CASE REPORT

A concurrent episode of two neoplasms in a toddler-age child

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ABSTRACT

Childhood neoplasms are relatively rare and represent only about 1- 2% of the total incidence of neoplasms in United States. Concurrent episode of childhood cancer is uncommon and usually related to a cancer genetic syndrome. Li Fraumeni Syndrome refers to an autosomal dominant condition that is manifested by the development of certain cancers in early childhood and an increased lifetime risk for developing multiple primary cancers including sarcoma, breast cancer, leukemia, bone cancer, and others. We report a case of a 21-month-old girl who was found to have orbital embryonal rhabdomyosarcoma and adrenocortical tumor concurrently.

Key words: Adrenocortical tumor, Li Fraumeni syndrome, orbital rhabdomyosarcoma

INTRODUCTION

Geneticists estimate that 5-10% of all cancers diagnosed in the pediatric age range occur in children born with a genetic mutation that directly increases their lifetime risk for neoplasia.[1] Importantly, identifying those mutations might help in implementing preventive measures in the affected patients.

LFS is a rare autosomal dominant hereditary cancer syndrome that results from germline mutations of the tumor protein gene (TP53) encoding a transcriptional factor able to regulate cell cycle and apoptosis when DNA damage occurs.[2]

CASE REPORT

A 21-month-old Hispanic girl presented to the emergency room with 10 days history of progressing left periorbital swelling. She was initially treated with antibiotics without improvement. The patient did not have any fever, vomiting, cough, eye discharge or sick contact.

On examination, she had swelling with proptosis at the left eye without erythema. There was a localized mass that was palpable, restricting the movement of the left eye. Incidentally, the patient found to have pubic hair Tanner stage III but no breast buds or clitoral hypertrophy. The remaining physical exam was unremarkable. There was a significant past medical history of a third-line family member with a diagnosis of uterine cancer at the age of 40 years and a second-line family member with a history of recurrent thyroid nodules.

Initial laboratory work up including complete blood count, basic metabolic panel, and liver function test were all normal. Computed tomography (CT) scan of the head revealed a single left orbital mass that has retro-orbital and postseptal extension. This mass measured 2.5 × 3.5 × 1 cm and was not associated with focal bone erosion or invasion to the optic nerve [Figure 1].

Because the patient had evidence of precocious puberty, the differential diagnosis at this point was broadened to include rhabdomyosarcoma, neuroblastoma, germ cell tumor or concurrent episode of childhood neoplasms. The patient subsequently underwent further evaluation with whole body positron emission tomography (PET) scan that showed another mass (6 × 6 cm) in the left suprarenal area [Figure 2]. Bone scan, bone marrow biopsy, and urine catecholamine were all negative.

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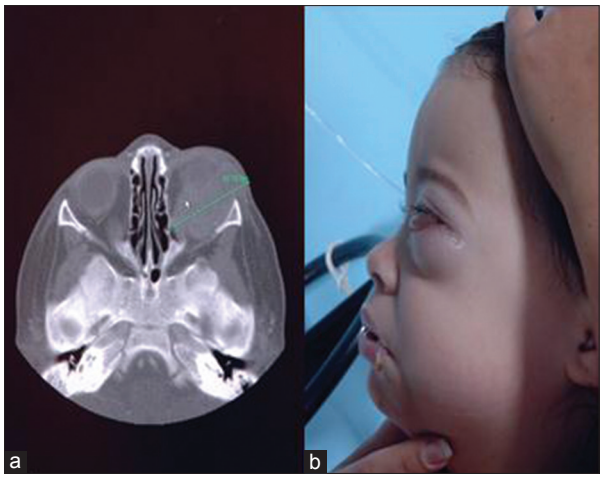

Figure 1: (a) The orbital Computed Tomography scan showing left retro-orbital mass. (b) Left eye proptosis at presentation (verbal permission was taken from the guardians)

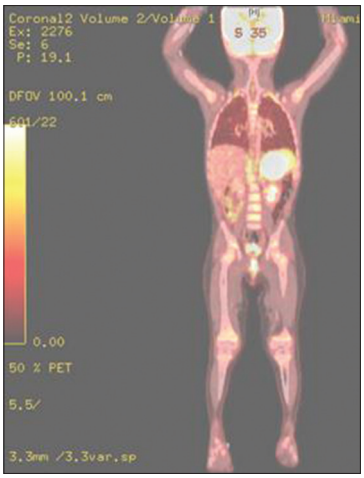

Figure 2: Positron Emission Tomography scan revealing a PET avid mass in the left suprarenal area.

Due to concern of adrenarche, the patient had endocrine work up that showed advanced bone age with significantly elevated dehydroepiandrosterone sulfate (DHEAS).

The previous finding raised the possibility that those two masses might be two different tumor entities. She underwent a subtotal surgical resection of the left retro-orbital lesion (about 75% of the tumor burden) and total surgical resection of the adrenal mass.

The pathologic evaluation of those masses revealed embryonal rhabdomyosarcoma from the orbital mass and a benign adrenocortical tumor (ACT) from the adrenal mass.

The diagnosis of LFS was suspected based on having two tumors that belong to LFS tumors spectrum that occurred before the age of 46 years. Genetic testing for TP53 mutation from peripheral blood revealed heterozygous change on the nucleotide-coding sequence c. 818G >A, which is a missense mutation in TP53 gene.

DISCUSSION

LFS was first described by Frederick Li and Joseph Fraumeni in 1969, which refers to an autosomal dominant condition that is manifested by the development of certain cancers in early childhood and an increased lifetime risk for developing multiple primary cancers including sarcoma, breast cancer, leukemia, bone cancer, brain tumors, lung cancer, laryngeal cancer and adrenal gland tumors. The majority of LFS cases are caused by TP53 germline mutation.[3]

An updated schema outlining clinical characteristics for TP53 testing (2009 Chompret Criteria for Germline TP53 Mutation Screening) has recently been issued[4,5]:

- Proband with tumor belonging to LFS tumor spectrum (e.g., soft tissue sarcoma, osteosarcoma, brain tumor, premenopausal breast cancer, adrenocortical carcinoma, leukemia, and lung bronchoalveolar cancer) before the age of 46 years and at least one first-degree or second-degree relative with LFS tumor (except breast cancer if proband has breast cancer) before the age of 56 years or with multiple tumors, or
- Proband with multiple tumors (except multiple breast tumors), two of which belong to LFS tumor spectrum and first of which occurred before age 46 years, or
- Patient with adrenocortical carcinoma or choroid plexus tumor, irrespective of the family history.

The surveillance screen of TP53 mutation carrier has proven to improve the overall survival by early detection of the new neoplasms. Villani *et al.*,[6] implemented a clinical surveillance protocol using frequent biochemical and imaging studies for asymptomatic TP53 mutation carriers. This study showed significant increase in the overall survival and the early detection of the new neoplasms in the surveillance group (*n*: 18) compared with the non-surveillance group (*n*: 15).

ACTs are rare in children and adolescents. The surveillance epidemiology end results data indicate about 14 new patient cases per year in individuals younger than age 20 years in the United States;[7] Because of the rarity of pediatric ACTs, no single pediatric oncology center has acquired extensive experience with this tumor.

Lefevre *et al.*,[8] analyzed the clinical characteristics and treatment outcomes of 42 children treated in several French hospitals over a 22-year period. They found a median age of 3.9 years, a predominance of girls (for unclear reason), presenting signs of virilization in more than 90% of patients,

and long-term survival of approximately 50%; tumor size was the most important prognostic factor. The prevalence of LFS or other associated constitutional genetic syndromes was not reported.

Because of the strong association between constitutional p53 mutations and a diagnosis of ACTs at a young age, genetic testing of these patients for p53 status should be considered.

Rhabdomyosarcoma has an annual incidence of 4.3 cases per million children[9]; the orbit is the primary site in approximately 10% of these tumors. From the ophthalmologist's standpoint, however, rhabdomyosarcoma is the most common malignant orbital tumor of childhood.

Based on data from the Intergroup Rhabdomyosarcoma Study, patients treated for embryonal tumors have 5-year survival rates of 87%, and those with primary orbital rhabdomyosarcoma approach 100% survival.[10,11] The treatment includes surgical resection, chemotherapy, and local control with radiation therapy.

Germline Tp53 mutations are found in approximately 23% of patients with rhabdomyosarcoma diagnosed at younger than 3 years.[12]

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