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Case report

Secondary malignancy following radiotherapy for thyroid eye disease

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ABSTRACT

Aim: To describe the first case of a secondary meningioma in a patient after radiation treatment for thyroid eye disease (TED). Secondarily to identify any additional cases of secondary malignancy resulting from radiotherapy for thyroid eye disease from our institutional experience.

Background: Thyroid eye disease (TED) is a self-limiting auto-immune disorder causing expansion of orbital soft tissue from deposition of glycosaminoglycans and collagen, leading to significant cosmetic and functional morbidity. Established management options for TED include: glucocorticosteroids, orbital radiotherapy, and surgical orbital decompression. Two large series on radiotherapy for TED have been reported without any cases of secondary malignancy.

Materials and methods: The case of a patient with visual failure, found to have a sphenoid wing meningioma after previous TED radiotherapy is described. We then reviewed 575 patients with at least 3-year follow-up receiving radiotherapy for TED at British Columbia Cancer Agency to identify other possible secondary malignancies.

Results: The patient had postoperative improvement in her vision without any identified complications. Three additional cases of hematologic malignancy were identified. The calculated risk in our population of developing a radiation-induced meningioma after TED with at least 3 years of follow-up of is 0.17% (1/575); with hematopoetic malignancies the risk for secondary malignancy is 0.7% (4/575).

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Conclusions: Our calculated risk for secondary malignancy (0.17%, 0.7%) is similar to the reported theoretical risk published in the literature (0.3–1.2%). There is real risk for the development of a secondary malignancy after radiotherapy treatment of TED and treatment options should include consideration for this potential.

1. Introduction

Thyroid eye disease (TED) is a self-limiting auto-immune disorder causing expansion of orbital fat and muscle from deposition of glycosaminoglycans and collagen, leading to a significant cosmetic and functional morbidity.[1] Established management options for TED are: oral or intravenous glucocorticosteroids, orbital radiotherapy, and surgical orbital decompression. The role of radiotherapy for TED remains controversial but has been used for over 60 years.[1]

Two large retrospective series on the safety of radiotherapy for TED have been performed by Wakelkamp et al.[2] and Marcocci et al.[3] These studies contain 363 patients with a minimum follow-up of 10 years and did not identify any single patient who developed malignancy within the irradiated field.[1] The calculated cumulative theoretical risk of developing secondary malignancy over a lifetime by Snijders-Keilholz et al.[4] is 1.2%.

The 1920s provided the first reports of post-radiation sarcomas in patients, demonstrating evidence of the carcinogenic effects of radiation.[5,6] Following these reports, Cahan subsequently developed the original criteria for the diagnosis of a post-radiation malignancy (specifically sarcoma). This has most recently been revised by Al-Mefty et al.[7] specifically for use with meningiomas and summarized in their manuscript as Table 1 (reproduced here):

1. Tumor must arise within the irradiated field
2. Histological feature must differ from those of any previous neoplasm
3. A sufficient latency or induction period following radiation must elapse before meningioma is diagnosed (5 years suggested)
4. No family history of phakomatosis
5. Tumor must not be recurrent or metastatic
6. Tumor must not be present prior to radiation therapy

The most frequent intracranial tumors resulting from irradiation are meningiomas, gliomas and sarcomas.[5] Post-radiation meningiomas are the most commonly reported radiation-induced neoplasms reported in the literature and there is some suggestion of increasing incidence due to the expanding indications for radiation therapy and increasing longevity of patients after radiation therapy.[5,7] The risk of developing a meningioma in post-radiation patients is described as 6–10× higher than the standard population.[8] Post-radiation meningiomas also differ in characteristics from spontaneous meningiomas having no female predominance and a younger age at presentation.[5] The mean latency for meningiomas after radiation has been reported up to 26.5 years[5,7] with suggestion that younger age at radiation treatment results in a shorter latency period.

1.1. *Case*

A 67-year-old right hand dominant female presented to the care of the Neurosurgery service at our institution with a generalized tonic clonic seizure. She had recently been investigated for right sided visual failure and been found on computed tomography (CT) (see Fig. 1) scan to have a large right sided sphenoid wing lesion, consistent with a meningioma. Magnetic resonance imaging (MRI) was performed and demonstrated an extensive dural tail along the middle cranial fossa. The lesion extended along the planum sphenoidale and across the diaphragma sella but not into the sella. The pituitary stalk was displaced to the contralateral side, along with the basal ganglia. The optic chiasm was also displaced with the right optic nerve difficult to visualize. There was no obvious intraorbital extension of the lesion. Flow voids from the supraclinoid internal carotid artery, the proximal middle cerebral artery and the proximal anterior cerebral artery were noted along the posterior margin of the tumor and appeared to be narrowed by the mass effect (MRI shown in Fig. 2). Formal cerebral vascular imaging was not performed.

The patient's past medical history was significant for hypertension, hypothyroidism with Graves' disease, a

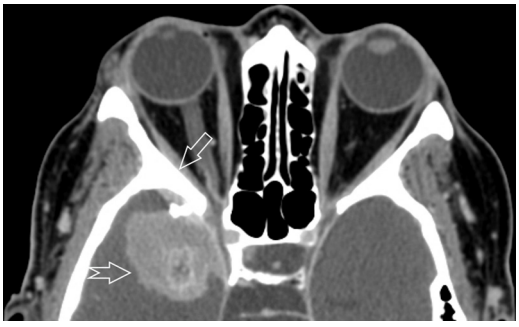

Fig. 1 – Axial computed tomography image without contrast, illustrating right sided sphenoid wing meningioma (notched arrow) measuring 5.4 cm × 4 cm × 5.3 cm (transverse × anterior-posterior × cranial – caudal). The bone along the right sphenoid wing, the anterior and posterior clinoid processes is hyperostotic (arrow). There was 1 cm of midline shift and vasogenic edema present in the right frontal and temporal lobes (not shown). The findings were consistent with meningioma and this was compared to the CT head from 10 years prior which had no evidence of lesion.