Journal of Neuro-Oncology (2006) 77: 73–77
DOI 10.1007/s11060-005-9009-9

Clinical–Patient Studies

Radiation induced meningioma with a short latent period following high dose cranial irradiation – Case report and literature review

Ajay Choudhary[1], Satyajit Pradhan[2], Mohammad Fakhrul Huda[1], Sureswar Mohanty[1] and Mohan Kumar[3]
[1]*Department of Neurosurgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005, Uttar Pradesh, India;* [2]*Department of Radiotherapy, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005, Uttar Pradesh, India;* [3]*Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005, Uttar Pradesh, India*

Key words: cranial irradiation, medulloblastoma, multiple meningiomas, radiation induced meningioma, radiation induced tumors, radiation therapy, second neoplasm

Summary

Radiation induced meningiomas (RIM) are rare late complications in patients who have received high dose irradiation for brain tumors. The mean latency period for induction of RIM in most of the series is 18.7 ± 10.2 years. There are only 9 reported cases of RIM following high dose cranial irradiation with unusually short latency periods of less than 5 years. Herein, we report a child diagnosed with RIM with an unusually short latency period of 14 months. An 11-year old male child underwent gross total resection of medulloblastoma. Following surgery he received high dose craniospinal irradiation. Postoperative computed tomography scan (CT scan) after 1 month did not show features of any residual tumor, recurrence or tumor at a new site. The child was asymptomatic for 14 months and then presented with complaints of headache and vomiting. CT scan head showed multiple solid homogenously enhancing lesions in bilateral basifrontal and right basitemporal region. Histopathology of the lesions turned out to be atypical meningioma.

Introduction

The concept of radiation induced tumors developed with the demonstration of tumor formation in an animal model by Lacassagne [1] in 1933. Several reports on radiation induced gliomas, sarcomas and meningiomas have followed since then. Currently, radiation induced meningiomas (RIM) are the commonest radiation induced tumors reported in the literature [2]. Harrison et al. [3] have classified RIM into three groups based on dose of radiation received, as follows: (1) low dose (< 10 Gy); (2) moderate dose (10–20 Gy); and (3) high dose (> 20 Gy). A sufficient latency or induction period following radiation has been crucial in the definition of the criteria for the diagnosis of RIM [4,5]. There has been a wide range of variation in the latency period following high dose radiation as reported in the literature, with shorter latent periods of 2 years [6] and 3.5 years [7] and a longer period of as much as 63 years [8]. Characteristically, RIMs occur in a younger population particularly, in those who have received high dose of radiation [3,9–11]. In the majority of series the diagnosis of RIM has been in the teens or early twenties with a mean latency period of 18.7 ± 10.2 years [3,9,11–13]. There is an inverse relationship between the dose of radiation received and the time to tumor formation [3,9,13,14]. As reported in the literature, nearly 75% of patients who received radiation during childhood developed RIM, thereby suggesting that the meninges in younger age group are particularly sensitive to the effect of radiation [15]. Herein, we report a case of RIM following high dose cranial irradiation with an unusually short latent period, which is one of shorter periods reported in the literature.

Case report

An 11-year old boy presented with complaints of headache, vomiting, difficulty in walking and occasional blurring of vision for a period of 6 months. Examination of the child revealed bilateral papilledema, truncal ataxia and overt cerebellar signs on both sides. The child had no history of any neurocutaneous disorder. Computed tomography scan (CT scan) head revealed a large, solid and enhancing midline posterior fossa tumor with mass effect and obstructive hydrocephalus (Figure 1).

He underwent a midline suboccipital craniectomy and gross total resection of tumor. The large tumor arose from the superior vermis, was firm in consistency, vascular and with a poorly defined plane of cleavage. The postoperative period was uneventful and patient improved neurologically except for mild gait ataxia. Histopathological examination of the operated specimen showed closely packed sheets and nodules of round to oval tumor cells having hyperchromatic nuclei and scanty cytoplasm. Mitotic figures were frequent. A diagnosis of medulloblastoma was made (Figure 2). The postoperative CT scan, done a month later, showed no sign of any residual disease or tumor at a new site

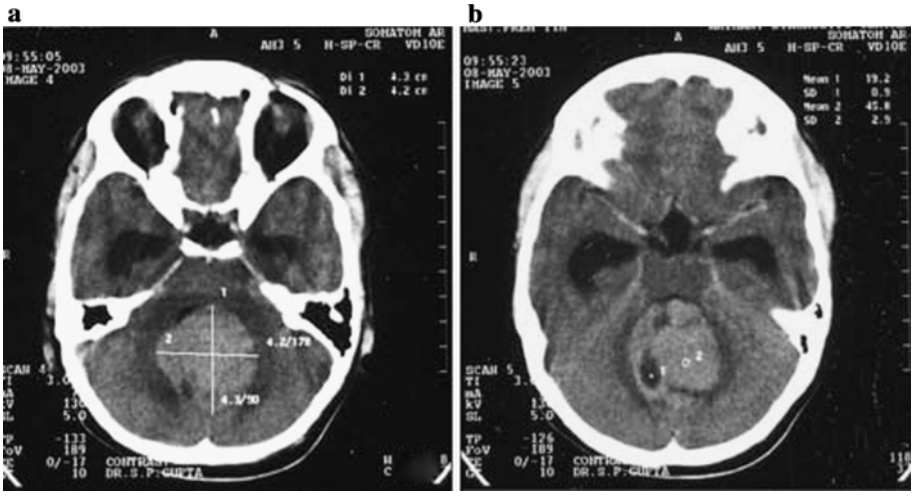

Figure 1. (a) and (b) A midline posterior fossa inhomogenously enhancing lesion with perilesional halo, significant mass effect and obliteration of fourth ventricle

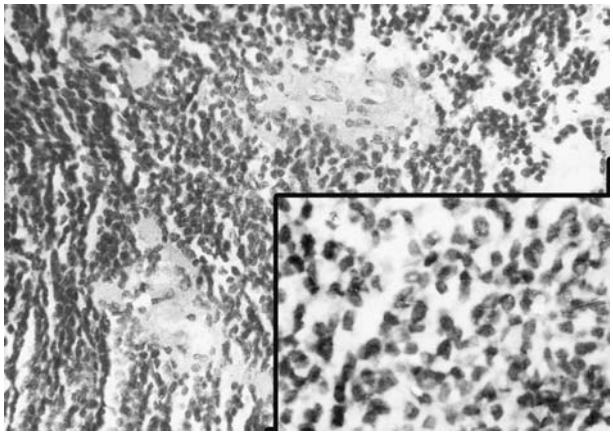

Figure 2. Photomicrograph of the first tumor showing diffuse closely packed sheets of tumor cells with intervening vascular channels (H & E stain, original magnification ×200). In inset: Higher magnification (H & E stain, original magnification ×400) showing monomorphic tumor cells.

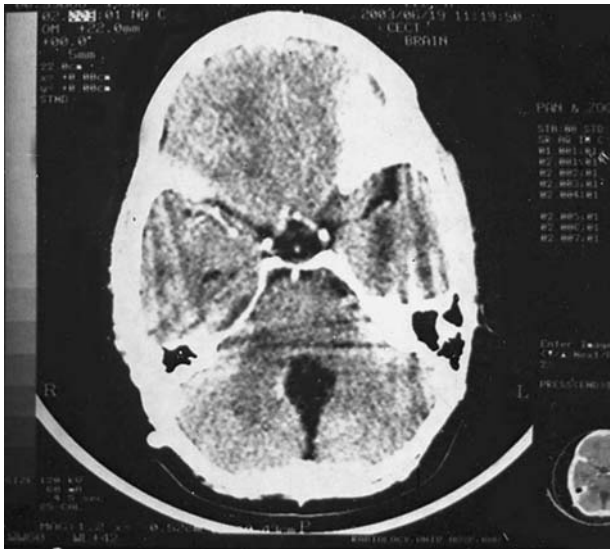

Figure 3. Postoperative follow-up CT scan showing no sign of any residual disease or tumor at a new site.

(Figure 3). The patient underwent craniospinal irradiation one month after surgery. A dose of 30 Gy in 20 fractions was delivered to the spine. Whole brain received 36 Gy in 18 fractions with a final boost of 18 Gy in 9 fractions to the posterior cranial fossa, by parallel opposed lateral portals.

Except for mild gait ataxia, the patient was asymptomatic and was under regular follow up. He underwent follow-up clinical examinations every 3 months. Follow-up CT scan was done 3 months after completion of radiotherapy. As a result of financial constraints on the part the patient, it had been decided to get a CT scan done every alternate visit. The second post radiotherapy CT scan was done during the third follow-up. Fourteen months following radiotherapy, the child presented with complaints of headache and vomiting. Repeat CT scan head showed multiple solid homogenously enhancing space-occupying lesions (SOL) in bilateral basifrontal and right basitemporal region (Figure 4). Presuming it initially as multifocal recurrence of medulloblastoma in other areas of the brain, chemotherapy was started using CCNU, vincristine and cisplatin. With the chances of an uncal herniation occurring due to the temporal mass, a simultaneous plan was made for decompression biopsy of right temporal SOL.

Right temporal craniotomy was performed. Grossly, the tumor was well defined, discrete, firm, vascular and was adherent to the basal dura. A gross total resection of right basitemporal tumor with coagulation of dural attachment (Simpson Grade 2) was done.

Histopathological examination of tumor specimen showed interlacing bundles and ill formed whorls of oval to spindle tumor cells having plump vesicular nuclei. Many of the nuclei showed prominent nucleoli. Mitotic figures were 3–4 per 10 high power fields. Reticulin stain revealed abundant pericellular reticulin fibres. A diagnosis of atypical meningioma was made (Figure 5). Subsequently, gross total resection of bilateral basifrontal tumor was also done (Simpson Grade 2). Thereafter, the patient has been on follow up for the last 6 months without any further neurological deterioration.

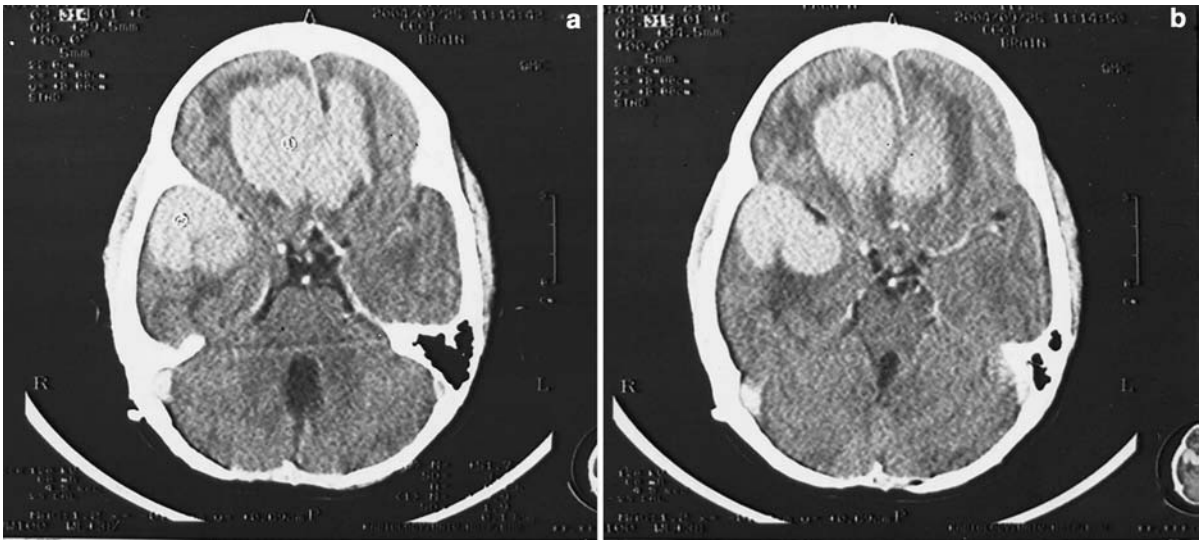

Figure 4. (a) and (b) CT Scan showing multiple solid homogenously enhancing space occupying lesion in bilateral basifrontal and right basitemporal region.

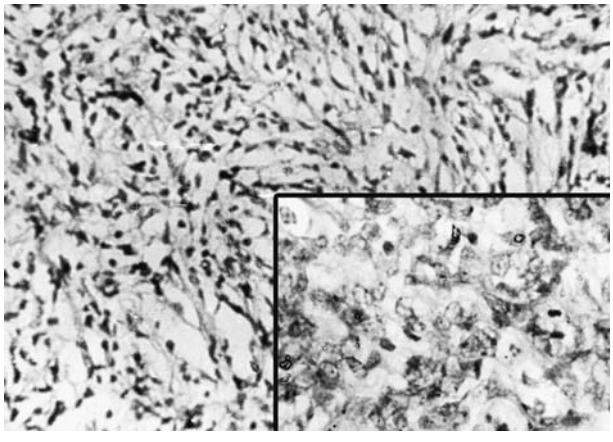

Figure 5. Photomicrograph of the second tumor showing fascicles and ill formed whorls of oval to spindle shaped tumor cells (H & E stain, original magnification ×200). In inset: Higher magnification (H&E stain, original magnification ×400) showing plump oval to spindle tumor cells with vesicular nuclei, prominent nucleoli and mitotic figures.

Discussion

Secondary intracranial meningiomas following high-dose cranial irradiation represent a rare but distinct clinical entity. RIM is characterized by a younger age at presentation, increased rate of multiplicity and recurrence after treatment and by an increased percentage of atypical or anaplastic histology, as compared to spontaneous meningiomas. The latency period is related to age at the time of radiation and varies inversely with radiation dose and biologic aggressiveness [3,9,13]. RIM following high dose radiation has been reported following a latency period ranging from 3.5 to 63 years [7,8]. Horanyi [16] has reported a low latency of 2 years following moderate dose irradiation of 20 Gy delivered for the treatment of tinea capitis. In the present case the latency period has been only 14 months. Survey of literature of cases of RIM with a latency period of 60 months or less for induction following irradiation is presented in Table 1. Of all the patients whose age is known, only one patient was a young adult and the rest were in the pediatric age group with the majority of them below 5 years of age at the time of cranial irradiation following a diagnosis of brain tumor. Our patient was 11 years of age at the time of irradiation. The present case has the shortest latent period second only to the latency period of 12 months that has been reported by Bliss et al. [19].

It has been demonstrated that the difference in latencies between low and high dose irradiated populations is statistically significant [22,23]. The diminishing latency period with increasing dose is indicative of a dose response relationship and lends additional support for the presumed induction of meningioma by radiation. The greater chromosomal injury invoked by higher radiation dosage elicits more rapid loss of cellular control mechanisms and earlier expression of the neoplastic phenotype [3,24,25]. However, the calculation on pooled data by Strojan et al. [11] indicated an insignificant correlation between latency period and radiation dose and they considered the relationship latency-dose not persuasive enough to be characteristic of secondary meningiomas.

More convincing is the relation of latency period to patients' age at the time of cranial irradiation. From reported data the majority of patients with secondary meningioma were irradiated before the age of 17 years and those irradiated at age of 5 years or less had significantly shorter interval to tumor formation than others [11]. Strojan et al. [11] assumed that more chromosome injury is invoked by radiation in the developing nervous tissue of young.

There is a relation between tumor histology and latency period as calculated from pooled data. As a result of more pronounced proliferative activity shorter latency was associated with atypical or anaplastic tumors [11]. Theoretically, following the results of cell kinetics measurements, the latent period could probably be less

Table 1. RIM following high dose irradiation after a short latent period – Literature survey

Sl. No.	Authors and year	Patient Sex & Age in yrs at RT	Primary tumor	RT dose in Gy	Latent period in months	Comment
1	Mann et al. 1953 [17]	4 F	Optic nerve glioma	65	48	Basifrontal
2	Moss et al. 1988 [18]	4 M	Medulloblastoma	46	60	–
3	Rusyniak et al. 1992 [7]	21 M	Lt pontine glioma	55	42	Lt. Temporal
4	Bliss et al. 1994 [19]	? ?	Rec. Pit. Adenoma	HD	12	Skull base
5	Kano et al. 1994 [6]	7 M	Craniopharyngioma	50	24	Rt. temporal
6	Mack and Wilson 1993 [13]	2 F	Medulloblastoma	48.25	60	Convexity meningioma
7	Starshak 1996 [20]	4.5 M	Medulloblastoma	HD	26	Parasaggital
8		9 F	Pineoblastoma	HD	42	Parasaggital
9	Duffner et al. 1998 [21]	< 3 ?	Medulloblastoma	53.2	35	–
10	Choudhary et al. (Present case)	11 M	Medulloblastoma	54	14	Multiple skull base

HD – High dose; Lt. – Left; Pit. – Pituitary; Rt. – Right; RT – Radiotherapy; Rec. – Recurrent; yrs – years.

than a year [11,15]. The mitotic labeling index (LI) is predictive of tumor growth rate. For recurrent tumors, the time to detection for LI of 1%, 3%, and 5% would be 2–4 years, 6–12 months and 3–6 months respectively [15]. In the series published by Mack and Wilson [13], 4 of the 10 RIM were characterized as being other than benign: one had an unusually high LI (3%) two were microscopically aggressive or invasive and one was atypical.

The carcinogenic effect of radiation is limited to cells that have undergone mutation leading to cancer but have not been killed by radiation. As a result, the highest incidence of radiation induced tumors occur at the periphery of the field which receive a dose lesser than that at the center [10,25]. In the present case the whole brain has been irradiated to 36 Gy and the site of the primary disease in the posterior fossa received a dose of 54 Gy. The meningiomas have manifested in the basitemporal and basifrontal regions. The incidence of multiple meningiomas in the radiation-induced group is higher compared to that of non-RIM group [3,9,14]. Multiple meningiomas were also seen in the present case.

Conclusions

RIM is a clearly recognizable clinical entity. The most susceptible population are young children, most likely because of the extensive chromosome damage induced by radiation in the developing nervous system.

There appears to be a distinct relationship between age and latency period. There is contradiction with regard to dose of irradiation and the time to tumor formation. In the present day, as many of the children with brain tumors are long-term survivors, it is absolutely necessary to limit the volume of irradiation and thereby dose to adjoining normal tissues. In view of the chances of a short latent period for meningioma induction, close follow-up with a scope for immediate surgical intervention, where feasible, is warranted. This is especially with respect to the developing and underdeveloped countries where, unlike that in developed countries, exists a problem with regard to regular follow up.

References

1. Lacassagne A: Condition dans lesquelles ont ete obtenus, chez le lapin, des cancers par action des rayons X sur des foyer inflammetories. Compt Rend Soc Biol 112: 562–564, 1933
2. Sadetzki S, Modan B, Cherit A, Freedman L: An iatrogenic epidemic of benign meningioma. Am J Epidemiol 151: 266–272, 2000
3. Harrison MJ, Wolfe DE, Lau TS, Mitnick RJ, Sachdev VP: Radiation-induced meningiomas: experience at the Mount Sinai Hospital and review of the literature. J Neurosurg 75: 564–574, 1991
4. Cahan WG, Woodard HQ, Higinbotham NL, Stewart FW, Coley BL: Sarcomas arising in irradiated bone Report of eleven cases. Cancer 1: 3–29, 1948
5. Al-Mefty O, Topsakal C, Pravendkova S, Sawyer JR, Harrison MJ: Radiation induced meningioma: clinical, pathological, cytokinetic, and cytogenetic characteristics. J Neurosurg 100: 1002–1013, 2004
6. Kano T, Zama A, Ono N, Nakamura T, Tamura M, Ohe T, Nakazato Y: A juvenile case of radiation induced meningioma two years after radiation for craniopharyngioma. No Shinkei Geka 22: 367–370, 1994
7. Rusyniak WG, Marchese MJ, Nelson CN: Benign meningioma with a short latency period following irradiation. Surg Neurol 38: 261–264, 1992
8. Kleinschmidt-DeMasters BK, Lillehei KO: Radiation induced meningioma with a 63 year latency period. J Neurosurg 82: 487–488, 1995
9. Musa BS, Pople IK, Cummins BH: Intracranial meningiomas following irradiation – a growing problem? Br J Neurosurg 9: 629–637, 1995
10. Epstein R, Hanham I, Dale R: Radiotherapy induced second tumors: are we doing enough to protect young patients? Eur J Cancer 33: 526–530, 1997
11. Strojan P, Popovic M, Jareb B: Secondary intracranial meningioma after high dose cranial irradiation: report of five cases and review of literature. Int J Radiat Oncol Biol Phys 48: 65–73, 2000
12. Domenicucci M, Artico M, Nucci F, Salvati M, Ferrante L: Meningioma following high dose radiation therapy. Case report and review of literature. Clin Neurol Neurosurg 92: 349–352, 1990
13. Mack EE, Wilson CB: Meningiomas induced by high-dose cranial irradiation. J Neurosurrg 79: 28–31, 1993
14. Softer D, Pittaluga S, Feiner M, Beller AJ: Intracranial meningiomas following low dose irradiation to the head. J Neurosurg 59: 1048–1053, 1983
15. Wilson CB: Meningiomas: genetics, malignancy, and the role of radiation in induction and treatment. J Neurosurg 81: 666–675, 1994
16. Horanyi B: Roentgen-besugarzas hatasara Keletkezett meningeoma gyermeken. Magyar Radiol 17: 1–7, 1965
17. Mann I, Yates PC, Ainslie JP: Unusual case of double primary orbital tumor. Br J Ophthalmol 37: 758–762, 1953

18. Moss SD, Rockswold GL, Chou SN, Yock D, Berger M: Radiation induced meningioma in paediatric patients. Neurosurgery 22: 758–761, 1988
19. Bliss P, Kerr GR, Gregor A: Incidence of second brain tumors after pituitary irradiation in Edinburgh 1962–1990. Clin Oncol 6: 361–363, 1994
20. Starshak RJ: Radiation-induced meningioma in children: report of two cases and review of literature. Pediatr Radiol 26: 537–541, 1996
21. Duffner PK, Krischer JP, Horowitz ME, Cohen ME, Burger PC, Friedman HS, Kun LE: Second malignancies in young children with primary brain tumors following treatment with prolonged postoperative chemotherapy and delayed irradiation: a Pediatric Oncology Group study. Ann Neurol 44: 313–316, 1998
22. Iacono RP, Apuzzo ML, Davis RL, Tsai FY: Multiple meningiomas following radiation therapy for medulloblastoma Case report. J Neurosurg 55: 282–286, 1981
23. Rubinstein AB, Shalit MN, Cohen ML, Zandbank U, Reichenthal E: Radiation – induced cerebral meningioma: a recognizable entity. J Neurosurg 61: 966–971, 1984
24. Salvati M, Cervoni L, Puzzill F, Bristot R, Gagliardi FM: High dose radiation-induced meningiomas. Surg Neurol 47: 435–442, 1997
25. Dorr W, Herrmann T: Cancer induction by radiotherapy: dose dependence and spatial relationship to irradiated volume. J Radiol Prot 22: A117–121, 2002

Address for offprints: Satyajit Pradhan, 8 GF, Old Medical Enclave, Ved Vyas Colony, Banaras Hindu University Campus, Varanasi 221 005, Uttar Pradesh, India; Tel: +91-542-2368655; ; E-mail: drsatyajit @yahoo.com