Nevoid basal cell carcinoma syndrome and fetal rhabdomyoma: A case study

Joseph Watson, DO; Kalpana Depasquale, DO; Mahmoud Ghaderi, DO; Seth Zwillenberg, MD

Abstract
Fetal rhabdomyoma is not generally considered part of nevoid basal cell carcinoma syndrome. However, a review of the literature revealed five patients with this syndrome who also had fetal rhabdomyomas in various locations. We report the first patient with nevoid basal cell carcinoma syndrome and a fetal rhabdomyoma of the tongue. We recommend that embryonal rhabdomyosarcoma be ruled out to avoid overly aggressive treatment of these patients.

Introduction
Extracardiac rhabdomyomas are rare, benign tumors that show striated muscle differentiation. They are distinct from cardiac rhabdomyomas, which are hamartomatous proliferations often associated with tuberous sclerosis. Extracardiac rhabdomyomas can be divided into three groups: fetal, adult, and genital. Fetal rhabdomyomas (FR) are very rare tumors that primarily affect infants and children. They occur principally in the soft tissue or mucosa of the head and neck, although more distal sites have been reported. Histologically verified FR of the tongue has also been reported. However, no one has reported an FR of the tongue in a patient with nevoid basal cell carcinoma syndrome (NBCCS). First characterized by Gorlin and Goltz in 1960, the syndrome is an autosomal-dominant disorder characterized by the occurrence of numerous basal cell carcinomas in childhood, keratocysts of the jaw, ectopic calcifications, palmar and plantar pits, various other neoplasms, and other stigmata of maldevelopment. We present the first patient with NBCCS and an FR of the tongue.

Case report
At birth, a term, male infant was noted to have multiple congenital abnormalities, including cleft lip and palate and a mass on the left side of his tongue (figure 1). The mass appeared to fit into the defect in the hard palate. The infant was unable to suck and was, therefore, placed on orogastric tube feedings. Magnetic resonance imaging (MRI) of the head and neck showed a 2 × 2 × 3-cm lobulated mass within the superior, anterior aspect of the tongue (figure 2). The mass was isointense to the tongue on T1-weighted images and hyperintense on T2-weighted images. We suspected that the patient had inherited NBCCS from his father, which was later confirmed by chromosomal analysis.

The infant exhibited the following manifestations of NBCCS: broad nasal bridge, bifid ribs, palmar and plantar pits, hypertelorism, iris coloboma, macrocephaly, and cleft lip and palate. The patient was taken to the operating room for excisional biopsy of the tongue mass. The mass was well demarcated and superficial, and did not show deep invasion of the intrinsic musculature of the tongue. It was easily removed using an electrocautery device, and the defect was closed with interrupted absorbable sutures (figure 3). Permanent sections were consistent with fetal rhabdomyoma, and immunohistochemical evaluation revealed that the markers desmin, muscle-specific actin, and myogenin were present. The patient did well postoperatively and was started on oral feeds via a cleft palate nipple on postoperative day 2.

Discussion
NBCCS is also known as Gorlin-Goltz syndrome, Gorlin’s syndrome, and basal cell nevus syndrome. Its initial description in 1960 by Gorlin and Goltz included the classic features of basal cell carcinoma, odontogenic keratocysts, and bifid ribs. Since then, much more has been recognized about the syndrome. It has autosomal-dominant inheritance with complete penetrance and variable expressivity. The syndrome’s gene has been mapped to chromosome 9q23.1-q31, a tumor-suppressor gene. Approximately 35 to 50% of cases represent new mutations in this gene.

Patients with NBCCS often have frontal bossing and a
broad nasal bridge. However, true hypertelorism is seen in only 5% of patients. Basal cell carcinomas most often proliferate between puberty and 35 years of age. They vary in number from a few to literally thousands and most often involve the face, back, and chest. Only after puberty do the lesions become invasive. Multiple odontogenic keratocysts of both the maxilla and mandible appear after the seventh year of life. Sixty-five to 80% percent of patients have palmar and plantar pits. Other common abnormalities include ectopic calcifications of the falx cerebri, tentorium cerebelli, and diaphragma sellae, and rib abnormalities, such as bifid, fused, or hypoplastic ribs.

Less common abnormalities include various ocular problems, such as congenital cataracts and colobomas. Cleft lip and palate have an estimated frequency of about 5%. Other neoplasms found less commonly in NBCCS include medulloblastoma, meningioma, cardiac fibroma, and ovarian fibroma.

Extracardiac rhabdomyomas are extremely rare tumors comprising less than 2% of all neoplasms showing striated muscle differentiation. The three commonly recognized subtypes (fetal, adult, and genital) are morphologically distinct. Another ill-defined morphologic variant characterized by prominent neural involvement similar to a neuromuscular choristoma has also been described. The fetal subtype is predominantly found in the head and neck regions, with the postauricular area the most common site. Other reported locations include the face, tongue, orbit, nasopharynx, parotid gland, larynx, parapharyngeal space, posterior mediastinum, and retroperitoneum. FR is benign and tends to be a well-demarcated, unencapsulated, slow-growing, solitary mass. The majority of FRs occur in children; however, adults are frequently affected, as well.

Histologically, two related types of FR can be distinguished: myxoid, or classic, and cellular, or intermediate. As seen in our patient, tumors of the cellular variant consist of haphazardly arranged bundles or elongated spindle cells with very little stroma (figure 4). Characteristically, mild nuclear pleomorphism is seen. The cells are relatively immature and not always readily recognizable as skeletal muscle. However, cross-striations can sometimes be demonstrated, and round eosinophilic cells that

Figure 1. The mass of the fetal rhabdomyoma in our case involved the anterior two-thirds of the tongue.

Figure 2. T1-weighted coronal magnetic resonance image shows the tongue mass and cleft palate defect.

Figure 3. Postexcision image shows the closed defect.
are recognizable as myoblasts are scattered throughout the tumor. The skeletal muscle origin of the myxoid type is readily apparent. Many of the well-differentiated muscle cells closely resemble mature, non-neoplastic skeletal muscle cells. They are haphazardly arranged and are interspersed with round or oval cells in a myxoid to fibromyxoid stroma. Immuno-histochemical evaluation of muscle-specific proteins is important in the diagnosis of FR. Desmin and muscle actin markers are consistently present in many of the tumor cells, including cells that appear undifferentiated. Myogenin is also present but is restricted to more differentiated myoblasts.

The main differential is with well-differentiated embryonal rhabdomyosarcoma. Unlike rhabdomyosarcoma, which has infiltrative margins and invades normal tissue, FR is relatively well-circumscribed and does not invade or destroy adjacent soft tissue or bone. Rhabdomyosarcoma frequently has areas of necrosis, mitotic figures, and nuclear atypia. FR rarely has necrotic areas and mitotic figures, and nuclear atypia is absent. Distinguishing FR from rhabdomyosarcoma is of utmost importance because failure to recognize this tumor could lead to unnecessary, aggressive treatment. FR is a benign condition, and surgical excision is the treatment of choice.

A review of the literature found five reported cases of FR and NBCCS. Schweisguth et al reported a preterminal FR in an infant with NBCCS. The patients reported by Dahl et al and Klijianienko et al each had multiple FRs. In 1992, DiSanto et al reported a 6-year-old with a large mass in the posterior mediastinum and retroperitoneum; and in 1996, Hardisson et al reported a patient with a retroperitoneal FR. The patient with multiple masses reported by Klijianienko et al was the only patient with a FR of the head and neck region. The first mass was excised from the preterminal and lower neck at age 1. This was followed by the excision of FR from the mandibular angle and parapharyngeal space at ages 7 and 26, respectively.

In summary, it is very rare to find an FR in a patient with NBCCS. Only five cases have been reported in the literature, and only one of these patients had an FR in the head and neck region. Our patient with NBCCS is the first reported to have an FR of the tongue. To avoid overly aggressive treatment and ensure that proper treatment is provided for patients with NBCCS, embryonal rhabdomyosarcoma must be ruled out.

References