

# Multiple atypical recurrent meningiomas 13 years after radiotherapy for unilateral retinoblastoma: case report and review of the literature

## *Mnogie atypowe nawrotowe oponiaki po 13 latach od radioterapii z powodu jednostronnego siatkówczaka: opis przypadku i przegląd piśmiennictwa*

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### Abstract

Radiotherapy is an important treatment modality for intracranial malignancies. Improved survival rates were achieved via a combination of surgery, chemotherapy and radiotherapy. On the other hand, improved survival rates made long-term complications of radiotherapy more apparent. Secondary neoplasms due to cranial irradiation are encountered more commonly in neurosurgical practice. Radiation-induced meningiomas are recognized as a common late complication of radiotherapy. However, radiation-induced meningiomas after radiotherapy for retinoblastoma have been reported rarely. Herein we report a patient who harboured multiple meningiomas 13 years after radiotherapy for unilateral retinoblastoma, which were recurrent despite surgical removal and chemotherapy.

**Key words:** radiotherapy, meningioma, radiation-induced tumour, secondary brain neoplasms in children, retinoblastoma.

### Streszczenie

Radioterapia jest ważną metodą leczenia złośliwych guzów śródczaszkowych. Dzięki łącznemu stosowaniu leczenia chirurgicznego, chemioterapii i radioterapii osiąga się zwiększony odsetek przeżyć, ale jednocześnie sprawia to, że częściej ujawniają się odległe powikłania radioterapii. Guzy wtórne do napromieniania w obrębie głowy są znanymi i częstymi powikłaniami radioterapii. Rzadko opisywano jednak oponiaki wywołane napromienianiem prowadzonym z powodu siatkówczaka. W niniejszym artykule opisano przypadek pacjenta, u którego po 13 latach od radioterapii z powodu jednostronnego siatkówczaka wystąpiły mnogie oponiaki, które miały charakter nawracający mimo leczenia chirurgicznego i chemioterapii.

**Słowa kluczowe:** radioterapia, oponiak, guz wywołany napromienianiem, wtórne guzy mózgu u dzieci, siatkówczak.

### Introduction

In the last three decades, a combination of surgery, new chemotherapy regimens and radiotherapy has improved survival rates in the management of malignancies. However, longer survival allowed late effects of radiotherapy to become apparent. Long-term effects

of radiotherapy such as radiation necrosis, arteritis, leukoencephalopathy and radiation-induced tumours are well known [1-3]. Radiation-induced meningiomas are usually aggressive and multiple, with a high recurrence rate after surgical treatment [1,3-6]. We present a case of a patient who harboured multiple atypical meningiomas, which were recurrent after surgical resection,

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13 years after the initial radiotherapy for unilateral retinoblastoma.

## Case report

A 13-year old boy was admitted to our outpatient clinic with severe headache continuing for the last three months. His neurological examination was normal.

He had been diagnosed in our institution with a unilateral retinoblastoma of the right eye, when he was 6 months old. No tumour invasion was detected in the contralateral eye or in the cranium. Enucleation of the involved eye was then performed. The pathological examination was consistent with retinoblastoma. The patient was then treated with multimodal chemotherapy for a period of 6 months, and right orbital radiotherapy of a total dose of 40 Gy in 20 fractions.

After 13 years of a disease-free follow-up period, the patient presented with severe headache. Gadolinium-enhanced magnetic resonance imaging (MRI) scan revealed an extra-axial mass lesion in the right mid-cranial fossa, with homogeneous diffuse contrast enhancement (Fig. 1). Surgery was planned and the lesion was totally removed along with the affected dura (Fig. 2). The patient's postoperative course was uneventful. The pathology report was consistent with atypical meningioma (WHO grade II). The mean proliferation index was high (Ki-67 20%).

Systemic chemotherapy of 3 courses (vincristine 1.5 mg/m<sup>2</sup>, cyclophosphamide 600 mg/m<sup>2</sup>, cisplatin

100 mg/m<sup>2</sup>, etoposide 150 mg/m<sup>2</sup>) was given, and the patient was followed up by both neurosurgery and oncology outpatient clinics. Fifteen months after the surgical resection, the patient experienced severe headache and visual deterioration in his left eye. Neurological examination was normal. Control MRI scans indicated a bifrontal extra-axial mass lesion with compression to the left optic nerve, and bilateral internal carotid artery (ICA) and cavernous sinus infiltration (Fig. 3). A bicoronal incision, with use of the existing right pterional craniotomy and an additional right frontal craniotomy, 2 cm crossing the midline, was performed; the lesion was subtotally removed with the affected dura, as the bilateral adhesion of tumour to ICA made a total resection impossible. The postoperative MRI scan showed a remnant of the tumour left on the planum sphenoidale and tuberculum sella level. The patient was discharged from hospital on the sixth postoperative day with no neurological deficit. The pathology report was consistent with atypical meningioma. The mean proliferation index was 25-30% (Ki-67).

## Discussion

Radiation-induced tumours (RITs) are a well-known late complication of cranial radiotherapy. The actual incidence of RITs is not exactly known, but considered to be low. The most common RITs are meningiomas, low or high grade gliomas, and sarcomas [1,7]. Meningiomas are tumours of the brain and spinal cord, arising

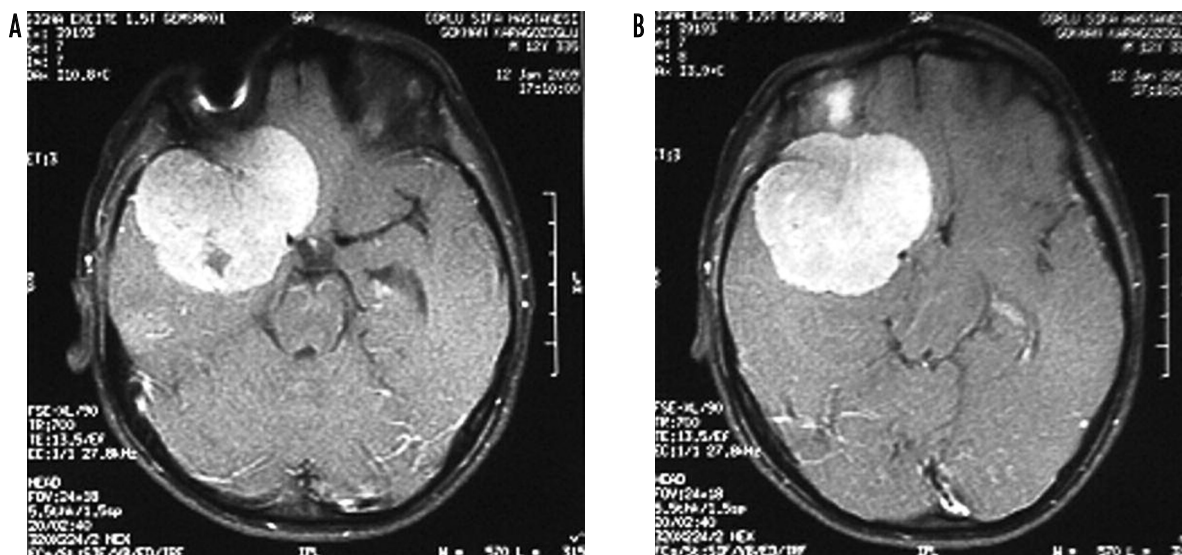


Fig. 1. Gadolinium-enhanced magnetic resonance imaging scan revealed an extra-axial mass lesion (58 × 62 × 50 mm) in the right mid-cranial fossa, with homogeneous diffuse contrast enhancement

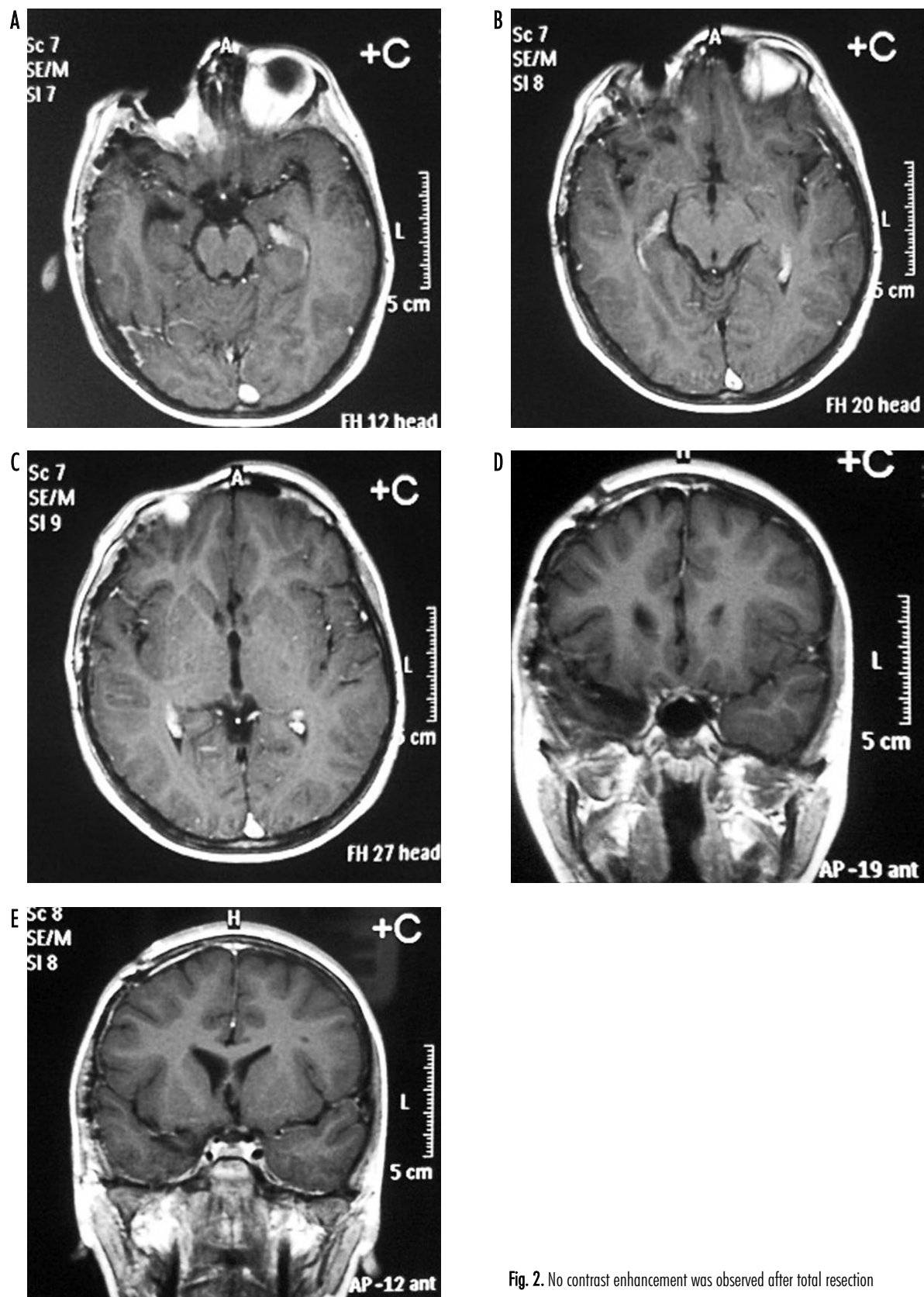
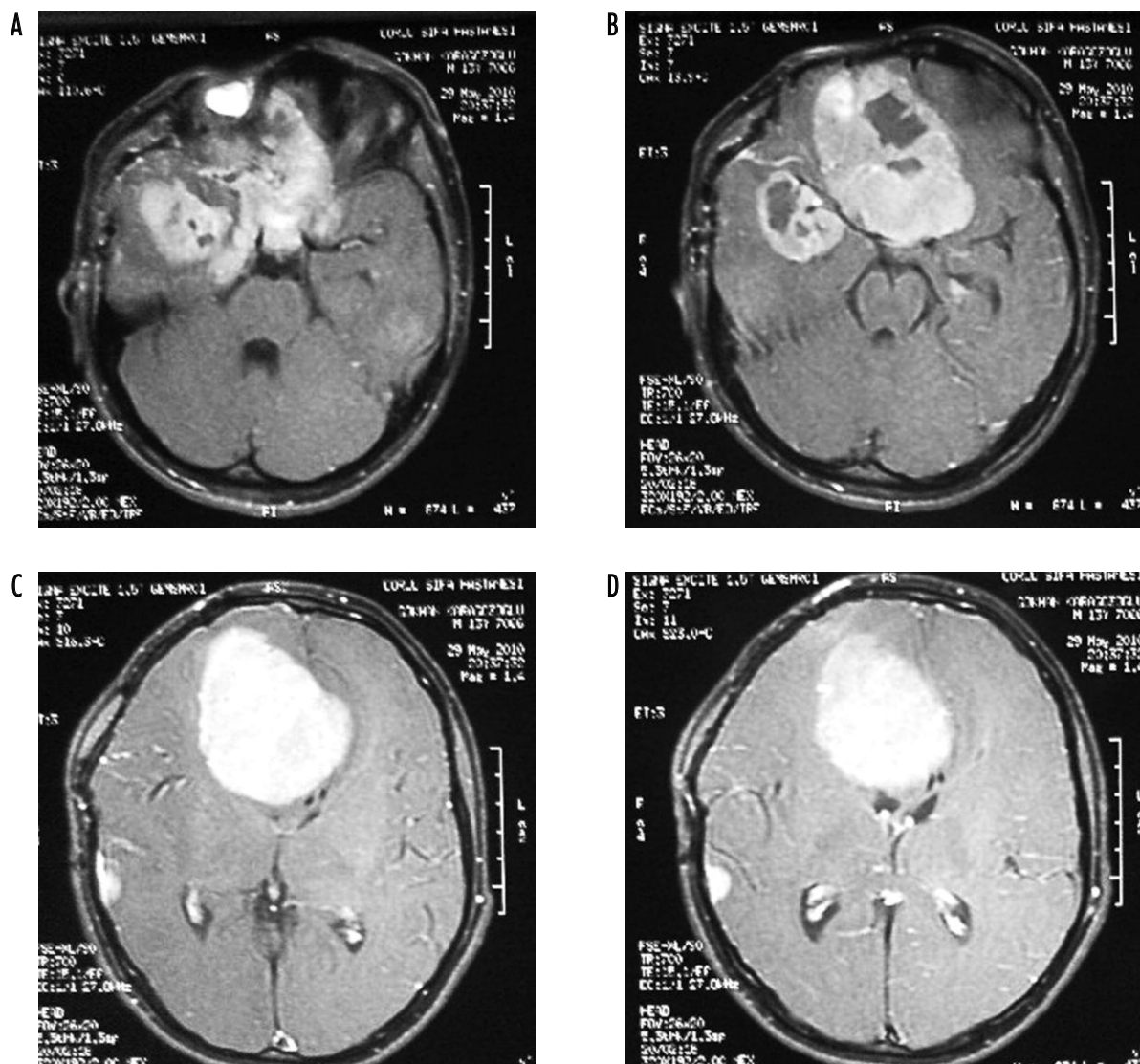


Fig. 2. No contrast enhancement was observed after total resection



**Fig. 3.** Bifrontal extra-axial mass lesion (55 × 62 × 57 mm) with compressed left optic nerve, and bilateral internal carotid artery and cavernous sinus infiltration

from the arachnoid cap cells on the external layer of the arachnoid membrane [8]. The arachnoid tissue is sensitive to irradiation, and especially in the paediatric age group, it is open to oncogenic stimulation [9]. Meningiomas are comparatively rare in infants and children, with an incidence from 0.4% to 4.6%, mostly associated with neurofibromatosis and previous irradiation [10,11].

Retinoblastoma is the most common primary intra-ocular malignancy in children. Two different forms of retinoblastoma are known: hereditary and nonhereditary. The hereditary form tends to be bilateral and familial with an autosomal dominant inheritance pattern, whereas the nonhereditary form is expected to be uni-

lateral and caused by somatic mutations in a single retinal cell [12,13]. Tumours following radiotherapy for retinoblastoma have been reported only in a limited number of publications [14-21]. Hereditary (bilateral) retinoblastomas in children caused by germline mutations in the *RB1* gene also increase the risk of developing a non-malignant second primary tumour. In contrast, most patients with unilateral retinoblastoma (> 85%) do not have these mutations [2]. Although there is an elevated risk for second primary tumours in patients with unilateral retinoblastoma, it is considerably lower than in patients with bilateral retinoblastoma.

The criteria for a tumour to be defined as radiation-induced was previously described [7,22]. There are many

risk factors which may be responsible for the development of an RIT, such as radiation type and dose, additional chemotherapy, tissue vulnerability, underlying disease, age at irradiation, genetic predisposition to malignancies and genetic polymorphism in certain enzymes [23,24].

Harrison *et al.* [5] classified radiation-induced meningiomas into 3 categories: those due to high dose (> 20 Gy), intermediate dose (10-20 Gy) and low dose (< 10 Gy). Patients exposed to irradiation at younger ages tend to develop meningioma in a shorter period and high dose radiation is established as an independent risk factor [25]. Harrison *et al.* [5] reported a latency period of 35.2 years after low dose irradiation, 26.1 and 19.5 years after intermediate and high dose irradiation, respectively. Similar latency periods have been reported by many authors. Although the latency period of 13 years in our case seems short in comparison to the relevant literature, it is consistent with the data published by Ghim *et al.* (10.8 years), where the patients were exposed to radiation at early ages [26].

Surgical removal of these lesions is the first treatment of choice. Radiation-induced meningiomas have a tendency to recur, but it is a known fact that recurrence is one of the main problems related to skull base meningiomas even without a radiation effect. Despite total surgical removal, recurrence may occur and in that case anatomical barriers do not have an influence on tumours growth [27]. So, dissection of these recurrent tumours from vital anatomical structures is challenging. Also in our case, recurrence occurred within 15 months despite total surgical removal. Complete removal of recurrent radiation-induced meningiomas is not always possible due to the aggressive nature of the tumour and due to prior radiotherapy. The tendency for multiple lesions, and bone and vascular involvement makes total surgical removal impossible in certain recurrent cases as well as in our case.

Interestingly, patients with radiation-induced meningiomas may benefit from radiotherapy or stereotactic radiosurgery, although these tumours were induced by radiation therapy. However, because of the former high-dose radiation exposure of our patient and the size of the irradiation field, stereotactic radiosurgery or conventional radiotherapy was not considered as a treatment option. With systemic chemotherapy, 15-month survival was achieved until the recurrence. After resection of the recurrent meningioma, additional systemic chemotherapy was planned.

In the treatment of malignant diseases of childhood such as lymphoma, leukaemia, gliomas, retinoblastoma

and medulloblastoma, great progress in the survival rates has been achieved with combined oncological treatment modalities. Despite the advances in radiation dose delivery technologies, still total radiation doses as high as 50-60 Gy are delivered to the patients for longer survival [28]. As the patients' disease-free survival gets longer, new problems occur, such as radiation necrosis or radiation-induced tumours. We believe that the actual incidence of this pathology is higher than it was reported earlier in the literature and in the future it will become a more serious problem in the management of cranially irradiated patients.

## Disclosure

Authors report no conflict of interest.

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