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Meningioma in the pediatric population

James E. Baumgartner[1] and Jeffrey M. Sorenson[2]
[1] *The University of Texas M.D. Anderson Cancer Center, Department of Neurosurgery, Houston, TX;*
[2] *University of Kentucky Chandler Medical Center, Department of Surgery, Lexington, Kentucky, USA*

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Abstract

Pediatric meningiomas are rare. They are usually seen in association with neurofibromatosis type 2 (NF-2) or following radiation therapy. The tumors are more frequently intraventricular, cystic, and infratentorial than are those in adult patients. Pathologically they are more histologically aggressive than in adults and tend to recur more frequently. Complete resection is the surgical goal. The treatment of subtotally resected meningiomas, particularly in NF-2, remains controversial.

Introduction

Meningiomas in the pediatric population are uncommon, accounting for less than 3% of pediatric brain tumors and 2% of all meningiomas in most centers [1–5]. Affected children often have NF-2 or a history of prior skull irradiation for tinea capitis, leukemia, or brain tumors [4–8]. Pediatric meningiomas differ from those in adults, and their management presents unique challenges.

Clinical materials and methods

The records of all patients 18 years old or less with a diagnosis of meningioma seen at M.D. Anderson Cancer Center from 1964 to 1994 were reviewed after searching the tumor registry database. Patients with meningeal sarcomas were excluded. Followup information was obtained from outpatient clinic notes.

Results

Presentation

Between 1964 and 1994, 14 cases of meningioma in children were seen at M.D. Anderson Cancer Center. These cases accounted for 4% of all patients diagnosed with meningioma. Complete records were not available for 3 patients, thus 11 patients were considered in detail (Table 1). Age at diagnosis ranged form 2 to 17 years, with a median of 11 years. The male/female ratio was 1.2 : 1. Four patients presented with epilepsy, 3 with headache, 3 with a palpable skull mass, 3 with motor deficits and 2 with visual deficits. Three patients met diagnostic criteria for NF-2. Stigmata of NF-2 did not appear in 1 patient until 11 months after resection of her meningiomas (Fig. 1:e & f). Two patients had a history of prior whole brain irradiation (3000 to 3500 cGy) in early childhood, 8 and 10 years prior to presentation with meningioma. Two patients with NF-2 had simultaneous multifocal tumors. Of the intracranial tumors, 10 were supratentorial, and 2 were infratentorial. Except for 1 intraventricular tumor and another involving only scalp and skull, all tumors had a dural base. One tumor had a cystic component.

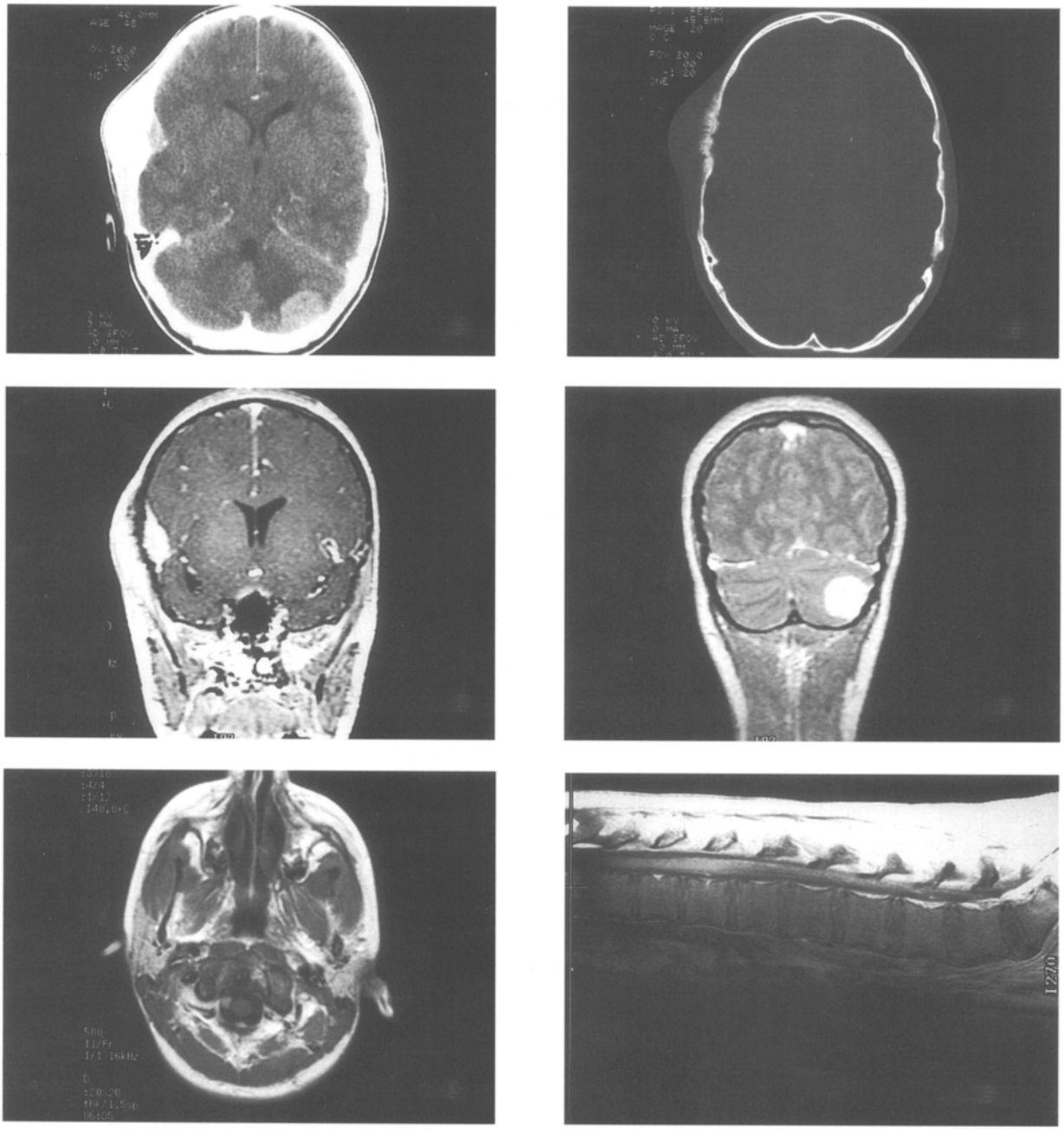

Fig. 1. a: Contrast enhanced CT scan revealing multifocal meningiomas (arrows)
b: CT scan windowed for bone revealing hyperostosis associated with the supratentorial (closed arrow), but not infratentorial (open arrow) meningiomas.
c: Contrast enhanced, coronal T1-weighted MR image demonstrating the supratentorial tumor.
d: Contrast enhanced, coronal T1-weighted MR image demonstrating the infratentorial tumor.
e: Contrast enhanced, axial T1-weighted MR image demonstrating a mass in the foramen magnum (arrow) not seen on scans 11 months earlier.
f: Contrast enhanced, sagittal T1-weighted MR image demonstrating masses throughout the cauda equina not seen on scans 11 months earlier.

Table 1. Pediatric patients with meningioma at M.D. Anderson Cancer Center*

No	Sex	Presentation	Site	Classification	Treatment	Outcome	Notes
1	7/M	hemiplegia, epilepsy, HA, papilledema	lateral ventricle	typical	GTR	visual field deficit, no epilepsy or HA, slight hemiparesis	occipital meningocele
2	14/F	facial palsy	sylvian fissure	malignant	STR, XRT	recurrence, death at 4 mo	whole brain irradiation at age 4 for leukemia
3	2/F	epilepsy	suprasellar	typical	STR	recurrence, blindness, death at 2.5 yrs	
4	8/F	epilepsy	convexity	malignant	GTR, XRT	stable at 5 yrs	
5a	15/M	weakness	cervical	unknown	GTR	recurrence in 14 yrs. GTR. now has recurrence at 1 hr.	NF-II
5b	17	epilepsy, visual change	parasagital & convexity	typical, atypical	GTR	convexity recurrence at 10 yrs. GTR.	
6	14/M	scalp lesion	parietal scalp & skull	malignant	GTR, XRT, Chemo	local recurrence & pulmonary mets, death at 2.5 yrs	
7	10/F	incidental	parafalcine	atypical	GTR	stable at 8 mo	radiotherapy at age 2 for recurrent medulloblastoma
8	17/M	blindness, HA	suprasellar	atypical	STR	blindness, stable	cafe au lait spots
9	17/M	visual change, HA	parafalcine	atypical, cystic	GTR	recurrence at 4 yrs. GTR.	
10	11/M	neck mass	skull base	–	observation	stable at 5 yrs	NF-II
11	11/F	skull mass	convexity, cerebellar	atypical	GTR	stable at 2.0 yrs	NF-II

*HA = headache, GTR = gross total resection, STR= subtotal resection, XRT= radiation therapy, Chemo = chemotherapy, NF = neurofibromatosis

Pathology

Histopathologically, four patients had typical meningiomas, 4 had atypical meningiomas, and 3 had malignant meningiomas. Case 5a was not classified beyond meningioma. In 1 patient (case 5b), multifocal meningiomas had different histologic classifications. BUDR labeling was 4.9% in the only pediatric meningioma tested (NF-2, atypical, case 11).

Surgery

All patients except case 10 had surgical treatment (Fig. 2). This patient's tumor originated in the hypoglossal fossa and encased the carotid artery. It appeared to threaten several cranial nerves. No new cranial nerve deficits were found on serial exams, and the mass was unchanged on serial MRI studies over 2 years. The patient had previously undergone removal of an acoustic neuroma and fulfilled criteria for NF-2.

Two of 4 patients with typical meningiomas had gross total tumor resections (GTR), and 2 had subtotal resections (STR). Both subtotally resected typical meningiomas were suprasellar. All 4 atypical meningioma patients had GTRs. Two of 3 patients with malignant meningiomas had a GTR and 1 of 3 a STR. The subtotally resected malignant meningioma was in the sylvian fissure.

Outcome

None of the 4 typical meningioma patients received radiation or chemotherapy. One patient died 2.5 years after initial presentation, from recurrence of a subtotally resected suprasellar tumor. The remain-

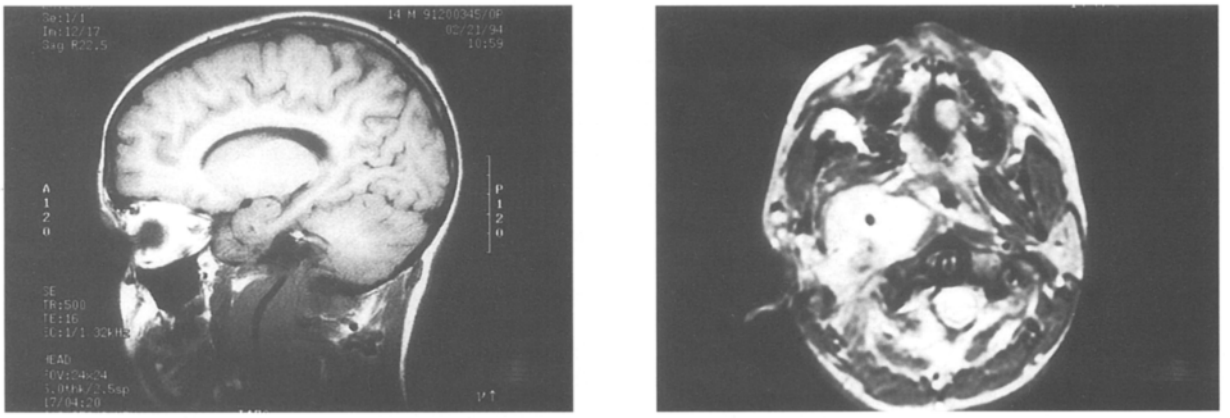

Fig. 2. Sagittal (a) and axial (b) T1-weighted MR images demonstrating a probable skull base meningioma encasing the carotid artery. The patient previously underwent resection of an acoustic neuroma and has NF-2.

ing 3 patients are stable an average of 7.1 years from presentation (case 1 was lost to follow-up 5 years after presentation). None of the 4 patients with atypical meningioma received radiation or chemotherapy. Two patients had local recurrences an average of 7 years from presentation. These were both managed with GTR. Both patients are stable an average of 9 months from their second operation. The remaining 2 patients are stable without evidence of tumor recurrence an average of 1.5 years form surgery. Two of 3 patients with malignant meningioma received standard focal radiation therapy (5000 to 6000 cGy over 5 to 6 weeks). Patient 2, who previously received whole brain radiation therapy for leukemia, was given an additional 3100 cGy after her meningioma was resected. One patient (case 6) received chemotherapy. Two of 3 patients with malignant meningiomas died an average of 17 months from presentation. A subtotally resected tumor recurred locally in the sylvian fissure causing death 4 months after presentation. A scalp tumor which recurred locally and with pulmonary metastasis was fatal 2.5 years after presentation. The remaining patient with malignant meningioma (case 4) did well for 5 years following presentation and then was lost to follow-up. This tumor was a papillary variant with brain invasion, but had relatively few mitotic figures.

Discussion

Meningiomas in the pediatric population differ from those in adults. They are more commonly cystic, intraventricular, and without a dural base [6, 9, 25]. In our series, 83% of intracranial meningiomas were supratentorial, similar to other reported series [6, 4, 9]. As in adults, pediatric spinal meningiomas are typically intradural, extramedullary, and thoracic (48% in children, 81% in adults), but a wider distribution along the spinal axis is seen in children [4, 26, 27]. Intraorbital meningiomas may also occur [6, 4]. Congenital meningiomas have been reported, but are rare [2, 25]. The female preponderance seen in adults is not found in children [3–6, 25]. Ferrante and coworkers reviewed 178 cases from the literature and found a male/female ratio of 1.3:1 [9]. The sex hormone binding characteristics of pediatric meningiomas have not yet been well-characterized, and it is unclear to what extent the hormonal status affects the sex ratio.

The location of the tumor determines its presentation. Supratentorial tumors often present with epilepsy, headache, visual changes, or motor deficits. Infratentorial meningiomas may present with difficulties with balance and coordination. With spinal meningiomas, presentation usually begins with pain and then is followed by motor or sensory deficit [4, 26, 27]. A child with proptosis may harbor an intraorbital meningioma. The combination of epilepsy, hemiparesis, hemianopsia, and papilledema should direct attention to the lateral ventricle [10].

A thin scalp may reveal bony changes in children. As in case 6, pulmonary metastasis may occur with malignant meningiomas [4].

Plain films may show hyperostosis, calcification, signs of increased intracranial pressure, or bony destruction [5, 6]. On CT scanning, hyperostosis is seen with 50% of tumors and 50% have intratumoral calcification. On MRI, pediatric meningiomas are generally large masses with well-defined margins isointense to grey matter on T1-weighted sequences. Cystic and necrotic areas, when present, have prolonged T1 and T2 relaxation times compared to solid portions of the tumor [28].

The causal relationship between radiation and pediatric meningioma is well-established. Modan and coworkers retrospectively studied nearly 11,000 patients who were irradiated for tinea capitis as children in Israel, finding a four-fold increased risk of meningioma in this group compared to a control group [7]. Moreover, the dose these patients received has been estimated to be less than 850 cGy [11]. Although scalp irradiation is no longer widespread, central nervous system (CNS) irradiation for leukemia and brain tumors is common in early childhood. Pediatric meningioma after irradiation for medulloblastoma, as in case 7, has been previously reported [5, 12]. The latency in the reported cases was 12 years and 8 years in our patient. Iacono *et al.*, suggest that latency may be dose-dependent, as meningiomas occurred an average of 20.8 years following high-dose CNS irradiation and 31.3 years following scalp irradiation for tinea capitis [8]. Radiation-induced meningiomas tend to occur within the field of irradiation, are histologically more aggressive, recur more often, and are more likely to be multifocal than sporadic meningiomas [11, 13].

Children with a meningioma should be evaluated for neurofibromatosis, as this may be the first indication of the presence of the disease. In our patient (case 11), eleven months after her initial surgeries, bilateral acoustic neuromas and cauda equina and foramen magnum neurofibromas were found on follow-up MR imaging. The prevalence of neurofibromatosis among children with meningioma is nearly 25%, and these patients may have a higher incidence of extracranial, intraocular, and multifocal meningiomas [4, 6, 14]. The association between NF-2 and meningioma is well-known, and they may share common mechanisms of pathogenesis. Seizenger and coworkers demonstrated loss of heterogeneity in the long arm of chromosome 22 in tissue from acoustic neuromas, neurofibromas, and a meningioma from a single patient with NF-2 [15]. Additional study revealed a loss of constitutional heterogeneity in 17 of 40 (43%) sporadic meningiomas tested at 4 loci on chromosome 22 [16]. Dumanski *et al.* showed that loss of constitutional heterogeneity in meningioma tissue was most commonly due to monosomy 22 (52%), but resulted from terminal deletions of the long arm of chromosome 22 in 11% of tumors [17]. These results suggest that the meningioma locus lies distal to, but near the myoglobin locus in the 22q12.3-qter.

The preoperative workup for children with a meningioma usually includes CT or MR imaging. Angiography with embolization is rarely necessary for children. Baseline and intraoperative somatosensory-evoked potentials are helpful when spinal cord compression is present. The goal of treatment is total resection. In an effort to prevent recurrence, the dural resection is widened until negative margins are obtained [18]. As in adults, recurrence and death are more likely with skull base lesions, incomplete resections, and malignant histopathology [4, 9].

If a total resection cannot be achieved, focal radiation therapy can forestall recurrence and may improve neurological deficits [19–22]. Potential adverse sequellae of radiation therapy, including secondary tumor induction, hormonal deficiency, and growth and intellectual retardation, must be seriously considered, particularly in younger children [23]. An aggressive initial STR may allow radiation therapy to be delayed. Postponement of radiation therapy until adulthood, however, does not necessarily prevent radiation-related complications [24]. It is not yet clear if radiation therapy in children with NF-2 potentiates the chromosome 22 changes and meningioma formation. Usually NF-2 related tumors have an indolent course and can be managed conservatively. Radiation therapy is reserved for unresectable tumors that show signs of progression. Although sarcoma chemotherapeutic protocols have been used for metastatic meningioma, a

role for chemotherapy in pediatric meningiomas is unproven. Isolated pulmonary metastasis can be managed surgically.

Several patients in this and other pediatric meningioma series were treated before modern neuroimaging and microsurgical techniques were available. In addition, some series included meningeal sarcomas; therefore, the reported mortality may be somewhat inflated [5, 10]. In addition, new modalities of radiotherapy show promise for patients previously considered intractable.

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Address for offprints: J. Baumgartner, M.D., Department of Neurosurgery, M.D. Anderson Cancer Center, 1515 Holcombe, Box 64, Houston, TX 77030, USA