Simpson	Local progression	Distant progression
1	20	Medulloblastoma	16	1	Convexity	4	0	+
2	29	Leukemia	20	0	Convexity	1	0	0
3	54	Lymphoma	17	0	Convexity	1	0	0
4	24	Leukemia	21	1	Falx cerebri	1	0	0
5	38	Astroscytoma	29	1	Cranial base	2	0	0
6	34	Leukemia	33	0	Convexity	2	+	0
7	27	Leukemia	25	1	Convexity	1	+	0
8	55	Cutaneous angioma	25	0	Convexity	1	+	0
9	28	Leukemia	22	0	Cranial basis	1	+	0

rarely spontaneously reported by patients. As grade 2 RAM is of rare occurrence, there is a lack of studies, which focused on this particular histological subtype. Moreover, the studies concerning RAM, were performed before the WHO 2007 classifications [23] and they mixed between all grades of meningiomas [27,31,37]. Our study aims to report the natural history of patients with radiation-associated grade 2 meningiomas operated in our institution.

2. Patient and methods

2.1. Population

This study is the retrospective analysis of prospectively collected data. The patient population is the same than from the previous paper [1]. This is a subgroup for further analyzing RAM and its natural history and outcome. Using the local database we studied the medical records of all patients who underwent the resection of a grade 2 meningioma at the Lille University Hospital between 1994 and 2011. Surgical resection has been measured using the Simpson Classification. Histological grading has been confirmed using the WHO 2007 classification [23]. Grade 2 meningiomas are defined by one or more of following criteria: (1) chordoid or clear cell histologic subtype, (2) 4–19 mitoses per 10 high-power field (HPFs), (3) brain infiltration, and (4) three or more of the following five histologic features: small cell change, increased cellularity, prominent nucleoli, sheet-like growth, or necrosis. The diagnosis of grade 2 RAM has been retained for patients with a medical history of cranial irradiation at least 1 year before, while other patients have been defined as sporadic grade 2 meningiomas. We noted if patients underwent early postoperative radiotherapy or not.

2.2. Clinical and radiological follow-up

Patients benefited from a close postoperative clinical and radiological (cranial MRI) follow-up every 4 months during 2 years and annually thereafter, to detect any tumor recurrence or progression. The size and the location of the tumor were evaluated by the neuro-radiologists of our institution. Adjuvant therapy and/or monitoring were systematically decided during a multidisciplinary team meeting.

2.3. Progression criteria

Local recurrence has been defined as the occurrence of a newly visible tumor (cranial MRI) in the surgical site or directly in contact with the surgical border. For patients with incomplete resection (Simpson 3–5), local progression was considered when the residual tumor increased in size. Distant recurrence was defined by the occurrence of a newly visible tumor on MRI at distance from the surgical site. Distant progression was defined by the increase in size of a known distant tumor in case of meningiomatosis. All tumor recurrences or progressions were confirmed by the neuro-radiologist of our institution.

2.4. Statistical analysis

Survival estimates have been computed using the Kaplan–Meier method. Comparisons of survival curves have been performed using the Log-rank test. Statistical analysis was performed using the SAS Software (Cary, NC, USA), V9.3.

3. Results

3.1. Population

Among all patients ($n = 167$) operated in our institution between 1994 and 2011 for a grade 2 meningioma, 9 harbored a RAM (5.3%). Among all patients, 4 harbored a meningiomatosis (2 or more tumors), while 5 patients harbored a single tumor. There were 6 men and 3 women with a mean age at diagnosis of 34 years old (range 20–55 years). No patient harbored a neurofibromatosis. The mean follow-up was 77 months (range 31–180 months). The indications for prior WBRT (Table 1) were leukemia ($n = 5$), lymphoma ($n = 1$), medulloblastoma ($n = 1$), astrocytoma ($n = 1$), cutaneous angioma ($n = 1$). The mean delay between initial cranial radiation therapy and the diagnosis of grade 2 RAM was 23 years (range 16–33 years).

3.2. Initial presentation

All patients were symptomatic as they were referred to our institution for the onset of progressive neurological symptoms: intracranial hypertension was noted in 5 patients, neurocognitive disorder in 3 patients, hemiparesis and aphasia in 1 patient, seizure in 5 patients and visual disturbance in 2 patients. Cranial MRI revealed a unique tumor in 5 patients and 2 or more tumors in 4 patients (meningiomatosis). Concerning the operated meningiomas, 6 were located on the convexity, 2 on the cranial basis and 1 on the falx cerebri.

3.3. Postoperative course

No excessive bleeding and no particular complication were noted during the procedures. The extent of resection was considered as Simpson 1 in 6 patients, Simpson 2 in 2 patients and Simpson 4 in 1 patient. Two patients experienced transient oculomotor nerve palsy after the resection of a meningioma located on cranial basis. No other complication has been reported. Histological findings revealed atypical meningioma in 7 patients, chordoïd meningioma in 1 patient and clear-cell meningioma in 1 patient. No patient benefited from early postoperative radiotherapy.