CASE REPORT

Anterior Skull Base Surgery for Secondary Malignancies in Retinoblastoma Survivors: Report of Two Cases

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ABSTRACT—With the improved survival rate of patients with retinoblastoma, the incidence of second malignancies has become substantial. We had two retinoblastoma survivors with secondary malignancies in the naso-ethmoidal complex, one a 21-year-old man with anaplastic carcinoma and the other a 16-year-old girl with malignant fibrous histiocytoma. They underwent repeated craniofacial surgery. Secondary malignancies arising at the nose and ethmoidal cells often invade the anterior skull base. The introduction of skull base surgery has provided wider surgical margins and increased the resultant likelihood of cure. Both patients have so far shown no evidence of recurrence.

Retinoblastoma (RB) is a malignant tumor of children with a current cumulative disease-related survival rate at 10 years in excess of 90%.¹ With the improved survival rate of patients with RB, the incidence of second primary tumors has become substantial. Secondary malignancies in association with RB are now thought to be the result of abnormal cell proliferation caused by an inactivation of the RB gene by a mutation at the long arm of chromosome 13 at the level band q14.² Irradiation may increase the risk of gene inactivation and shorten the latency period until the development of a secondary malignancy.

Malignancies occurring in the nasal cavity and ethmoidal cells often invade the anterior skull base bones and intracranial components. The techniques of skull base surgery have provided wider surgical margins, and the resultant more radical surgery, in patients with malignant tumors arising in this region. The skull base surgery team at the University of Tokyo Hospital has performed 51 skull base surgeries on 41 patients during the last 7 years. Out of these 41 patients, there were 2 with histories of irradiation for bilateral RB in their infancy who developed malignant tumors in this region. We re-

port their case histories and discuss the problems of treatment.

CASE REPORT

Case 1

A 21-year-old man presented with bilateral sensation of ear fullness of 3 months duration. He had a history of two episodes of meningitis 5 years previously. He had a history of bilateral RB: his right eye had been resected when he was 2 years old, and the left eye had been treated with external beam radiation of 78 Gy when he was 3 years old, leaving him blind.

Physical examination revealed a necrotic mass in the bilateral posterosuperior nose. The posterosuperior part of the septum was absent. Bilateral middle ear effusion was noted. Biopsy of the specimen from the left middle turbinate revealed anaplastic small cell carcinoma. CT revealed a mass with soft tissue density occupying the posterior ethmoid cells and extending inferiorly to the common meatus. A total of 52 Gy of electron

beam irradiation was applied over a 5-week period, but there remained a rough surfaced elevation in the posterior-most part of the nose at a locus which was compatible with an iso- to hypointensity mass extending from the posterior ethmoid tegmen to the clivus, as visualized on the T1-weighted magnetic resonance (MR) image.

Surgery was performed solely through a transfacial approach on May 20, 1992. Using a total rhinotomy incision,³ both ethmoid sinuses were visualized. Due to the defect of the posterior septum, excellent operative field was obtained. Extensive multiple defects at the ethmoidal tegmen were recognized. Microscopic resection of the tumor from the dural surface was applied. As the frontal lobe dura was very thin, it was torn in one place, resulting in cerebrospinal fluid (CSF) leak. The defect was successfully repaired with a free fascia lata graft.

Two years later, the patient developed a recurrence at the left posterior ethmoid sinus extending to the medial part of the orbit (Fig. 1). The second operation was performed on September 5, 1994 using bifrontal coronal incision and transfacial approach. The dura mater was maldeveloped and very thin, and it adhered to the arachnoid membrane. It was patched with a free fascia lata flap. There was no brain invasion. Frontal base bone was cut at the both orbital plates of the frontal bone with the left side more lateralward. The sphenoid sinuses were poorly pneumatized. The bilateral optic nerve was sectioned at the retro-orbital portion. Using Weber-Ferguson's incision, we performed a total en bloc removal of the nasal cavity and left partial maxillectomy with left orbital exenteration. The large defect of the anterior skull base, left orbit, and left maxillary sinus was filled with a rectus abdominis musculocutaneous flap, the feeding vessels of which were anastomosed with the left facial artery and vein. Pathologic specimens revealed poorly differentiated carcinoma.

This patient has been alive and well without recurrence for 22 months.

Case 2

A 16-year-old girl was referred for evaluation of bilateral nasal tumor. Her medical history was remarkable for bilateral RB. Her right eye had been enucleated when she was 1½ years old, followed by external beam of irradiation of 63 Gy. Her left eye also had been resected when she was 3 years old, followed by local placement of a Cobalt 60 source. Two months before presentation she had developed bilateral nasal congestion with bloody rhinorrhea. Transnasal biopsy confirmed the diagnosis of sarcoma of unknown type. As tumor development was very fast, preoperative irradiation of 36 Gy was applied.

The tumor, which bled easily, occupied both nasal cavities and protruded from both the right anterior nares and the right choana, so that it was suspended in the oropharynx. The resultant soft palate bulging was observed. The CT scan disclosed a mass with soft tissue density occupying bilateral nasal cavities and ethmoids with an extensive defect of the ethmoidal tegmen. The orbits and the maxillary sinuses were hypoplastic bilaterally. Due to the artifact produced by a metal holder for an artificial eye in the right orbit, informative MR scan was not obtained.

She underwent craniofacial surgery on September 28, 1993. Using a bifrontal craniotomy with partial frontal bone resection, we examined the anterior skull base from above. The tumor occupied the ethmoidal sinuses, extending to the bone of the eroded tegmen and adhered partially to the dura. The very thin frontal lobe dura was elevated to the planum sphenoidale. An osteotomy of the anterior skull base was made at the cribriform plate and the orbital roof to remove the ethmoidal sinuses en bloc. Then, the transfacial portion of the procedure was performed through a total rhinotomy approach, by which we successfully accomplished total ethmoidectomy and total removal of both nasal cavities. Complete en bloc resection of the tumor could then be

Figure 1. Postcontrast CT scan in Case 1 (recurrence). An enhancing mass is observed below the fascia-galeopericranial graft encroaching on the left medial orbit.

Figure 2. Postcontrast CT scan in Case 2 (recurrence). A mass with soft tissue density mass is present in the posterior right orbit. Bony defect is evident at the roof.

performed. The bony defect in the anterior skull base was covered with a galeopericranial flap.

Eighteen months later, she developed recurrence which was confirmed with routine follow-up CT study. The recurrent tumor extended from the posterior ethmoidal tegmen with invasion into the right medial orbit (Fig. 2).

Reoperation was performed on March 20, 1995 using bifrontal craniotomy and Weber-Ferguson lip splitting incision approach. Extensive dural invasion, including the area patched with the fascia lata flap in the previous operation, was recognized. An osteotomy from above was made laterally both at the lateral border of the right orbit and at the medial bony wall of the left orbit as well as posteriorly at the planum sphenoidale. The large defect of the anterior skull base, right orbit, and right maxillary sinus was filled with a rectus abdominalis musculocutaneous flap. This recurrent tumor was confirmed pathologically to be a malignant fibrous histiocytoma. One month postoperatively, single massive Linac x-ray irradiation (25 Gy) was performed to destroy any possible microscopic residual malignancy, because the posterior margin of the resected dura was close to the tumor.

This patient has been alive without disease for 16 months.

DISCUSSION

In RB survivors, the secondary malignancies arising from the nose and ethmoidal cells are very difficult to manage. Before the introduction of skull base surgery, most patients died within 5 months. Schwartz et al⁴ were the first to introduce skull base surgery for the second tumor in RB survivors. Smith et al⁵ reported that with an aggressive combined modality approach (radical surgery with postoperative radiotherapy) in the treatment of secondary sarcoma, three of four patients were without evidence of disease at 22 to 72 months fol-

low-up. Among three patients who did not receive aggressive treatment, there were no survivors.

It is evident that radical resection, including craniofacial resection, provides an opportunity to obtain cure. The presence of a mutation which can occur in the RB gene may cause development of a third tumor. Therefore, some experts insist that aggressive treatment will not do the patients any good. However, we think that for patients to obtain a better quality of life, keeping a tumor-free condition for a longer period is truly worthwhile.

Clear surgical margins may not be readily attained due to the close proximity of the diseased portions to critical structures, such as the internal carotid artery, or due to the diffuse nature of the tumor. Thus, because of overt or possible positive margins after the surgery, irradiation should be applied postoperatively. The fact that we did not obtain good results in preoperative irradiation for both patients also supports the propriety of postoperative irradiation, even though it may increase the risk of gene inactivation and development of a third malignancy.

Even when these procedures are performed, recurrence may occur. However, reoperation using skull base surgery technique can be effective, as our experience showed with these patients.

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