Title: Pediatric Basal Cell Carcinoma

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Case Presentation: Oct 19, 2011 – previously healthy 6-year-old girl referred for molluscum contagiosum affecting bilateral upper and lower eyelids, face, neck and chest. She has had a diagnosis of molluscum contagiosum since 2009. She was otherwise healthy. No other past medical history, past ocular history, or medications. She is allergic to amoxicillin (rash). She was born via elective caesarean section, chosen due to breech presentation, at 37.5 weeks at 6lb 13oz. There is no significant family history.

On exam: External – multiple flesh-colored papules on face, neck and chest measuring approximately 1-4mm in diameter

Visual acuity - 20/20 OD, 20/20-1 OS

Stereo – Titmus +fly, 3/3, 9/9

Extraocular movements – full

Orthoptic exam – orthophoric at distance and near

Pupils – equal and reactive, no afferent pupillary defect

Anterior segment – within normal limits OU

Dilated fundoscopic exam – within normal limits OU

Cycloplegic refraction - +1.00D OU

March 1, 2012 – surgical curettage of all visible lesions by #11 blade and scissors

Jan 10, 2013 – re-referral of now 7-year-old girl with again multiple molluscum contagiosum lesions of the face. She was started on cimetidine, referred to Dermatology, and surgical excision was planned.

Feb 5, 2013 – seen by dermatologist, who documented 20-30 brownish and yellowish papules in the infraorbital area; agreed with plan for surgical excision to rule out milia cysts vs. syringomas.

Feb 28, 2013 – excision of multiple lesions on bilateral upper and lower lids, 2 specimens sent for pathology

Diagnosis: "Proliferation of trichoblastic epithelium, favor basal cell carcinoma."

Microscopic Description: "The biopsy consists of a small fragment of tissue which contains a proliferation of trichoblastic epithelium with a peripheral palisade. This epithelium is present in a single solid nodule as well as several smaller nests. An immunohistochemical stain for Merkel cells (CK20) shows no evidence of these cells within the trichoblastic epithelium."

Pathologist Comment: "Proliferations of trichoblastic epithelium may represent either a basal cell carcinoma or a trichoepithelioma/trichoblastoma. These can be extremely difficult and at times

impossible to distinguish from one another. This child has one of these two entities and all things considered, a basal cell carcinoma is favored keeping the above limitation in mind. If this is a basal cell carcinoma, then it is possible that this child may have the basal cell nevus syndrome (Gorlin syndrome). It is assumed that xeroderma pigmentosum is not a consideration clinically. The amount of tissue present for assessment is small and the changes are not diagnostic. Repeat biopsies are suggested."

Post-Operative Course: The patient was referred to Dermatology, Oncology, and Genetics. Multiple biopsies of her lesions came back positive for basal cell carcinoma. Genetic testing for known mutations causing basal cell nevus syndrome in the PTCH1 and SUFU genes was negative. Currently no formal genetic diagnosis has been made. Photodynamic therapy (PDT) has been used to treat her lesions, with surgical excision reserved for lesions not amenable to PDT.

Discussion: In 1960, Gorlin and Goltz described the triad of multiple basal cell carcinomas, odontogenic keratocysts, and bifid ribs characteristic of Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome.1

The estimated prevalence is 1 in 57,000 to 256,000 individuals. There is equal sex predilection and it is transmitted in an autosomal dominant fashion with variable expression.1-2 Mutations in PTCH1, a tumor suppressor gene located in 9q22, 3-q31, has been linked to this disease.2 When basal cell carcinomas are found in young patients and on areas of the body not frequently exposed to ultraviolet light, basal cell carcinoma syndrome should be suspected and a thorough family history should be performed with referral to dermatology and appropriate tests for conditions associated with this syndrome.1,2

Treatment options for the basal cell carcinomas depend on the histologic type, location, and size of the lesion. As the lesions can be widely distributed and variable in size, the number of excisions/Mohs resections may be extensive and place a heavy burden on the patient. Topical options for localized disease include 5-fluorouracil (5-FU) and imiquimod.2 Currently, vismodegib, a first-in-class Hedgehog-pathway inhibitor, is approved for use in adults with advanced basal cell carcinoma and shows promising results.3 The phase 2 registration study, ERIVANCE BCC, showed that 43% of patients with locally advanced basal cell carcinoma and 30% of patients with metastatic disease showed improvement in their disease burden when assessed by independent reviewers.4 The 30-month results from ERIVANCE BCC found consistent results in treatment activity and safety of

vismodegib treatment.5 This study observed a median duration of response of 26 months in patients with locally advanced basal cell carcinoma.5

Discussion with multiple Tumor Boards at the citywide and provincial level determined the following recommendations in this rare childhood presentation:

- Minimal systemic investigations regarding basal cell carcinomas needed (just a Panorex film to look for dental cysts and a chest x-ray to look for bifid rib); chance of metastatic spread to other organs appears to be very small.
- No chemotherapy or other agents indicated at this time. Vismodegib has been used in adults but not reported for use in children. Vismodegib should only be used if there is a need to regress lesions that have grown too large for resection.
- Surgical excision of the lesions is the primary therapy.

- Further genetic testing, including whole exome sequencing, may be useful as a research level to identify an underlying genetic mutation.

With this case, we hope to share the treatment approach and results obtained in a relatively rare syndrome.

References

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