Intracranial Large Vessel Vasculopathy and Anaplastic Meningioma 19 Years After Cranial Irradiation for Acute Lymphoblastic Leukaemia

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A child was diagnosed in 1969 as having acute lymphoblastic leukaemia (ALL) and received chemotherapy. On bone marrow relapse in 1973, he was treated with cranial irradiation (20 Gy) in addition to chemotherapy. He continues in complete remission 19 years after his relapse. At age 25 years, he presented with headaches and left hemiparesis. Computerised tomograph demonstrated a large, enhancing right-sided intracranial tumour. Angiography was performed and showed the right internal carotid artery was occluded. Most of the right hemisphere was supplied from the external carotid via the middle meningeal artery. The left posterior cerebral artery and the left anterior cerebral artery were absent presumably as a result of radiation-induced arteritis. A

resection of an anaplastic meningioma arising from the right sphenoidal ridge was achieved. There was a rapid improvement in function and he returned to work. Vasculopathy of the large intracranial arteries has been described after high dose radiation. It may occur as in this case after moderate dose radiation. There is a correlation with meningioma. There is a possibility that large artery vasculopathy will be present in a proportion of patients irradiated for ALL. The long lag time between irradiation and the development of meningioma may mean that, as survivors of childhood ALL enter their third decade since cure, this tumour may be seen increasingly. © 1995 Wiley-Liss, Inc.

Key words: vasculopathy, meningioma, irradiation, ALL

INTRODUCTION

Radiation-induced meningiomas have been reported following both low dose irradiation for conditions such as tinea capitis and after high dose irradiation for intrinsic brain tumours [1]. Large intracranial vessel vasculopathy has been reported after high, but not low, dose irradiation [1–3]. An association between large vessel vasculopathy and radiation-induced meningioma has been reported [4]. How much either of these complications will affect survivors of childhood acute lymphoblastic leukaemia who received prophylactic irradiation is unknown.

CASE HISTORY

A child aged 2 years presented in December 1969 with anaemia and a white count of 15×10^6 /L. A diagnosis of acute lymphoblastic leukaemia (ALL) was made and he achieved a remission with prednisolone and vincristine. Maintenance consisted of courses of methotrexate, 6-mercaptopurine and cyclophosphamide. He received no central nervous system-directed therapy. Therapy was discontinued in February 1973.

In November 1973, he had an isolated bone marrow relapse and achieved a second complete remission with prednisolone and vincristine. Maintenance consisted of continuous 6-mercaptopurine and weekly methotrexate. He received cranial prophylaxis with intrathecal methotrexate and cranial irradiation. Cranial irradiation consisted of 20 Gy given in 11 treatments of 1.8 Gy over 16 days, both fields treated each day, from a 250 KV orthovoltage machine. Therapy was discontinued in November 1976. He continues in complete remission 19 years after his relapse and 23 years since diagnosis of ALL. He was without neurological symptoms, went to normal school and subsequently worked as a mechanic. However, he was noted to have persistent patchy alopecia and atrophic dry scalp skin.

In 1992, he presented with a two-week history of headache and left-sided weakness. At referral to the Neu-

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Fig. 2. Right common carotid angiogram. The internal carotid artery is occluded (arrow) just distal to the origin of the ophthalmic artery.

Fig. 1. Postcontrast axial CT scan. A large, uniformly enhancing right frontal tumour is seen consistent with a meningioma.

rosurgical unit, he was found to have a left hemiparesis and papilloedema. Computerised tomography demonstrated a large, enhancing right-sided intracranial mass arising out of the middle cranial fossa, typical of a meningioma (Fig. 1).

Angiography was performed to assess possible underlying radiation-induced vasculopathy and to define tumour blood supply. This showed complete occlusion of the right internal carotid artery just distal to the origin of the ophthalmic artery (Fig. 2). The anterior right hemisphere was almost completely supplied by the external carotid artery via collaterals from the middle meningeal, anterior meningeal and ethmoidal arteries. The middle meningeal artery supplied structures in the midline, including the motor strip (Fig. 3). The tumour also took its blood supply predominantly from this vessel. In addition, on the uninvolved left side, there was occlusion of the anterior and posterior cerebral arteries at their origins (Figs. 4,5). Supply to the left hemisphere was predominantly via an extensive network of collaterals arising from an hypertrophied middle cerebral artery.

At surgery, the tumour was found to arise from the left sphenoidal ridge. A near total excision of the tumour was performed with preservation of the middle meningeal artery. The need to preserve collateral circulation and the lack of a clear plane around the tumour prevented a total excision. Pathology revealed an anaplastic meningioma.



Fig. 3. Right external carotid angiogram. The middle meningeal artery (arrow) is hypertrophied and supplies midline structures via collaterals. Tumour blood supply is also seen to arise from this vessel.

He made an uneventful recovery from surgery and subsequently recovered good power on the left. He returned to work within 2 months.

DISCUSSION

This young man presents 19 years after cranial irradiation with a radiation-induced meningioma and large ves-

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Fig. 4. Left vertebral angiogram. The left posterior cerebral artery is occluded at its origin (arrow).



Fig. 5. Left carotid angiogram. The left anterior cerebral artery is occluded at its origin (arrow).

sel vasculopathy. This is an association only noted before with high dose irradiation [4]. Meningioma has been reported after prophylactic irradiation for ALL [5]. However, it appears to be rare, cerebral gliomas being more commonly associated.

This may, however, be a function of the time that these children have been followed and one might expect to see more radiation-induced meningiomas in these patients over the next decade. Craniospinal irradiation was only shown to dramatically decrease the risk of a subsequent central nervous system (CNS) relapse of ALL in 1971 [6]. Prior to this, CNS relapse was extremely common, occurring in up to 70% [7]. With cranial irradiation and systemic combination chemotherapy, childhood ALL became curable in 50% [6]. There are then a considerable number of long-term survivors from childhood ALL who were treated after 1971 and who received cranial irradiation. Follow-up time has therefore been less than 20 years in all but a handful of patients. However, the latency period for moderate dose irradiation was 26.1 years in the largest series of radiation-induced meningiomas [1].

The alopecia and atrophic scalp skin noted in this patient are virtually a hallmark of patients with radiationinduced meningiomas [5,8–10]. Whether long-term survivors of ALL who received irradiation and have alopecia would benefit from follow-up neuroimaging is unknown. Meningiomas, postirradiation, as in our patient, are often atypical and may behave aggressively as low grade malignancies [11,12].

It is possible that the occlusion of the right internal carotid was due to tumour compression but this would not explain the occlusion of the left posterior and anterior cerebral arteries. Although occlusive large vessel arteriopathy has never been documented with low dose (less than 10 Gy) [1], it is well-described after high dose radiation in both adults and children [13–15]. There is no literature on the likelihood of arteriopathy after the moderate dose (10 Gy to 20 Gy) used for cranial prophylaxis but as in this case it is obviously a possibility.

It may be that the low energy, 250 KV, used in this patient may have significantly contributed to the risk of arteriopathy and meningioma. Certainly the treatment of tinea capitis in Israel with superficial 60–100 KV resulted in a number of children treated with meningiomas in adult life [16]. Higher energy sources are now used, but a significant number of children were irradiated with orthovoltage in the 1970s. Now that magnetic resonance angiography is available, a study could be performed to assess whether large vessel arteriopathy is present in such patients. If arteriopathy is identified in a cohort of longterm survivors, regular scanning may indicate whether there is an association with meningioma after moderate dose radiation.

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