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Case Report

Giant Juvenile Fibroadenoma and Cowden Syndrome: A Case Report of the Surgical Management in Adolescence

Kelsey Baran[1], Heather Grant[2], Jessica Dahle[2], Colby Cayton[3], Benjamin Schalet[2] and Holly Mason[2]*

[1]*Department of Surgery, Berkshire Medical Center, USA*

[2]*Department of Surgery, University of Massachusetts Medical School-Baystate, USA*

[3]*University of Massachusetts Medical School-Baystate, USA*

Abstract

Giant Juvenile Fibroadenoma (GJF) comprises 1% to 8% of breast lesions in the adolescent population. Cowden Syndrome is a genetic condition that carries an increased lifetime risk of breast, thyroid and uterine cancer. We present a 10 year-old African-American female with rapidly enlarging bilateral breast masses. Genetic testing revealed a PTEN variant of undetermined significance. She was diagnosed with ductal carcinoma in situ at age 14 and treated with bilateral mastectomy with reconstruction. This case highlights the challenge of managing GJF in adolescents.

Keywords: Giant juvenile fibroadenoma; Cowden syndrome; Uterine cancer; Beckwith-wiedemann syndrome

Introduction

Cowden Syndrome (CS) is an autosomal dominant hereditary condition affecting 1 in 200,000 people characterized by germline mutations in tumor suppressor gene PTEN [1]. Some of the common features of CS include benign tissue growth, macrocephaly, developmental delay and increased risk of breast, thyroid and uterine cancers [2]. Women with CS have a 50% lifetime risk of developing breast cancer with recent reports suggesting a lifetime risk as high as 85% [3,4]. Current guidelines for screening have only been described in the adult population.

In this case, we present a 10 year-old female with multiple giant juvenile fibroadenomas who was diagnosed with PTEN Variant of Undetermined Significance (VUS) and underwent bilateral mastectomy after a diagnosis of Ductal Carcinoma *In Situ* (DCIS) discovered incidentally.

Case Presentation

The patient is a 10-year-old, African-American female who presented with a rapidly enlarging bilateral breast masses. Her pertinent history includes macrocephaly, autism, and stage IV Wilms tumor. Her family history was significant for a paternal aunt with juvenile fibroadenomas.

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***Corresponding author:** Kelsey Baran, Department of Surgery, Berkshire Medical Center, Pittsfield, MA, USA, Tel: +1-651-231-5885; E-mail: kbaran@bhs1.org

She underwent five surgical excisions over four years, including excision of a 10 cm fibroadenoma at the first surgery. Each follow up visit revealed new breast masses. Pathology from all excised masses revealed juvenile fibroadenoma. She was referred for genetic testing. Testing for Beckwith-Wiedemann Syndrome (BWS) was negative. PTEN testing revealed a Variant of Uncertain Significance (VUS), c.274G>T (p.Asp92Tyr). On her sixth surgical excision, she had11 masses removed from the right breast and 4 removed from the left breast. Pathology demonstrated a 15 mm focus of DCIS with positive margins. The remaining masses were benign but multiple areas of bilateral atypical ductal hyperplasia were identified.

The patient was treated with bilateral mastectomy with reconstruction. The genetic counselor placed her in a PTEN surveillance program due to the diagnosis of DCIS in addition to her other PTEN-associated diagnoses. She has since done well.

Discussion

A fibroadenoma is a benign breast tumor that often occurs in young women and arises from stromal and epithelial connective tissue cells. The giant juvenile fibroadenoma is a rare variant affecting adolescents, defined by a size greater than 5 cm, weight greater than 500 g, or replacement of at least 80% of the breast [5]. Giant juvenile fibroadenoma comprise 1% to 8% of breast lesions in the adolescent population, 0.5% to 2% of all fibroadenomas and are more common in African American population [6]. These tumors are associated with rapid growth and marked breast asymmetry and often require surgical management.

Fibroadenomas are associated with multiple genetic syndromes including CS [6]. CS is a rare, multisystem disease with an increased risk of breast, thyroid, and endometrial cancer [2]. It is an autosomal dominant condition with a loss-of-function germline mutation in the PTEN gene located on chromosome 10 [7,8]. The International Cowden Syndrome Consortium developed a scoring system that generates a probability of finding a PTEN pathogenic variant and is included in NCCN guidelines [9]. In children, macrocephaly and the

presence of autism or developmental delay, dermatologic features, vascular features or gastrointestinal polyps should prompt evaluation by a genetic counselor [9].

Benign breast lesions are common in CS affecting up to 75% of women; breast cancer is the most common malignancy affecting 30% to 50% in this population [2-4]. NCCN guidelines recommend monthly self-breast exams at age 18, clinical exam every 6-12 months starting at age 25, and annual mammography or MRI beginning at age 30 [9,10]. There are no current recommendations for breast cancer screening in women diagnosed with CS before the age of 18 or risk reduction measures. Surgical recommendations for women diagnosed with CS should be based on family history, residual breast cancer risk with age and life expectancy [11].

This case highlights the complexity of managing multiple benign breast lesions in an adolescent with a clinical history consistent with a PTEN mutation. Initially managed with excisional biopsies, she required frequent medical appointments and surgeries. After undergoing bilateral mastectomy with reconstruction, she has had improvement in her quality of life and reduced risk of future malignancy.

Conclusion

This case is unique in the literature and highlights the need for surveillance in young patients with multiple enlarging breast masses. We recommend treatment strategies on a case by case basis that consider genetic testing, screening exams prior to age 18, and an open dialogue about the risks and benefits of mastectomy.

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