**Radiation Induced Malignancy in Retinoblastoma: New Pathology in a Case Report**

Clara Draf, Madeleine R. Schaberg MD, Vijay K Anand MD, Gurston Nyquist MD, Syed Hoda

1Department of Otolaryngology, Head and Neck Surgery, Weill Cornell Medical College, New York, N.Y.
2Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York Presbyterian Hospital, New York, N.Y.

**Abstract**

**Objective**: Patients with a genetic history of retinoblastoma have an increased risk of developing a second neoplasm. When these secondary malignancies occur in the previously irradiated field of the primary tumor they are most commonly osteosarcomas, fibrosarcomas, and squamous cell carcinomas. We present the first case of a radiation induced adenocarcinoma in a patient after treatment for retinoblastoma.

**Methods**: This case study underwent a chart review, comprehensive history, physical exam, rigid nasal endoscopy, and radiographic imaging. A literature review of the MEDLINE database 1966-2009 using key words, retinoblastoma, radiation, and second malignancy was performed.

**Results**: Our case is a 29 year old man with a past medical history significant for surgical resection followed by irradiation at age 1 for retinoblastoma who presented with right sided epistaxis and nasal obstruction. Endoscopy revealed a mass in the right nasal cavity. MRI and CT revealed a mass filling the right nasal cavity and ethmoids with erosion through the cribriform plate. The patient underwent surgical resection and pathology revealed a sinonasal adenocarcinoma.

**Conclusions**: Second malignancies in patients with retinoblastoma tend to occur in the previously irradiated field of the primary tumor and contribute significantly to long term morbidity and mortality rates. This is the first case of a sinonasal adenocarcinoma occurring in the previously irradiated field. The endoscopic skull base surgeon plays a vital role as patient survival depends on the diagnosis and surgical management.

**Introduction**

- 250-350 children in the United States are diagnosed with retinoblastoma annually
- Retinoblastoma is a rare type of eye cancer which originates in the retina[1, 2]
- Retinoblastoma is differentiated into hereditary 30-40% and non-hereditary 60-70% [3]
- The genetic basis of retinoblastoma lies in a mutation of the tumour suppressor gene RB1, located on the long arm of chromosome 13
- Treatment, including different types of radiation therapy, chemotherapy regimens, intraocular laser- and cryo-coagulation have lead to a high rates of survival for retinoblastoma with the literature citing an average 93% 5 year survival [7, 8]
- It has also been shown that the level of expression of the mutated gene may predispose to the development of a second malignant neoplasm [9]
- Patients with retinoblastoma of hereditary origin have an increased risk of developing a second malignant tumor [9]
- Additionally these secondary neoplasms occur frequently in the field of radiation
- We present a patient case of hereditary retinoblastoma that subsequently developed a sinonasal adenocarcinoma 27 years post-radiation therapy

**Case**

- 29 year old male presented with a six month history of right sided nasal obstruction, rhinorrhea, epistaxis, and headaches
- Past medical history: treatment at age one for unilateral right sided retinoblastoma with external beam radiation up to a dose of 45 Gy
- Family history: positive for retinoblastoma in both parents and two siblings
- Social history: significant for 10 pack years of tobacco use
- Clinical exam: Patient with normal vision bilaterally except for small right medial visual field defect in left eye
- Nasal endoscopy: revealed a mass in the right nasal cavity, lying along the floor of the nasal cavity and emanating from beneath the middle turbinate
- Computed Tomography of the paranasal sinuses identified a soft tissue mass in the right nasal cavity, extending into the ethmoid air cells, sphenoid sinus, and eroding the cribriform plate
- Magnetic resonance imaging of the brain and maxillofacial region showed a similar heterogeneous mass with dural displacement but no gross erosion
- Intra-operative findings: The bulk of the tumor was in the nasopharynx and it extended into the superior posterior right septum and filled the right ethmoids and sphenoid, extending to skull base and cribriform plate. It invaded the dura beneath the right cribiform plate
- Surgery: Endoscopic resection of tumor, bilateral ethmoidectomy, sphenoidotomy, and closure of skullbase defect with fascia lata graft, medpore implant, and left nasoseptal flap
- Pathology revealed a sinonasal adenocarcinoma with papillary features.
- This was staged as a T4aN0M0 tumor and patient underwent post-operative chemotherapy and proton beam radiation which was completed in October 2009

**Discussion**

- Survivors of genetically transmitted retinoblastoma have an increased risk of developing a second nonocular tumor
- In addition these patients have an increased sensitivity to carcinogenic effects of radiation
- Whether a tumor is classified as radiation-induced is determined by following criteria:
  - The secondary neoplasm has to be located within the irradiated volume
  - It must develop at least three years after the irradiation of the primary tumor
  - The administered dose of radiation has to exceed 2 Gy
  - The pathology should have excluded a metastatic tumor process [12, 13]
- A long latency period is characteristic for radiation induced tumors and within this field the most common secondary neoplasms are: osteosarcomas, fibrosarcomas and squamous cell carcinomas
- Patients who have been diagnosed with retinoblastoma have an increased susceptibility to oncogenic processes due to a genetic predisposition
- In addition, therapeutic radiotherapy also increases the risk of developing a second primary malignancy even after a substantial amount of time, in this case 27 years

**Conclusions**

- Physicians treating these patients should be aware of the increased risk of developing second malignancies and perform life-long follow-up and screening
- This is the first case study reporting a sinonasal adenocarcinoma as a secondary neoplasm in a retinoblastoma survivor

**References**