Costello syndrome: A proposal for head and neck cancer screening

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ABSTRACT

Costello syndrome is a rare congenital disorder first described in 1971. It is characterized by prenatal polyhydramnios, severe postnatal failure to thrive, coarse facial features, non-progressive cardiomyopathy, loose skin, and developmental delay. Among the features of costello syndrome, the most characteristic is the predisposition to benign and malignant tumors. These include rhabdomyosarcoma, neuroblastoma, and bladder transitional cell carcinomas. Rhabdomyosarcoma, which accounts for 60% of the malignant tumors seen in costello syndrome, is reported to originate most commonly from the abdomen. Here, we present a case of a 2 year old male with features of costello syndrome presenting with nasopharyngeal rhabdomyosarcoma.

Given the propensity for multiple malignancies, tumor screening is crucial in costello patients. Therefore, in addition to the current tumor surveillance protocol, we believe that head and neck imaging should be included to screen for nasopharyngeal rhabdomyosarcoma.

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INTRODUCTION

Costello syndrome is a rare congenital syndrome first described in 1971. Since then, approximately 115 cases have been reported in the literature.[1] The syndrome presents with failure to thrive, developmental delay and unique facial characteristics. These include macrocephaly, downward slanted palpebral fissures, curly hair, low set ears, depressed nasal bridge, large tongue and hypertrophied gingiva.[2] Overall, these phenotypic features give rise to the characteristic coarse facial appearance.

Costello syndrome also affects multiple organ systems including musculoskeletal, skin and cardiac. These manifest as joint hypermobility, tightness of achilles tendon, redundant skin of neck, hands and feet, and cardiac abnormalities such as dysrhythmias and hypertrophic cardiomyopathy.[2]

The most intriguing feature of costello syndrome is the predisposition to certain malignancies. Of these, rhabdomyosarcoma is the most common. Rhabdomyosarcomas in costello patients most commonly involve the abdomen, pelvis and urogenital areas.[3] We describe, to our knowledge, the first reported case of nasopharyngeal rhabdomyosarcoma in a costello patient.

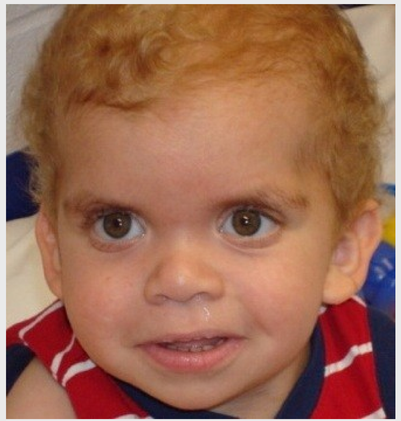

Figure 1: Picture of our 2-year old male patient illustrating the coarse facial features characteristic of costello syndrome. Notice the relative macrocephaly, curly yet sparse hair, strabismus, downward slanted palpebral fissures, depressed nasal bridge and low-set pinnae. Written permission for publication of this photograph was obtained.

RESULTS

A 2-year old full-term male was born with prenatal polyhydramnios, macrosomia, and coarse facial features (Figure 1). Given the patient's phenotypic features, there was suspicion of a congenital syndrome and workup revealed the diagnosis of costello syndrome at 6 months of age. Over time, patient was noted to have failure to thrive and respiratory distress initiating an evaluation by otolaryngology. Direct laryngoscopy and bronchoscopy at the time revealed tracheal papillomas and subglottic stenosis requiring balloon dilations.

At age one, patient was re-evaluated for increased work of breathing. Clinical examination demonstrated an obstruction in the nasopharynx. He underwent nasal endoscopy to evaluate the adenoids and to rule out an obstructive malignant neoplasm. Nasal endoscopy revealed a necrotic mass (Figure 2) of the right nasopharynx obstructing the right choana. Histologic examination of the biopsy specimen revealed embryonal type rhabdomyosarcoma.

The tumor stage at diagnosis was T1N0M0, and the patient received and completed chemotherapy followed by radiation. To date, our patient has been without evidence of clinical recurrence.

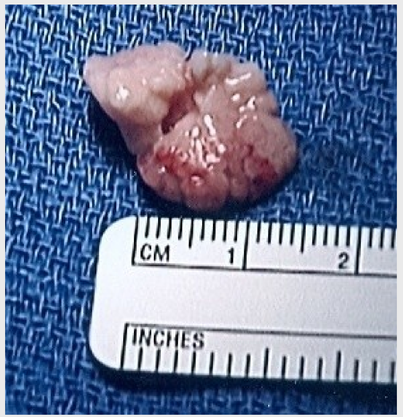

Figure 2: Necrotic nasopharyngeal mass

DISCUSSION

Costello syndrome is a rare congenital disorder. The genetic mutation that causes costello syndrome was first discovered in 2005. This gene was identified as HRAS, an isoform of the RAS family of genes, which are protooncogenes involved in cellular signal transduction. Costello syndrome is caused by de-novo point mutations in HRAS, resulting in uncontrolled cell growth and proliferation.[4] Although in malignant tumors of the general population, HRAS mutations are only identified in tumor cells, in costello syndrome every single cell of the individual has the identical HRAS mutation accounting for the tumor predisposition in these patients.[4]

The predisposition to tumors in costello syndrome includes both benign (papillomas being the most common) and malignant tumors. The malignant tumors seen in costello syndrome include rhabdomyosarcoma, neuroblastoma, and transitional cell carcinoma of the bladder.[3] The risk of developing these malignant tumors is reported to be 10-15%, with rhabdomyosarcoma being the most common, accounting for approximately 60%.[4]

To date, eleven cases of rhabdomyosarcoma associated with costello syndrome have been reported in the literature. Eight have originated in the abdomen, pelvis or urogenital regions, one in the foot, one in the orbit and one in the parameningeal region.[1] To our knowledge, this is the first reported case of nasopharyngeal rhabdomyosarcoma.

Given the propensity for multiple malignancies, tumor screening is crucial in costello patients. Since the most common sites of rhabdomyosarcoma are the abdomen and pelvis, the current screening includes abdominal and pelvic ultrasounds every 3-6 months from birth until 8-10 years of age.[2] However, there has been no proposed head and neck cancer screening in costello patients.

Rhabdomyosarcoma is a chemo-radiosensitive malignancy, and therefore, early diagnosis with head and neck screening is crucial. We recommend adding head and neck MRIs every 6 months starting at the time of diagnosis to the current screening protocol. We also encourage tympanometry every 6 months in order to detect middle ear effusion (missed on physical examination), which would raise suspicion for a nasopharyngeal mass.

CONCLUSIONS

In conclusion, costello patients are predisposed to developing head and neck rhabdomyosarcomas, and with our recommended screening protocol, we can detect and initiate treatment sooner and therefore, improve survival.

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