Multiple neoplasms following craniospinal irradiation for medulloblastoma in a patient with nevoid basal cell carcinoma syndrome

Case report

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A 28-year-old man presented to the authors’ hospital with multiple intracranial tumors. At 2 years of age, he had undergone resection of a medulloblastoma and received adjunctive craniospinal irradiation. Subsequently, he was diagnosed with nevoid basal cell carcinoma syndrome, Gorlin’s syndrome. Since his first presentation, he has required surgery for multiple basal cell carcinomas, an osteochondroma of the rib, two meningiomas, a trigeminal schwannoma, and a pleomorphic liposarcoma, all of which arose within the radiation field. Despite this impressive list of benign and malignant neoplasms, the patient is relatively well and leads a normal life. The authors examine the relationships between Gorlin’s syndrome and radiation therapy and the subsequent development of tumors.

KEY WORDS • Gorlin’s syndrome • radiation-induced tumor • pleomorphic liposarcoma

The formation of tumors in patients who received therapeutic irradiation is a well-documented phenomenon. The criteria that must be met to classify a tumor as radiation induced include location within the irradiated field, long latency period (years–decades), and a histological appearance distinct from the original tumor. Intracranial neoplasms that have been associated with a history of irradiation include meningiomas, sarcomas, and gliomas.

Nevoid basal cell carcinoma syndrome is an autosomal dominant disorder (40% of new cases are sporadic) that is characterized by early basal cell carcinomas, craniofacial anomalies (left lip/palate, hypertelorism, keratohyalin cysts of the mandible, and frontal bossing), and skeletal anomalies (scoliosis, bifid ribs, and metacarpal dysmorphisms). Approximately 5% of patients with this disorder have childhood medulloblastomas.

We present an interesting case of nevoid basal cell carcinoma syndrome in a patient who received craniospinal irradiation following resection of a medulloblastoma. Subsequently, he developed several tumors, both benign and malignant, which necessitated multiple operative procedures. We provide a review of the literature.

Case Report

History. This 28-year-old man first underwent resection of a cerebellar medulloblastoma at the age of 2 years. He required shunt placement to treat hydrocephalus. The patient then underwent radiation therapy, receiving 40 Gy to the cranium and 20 Gy to the spinal canal. He was also found to have spina bifida occulta with a sacral lipoma, which has not required surgery. At the age of 12 years, the patient underwent resection of the anteromedial portion of his third rib because of an osteochondroma. He did well following these procedures; however, he required numerous excisions of basal cell carcinomas and squamous cell carcinomas, primarily of the head and trunk, within the radiation fields. At the age of 26 years, the patient underwent magnetic resonance imaging of the brain because of depression (Fig. 1 left). The study revealed a large left petroclival mass, left anterior temporal mass, and smaller right anterior temporal mass, as well as extensive calcification of the falx cerebri and tentorium. A small extracranial mass in the right parietal region was also noted (Fig. 1 right).

Operations. The two left-sided lesions were resected and found to be a trigeminal schwannoma and a meningioma. Postoperatively, the patient required a tracheostomy and percutaneous feeding tube, both of which were temporary, and he sustained a right-sided hemiparesis caused by brainstem edema. These deficits improved with therapy. The right-sided lesions progressed in size (Fig. 2) and were resected 14 months later. The intracranial and scalp tumors were determined to be a meningioma and a pleomorphic liposarcoma, respectively. Although the margins of the sarcoma did not show any evidence of tumor, the patient was returned to the operating room for a wide
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resection, rotational flap and split thickness skin graft, because of the malignant nature of this lesion. He sus-
tained no new neurological deficits from these procedures.

**Postoperative Course.** Radiation therapy was not given
to the scalp because of the history of radiation therapy.
Currently, 1 year after his last procedure, the patient
has returned to his previous employment as a cashier in a
bookstore. Neurologically, he has decreased sensation of
the left side of the face with an absent corneal reflex, left-
sided hearing loss, facial asymmetry due to mandibular
dysplasia, and a mild right hemiparesis with right-sided
hyperreflexia. There is no evidence of either recurrence or
metastasis of the pleomorphic liposarcoma or the other
tumors (Fig. 3).

**Discussion**

Nevoid basal cell carcinoma syndrome was first delin-
eeated by Gorlin and Goltz in 1960. Linkage analysis and
heterozygosity studies have mapped the responsible gene
to chromosome 9q22.3-q31. The incidence of medul-
loblastoma in this population has been estimated to be
between 5% and 20%. Conversely, the estimated inci-
dence of Gorlin’s syndrome in patients with medulloblas-
toma is 1 to 2%. It has been noted that patients with
Gorlin’s syndrome tend to have a better prognosis with
regard to medulloblastoma, despite its occurrence gener-
ally before the age of 2 years. This may be an erroneous
concept because Gorlin’s syndrome is typically not diag-
nosed until the second decade of life, and the patients with
Gorlin’s syndrome and more aggressive medulloblastoma
may not survive to diagnosis, thus selecting out the more
favorable tumors.

Meningioma has been described in association with
Gorlin’s syndrome in the past, including a case report of
multiple meningiomas. In the two prior cases of menin-
gioma associated with irradiation and Gorlin’s syndrome,
there has been histological evidence of malignancy that is
absent in our case.

The patient had a large trigeminal schwannoma that has
not been previously reported in association with Gorlin’s
syndrome. Schwannomas have rarely been described after
irradiation, although the relative risk of schwannoma
after irradiation for tinea capitis has been reported to be
significantly higher than that for meningioma.

Benign radiation-induced tumors occur when the radia-
tion is low dose, typically less than 10 Gy, as was used in
the first half of this century for tinea capitis. High-dose
radiation for the treatment of malignancies commonly
causes other malignant tumors of the soft tissue, typically
sarcomas. This patient had a pleomorphic liposarco-
ma of the scalp, an extremely rare location for this tumor.
Although it has been reported in the axillary region in
association with radiation, there are no such reports of this
lesion in the scalp following cranial radiation.

Multiple primary tumors of the head and neck and of
the central nervous system (CNS) of different histological

![Fig. 1. Gadolinium-enhanced T1-weighted MR images, axial views, demonstrating (left) bilateral temporal fossa meningiomas and left trigeminal schwannoma and (right) a small scalp mass in the right parietal region.](image1)

![Fig. 2. Gadolinium-enhanced T1-weighted images, axial views, demonstrating (left) interval enlargement of the right temporal fossa meningioma and left trigeminal schwannoma, and (right) an interval increase in the right parietal scalp mass.](image2)

![Fig. 3. Gadolinium-enhanced T1-weighted MR image, axial view, demonstrating no recurrence of the bilateral meningiomas or the trigeminal schwannoma.](image3)
types do occur but rarely in this number except in the phacomatoses. 3,6,9,17 This patient has had four primary CNS tumors of three different histological types in addition to multiple soft-tissue tumors of the scalp. We know of no other case with such an array of tumor types.

The patient clearly has Gorlin’s syndrome, a syndrome in which there is a known predisposition to develop tumors of the CNS and other systems. Each of this patient’s tumors has been previously described in association with irradiation. With the exception of the medulloblastoma, all of these tumors fulfilled the criteria to be considered radiation induced: they were of different histological types from the primary tumor, occurred after a considerable length of time, and arose within the field of irradiation. Whether the stimulus for these tumors to grow lies in the genetic code of the patient with Gorlin’s syndrome or whether it is a result of irradiation is as yet unclear. Most likely, it is a combination of the two factors. Patients with Gorlin’s syndrome develop basal cell carcinoma in large numbers. There have been reports of malignancies induced by irradiation of these basal cell carcinomas, and their current therapy does not include therapeutic irradiation. 14,20 Between 5% and 20% of patients with Gorlin’s syndrome will suffer from a medulloblastoma. 4 In past years this was treated with surgical excision and irradiation. Current strategy increasingly favors chemotherapy because of the deleterious effects of irradiation on the developing CNS and the demonstrated increase in survival with chemotherapy. 19 In light of this propensity to grow more tumors in the field of irradiation, it would seem prudent to minimize the radiation dosage when possible in the Gorlin’s syndrome population with medulloblastoma. This may prove difficult in light of the previously mentioned delay in making the diagnosis of Gorlin’s syndrome in the infant with medulloblastoma. Fortunately, the trend is toward the substitution of chemotherapy for at least some of the radiation dose in younger patients.

We believe that this case of Gorlin’s syndrome is noteworthy for a number of reasons. The patient has the largest variety of primary tumors of the CNS and head and neck thus far reported. This is the first report of a patient with Gorlin’s syndrome and an intracranial schwannoma or pleomorphic liposarcoma. Schwannomas are rarely associated with irradiation.

References


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