Case Report

Ovarian Torsion in an Adolescent with Beckwith-Wiedemann Syndrome and Unilateral Tubo-ovarian Hyperplasia

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A B S T R A C T

Background: Beckwith-Wiedemann syndrome (BWS) is the most common pediatric overgrowth syndrome. BWS has a broad phenotypic presentation along with an increased propensity to develop various embryonal tumors. There are very few reported cases of gonadal hyperplasia in BWS patients in the existing literature.
Case: We describe a 13-year-old girl with BWS who presented with an episode of abdominal pain and was found to have torsion and necrosis of a markedly hyperplastic right ovary and fallopian tube. We present a brief literature review on ovarian hyperplasia in BWS patients for which we used an online search of the databases PubMed, Embase, Ovid Medline, and Cochrane.
Results and Conclusion: Through an extensive literature search, we only found 3 previous reports of ovarian hyperplasia in BWS patients, all in postmortem specimens. Our case highlights a potentially important aspect of visceral organ hyperplasia in patients with BWS that could remain indolent until adolescence and might present as an abrupt-onset abdominopelvic catastrophe.
Key Words: Beckwith-Wiedemann Syndrome (BWS), Tubo-ovarian hyperplasia, Torsion

Introduction

Beckwith-Wiedemann Syndrome (BWS) is a rare syndrome which presents with overgrowth of various parts of the body and an increased propensity to develop certain types of embryonal cancers in childhood, commonly Wilms tumor and hepatoblastoma.[1] The clinical presentation varies widely, ranging from an array of abdominal wall defects like omphalocele and umbilical hernia early in life, to hyperplasia of various other organs of the body as the child grows older. The commonly hyperplastic organs are tongue (macroglossia), limb hyperplasia, and visceromegaly (commonly liver, spleen, kidneys, adrenals, and pancreas). There are very few cases of gonadal hyperplasia reported in the literature in patients with BWS.

Case

Our patient was a 13-year-old Caucasian girl with BWS. She was born at 34 weeks of gestation by Cesarean section because of to pre-eclampsia, with a birth weight of 2485 g. She was noted to have isolated, right-sided hemihypertrophy. She was evaluated by genetics department because of hemihypertrophy and was subsequently diagnosed with BWS resulting from paternal uniparental disomy. Her blood lymphocyte chromosomal analysis showed 46, XX karyotype. BWS testing confirmed abnormal methylation at 11p15 resulting from loss of the maternal allele. She had her first abdominal ultrasound examination and α-fetoprotein (AFP) level checked at 3 months of age. Abdominal ultrasound was normal. AFP was 2085 ng/mL, which was believed to be normal for age (corrected for 6 weeks premature) by the pediatric oncology team. At the age of 12 months, computed tomography imaging of the neck, chest, abdomen, and pelvis was done because of rising AFP level from 50.5 ng/mL to 55 ng/mL within a month's time. This was normal with no evidence of tumor in her liver, kidneys, or adrenals. After then, she was followed-up in the pediatric oncology clinic with every-3-month abdominal ultrasound examination and serum AFP level test until the age of 4 years. Thereafter, screening abdominal ultrasound examinations were done periodically until she turned 8 years. All her laboratory values and ultrasound examinations were unremarkable.

At the age of 13 years, she presented to a local emergency department (ED) with 4 days' history of worsening right lower quadrant abdominal pain and nausea followed by fever of 103°F. The computed tomography scan done at the ED showed a large, 12-cm mass in the right pelvic cavity pushing the other pelvic structures to the left (Fig. 1). The patient was transferred to our center because of concern for neoplastic mass in view of her history of BWS. On arrival to our center, initial lab work was done including the values for various embryonal tumor markers. Initial complete blood count showed white blood cell count of 16.44 × 10^3/μL,

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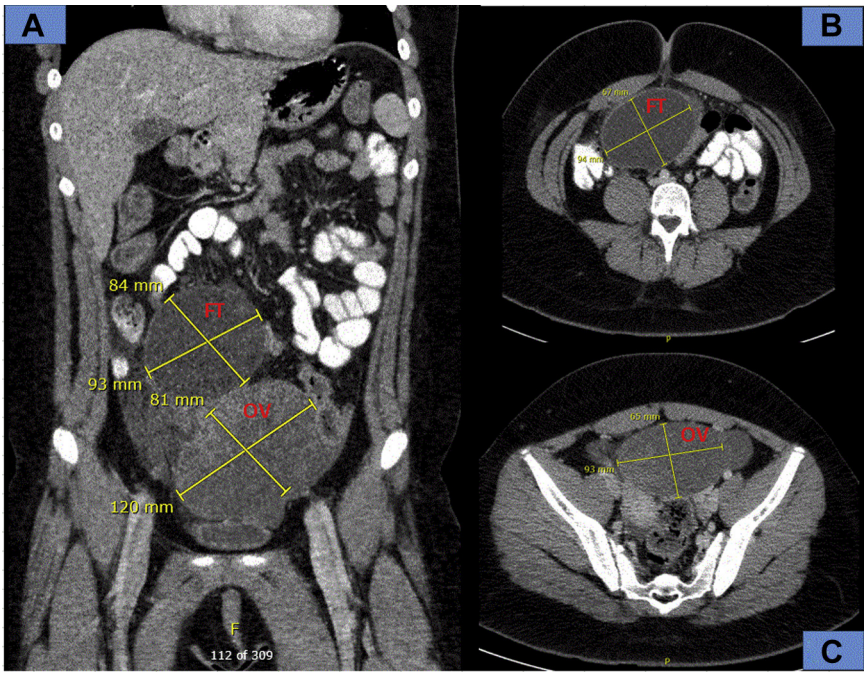

Fig. 1. Computed tomography image of the abdomen and pelvis with contrast showing coronal view on the left (A), and transverse views on the right (B and C). (B) Cut section through the hyperplastic right fallopian tube (FT); and (C) transverse section through the enormously hyperplastic right ovary (OV).

hemoglobin 9.9 g/dL, platelets 296 × 10^3/μL, and absolute neutrophil count of 12.2 × 10^3/μL. Comprehensive metabolic profile including electrolytes, renal function tests, liver function test, lactate dehydrogenase, uric acid, magnesium, and phosphorus were within normal range. Blood culture was sent, and the patient started empiric intravenous antibiotics. Ultrasound of the pelvis was done, which revealed a solid cystic-appearing 12.2 × 9.8 × 5.7 cm right adnexal mass with surrounding free intraperitoneal fluid. No blood flow was identified to the right ovary. The patient was evaluated by the surgical team and was taken to the operating room because of concern for ovarian torsion. Exploratory laparotomy revealed a 12.5 × 9 × 4.3 cm ovarian complex attached to a dilated fallopian tube measuring 14 cm in length and 8 cm in greatest diameter, weighing 715 g (Fig. 2). The left ovary and the fallopian tube were noted to be of normal morphology using visual inspection during the surgery. The specimen was sent for pathological exam. Peritoneal fluid cytology was negative for malignant cells. Blood AFP, human chorionic gonadotropin, inhibins A and B, carcinoembryonic antigen, carcinoma antigen 125, and carcinoma antigen 19-9 were all normal.

The gross morphological examination of the mass revealed the hyperplastic right tubo-ovarian complex with a smooth, purple, dull, necrotic appearance. Surface papillations were absent. The cut surfaces were solid, homogeneous, dull, and hemorrhagic with no viable areas (Fig. 3). Histologic examination showed hyperplastic tubo-ovarian complex with marked vascular ectasia, edema, hemorrhage, fibrinopurulent inflammation, necrosis, and hydrosalpinx. No findings suggestive of neoplastic changes were identified. The patient had an uneventful postoperative course and was discharged home on the second postoperative day.

Summary and Conclusion

We present a 13-year-old girl with BWS who presented to the ED with an acute abdomen and was found to have a severely hyperplastic right tubo-ovarian complex that had undergone torsion and necrosis. We searched the databases

Fig. 2. A gross picture of hyperplastic spherical right ovary (OV) measuring 12.5 × 9 × 4.3 cm attached to a markedly dilated right fallopian tube (FT) measuring 14 cm in length and 8 cm in greatest diameter. The entire specimen weighed 715 g.

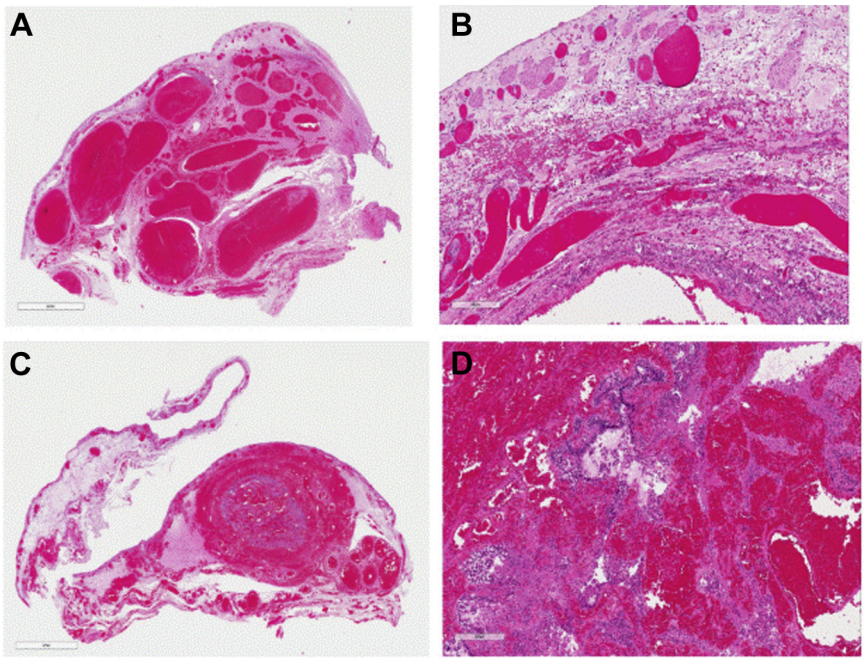

Fig. 3. Microscopic pictures of ovary (A and B) and fallopian tube (C and D) showing marked vascular ectasia, edema, hemorrhage, necrosis, and fibrinopurulent inflammation. The fallopian tube also showed hydrosalpinx. No neoplastic cells were identified.

PubMed, Embase, Ovid Medline, and Cochrane with key search words "Beckwith-Wiedemann syndrome," "Ovarian overgrowth," and "Ovarian hyperplasia" with the aim of identifying all reports describing ovarian hyperplasia/overgrowth in BWS patients. We also selected additional relevant articles listed in the references of the identified articles. Individual reports were reviewed in their entirety to extract characteristics of the patients described. The findings are summarized in this section.

BWS is a rare disorder of growth dysregulation and tumorigenesis, with an estimated incidence of 1 in 13,700 in male and female individuals.[1] However, the incidence could be underestimated because patients with milder phenotypes often go undiagnosed. Genetically, approximately 15% of cases are reported to be inherited in an autosomal dominant pattern with variable penetrance. The rest occur sporadically because of complex genetic and epigenetic alterations on chromosome 11p15.5, most commonly gain of methylation at 1 imprinting control region, imprinting center 1 (H19/IGF2: IG-DMR), or loss of methylation at a second imprinting control region, imprinting center 2 (KCNQ1OT1: TSS-DMR).[2] Overgrowth has been attributed to this complex group of genetic and epigenetic alterations. BWS has a wide and heterogeneous clinical spectrum. Some patients present with the full clinical picture, whereas others have just 1 or 2 phenotypic characteristics. The common presenting features are pre- and postnatal somatic/visceral overgrowth, macrosomia/macroglossia, neonatal hypoglycemia, omphalocele/umbilical hernia/diastasis recti, and anterior linear ear lobe creases/posterior helical ear pits. The common hyperplastic visceral organs reported in the literature are liver, spleen, kidneys, adrenal glands, and pancreas. In addition, children with BWS have an increased propensity to develop embryonal tumors with reported risk ranging from 4% to 21% on the basis of genetic and epigenetic causes of BWS.[3] The most common tumors reported are Wilms tumor and hepatoblastoma. Adrenocortical carcinoma, neuroblastoma, and rhabdomyosarcoma are other less commonly reported malignancies in patients with BWS.[4] The occurrence of benign overgrowth and the malignancies plateaus by 8 years of age.

Ovarian hyperplasia in BWS patients is sparsely reported in the existing literature. In this case report, we present a case of an adolescent girl with BWS, who presented in early puberty with an enormously hyperplastic ovary leading to torsion and necrosis of the entire ovary. She previously had negative screening for AFP and serial abdominal ultrasound examinations. There is a possibility that the enlarged tuboovarian complex could be due to spontaneous torsion. However, on the basis of the pathology findings in the background of BWS, it was believed most likely to be the result of a largely hyperplastic ovary, which induced torsion and necrosis causing severe pain and reactive fever. Of note, the contralateral ovary and fallopian tube were noted to be normal according to visual inspection by the surgical team.

In our literature search, we found just 3 reports of ovarian hyperplasia, all of which were reported in postmortem findings in prepubertal girls. J.B. Beckwith, an American pathologist, initially presented 3 postmortem cases with macroglossia, omphalocele, cytomegaly of the fetal adrenal cortex, renal medullary dysplasia, and visceromegaly before the Western Society for Pediatric Research in Los Angeles in 1963.[5] His original series described a female patient with bilateral enlarged ovaries to twice their normal size with normal follicular activity and large masses of Leydig cells present in the hilus. Subsequently, Irving described a case series of 11 patients (5 male and 6 female) admitted to Liverpool Neonatal Surgical Center with

exophthalmos and macroglossia.[6] Two female patients brought to autopsy were found to have bicornuate uterus. One of them was found to have long, attenuated ovaries on autopsy, which showed numerous follicular cysts up to 3 mm in diameter with increased stromal bulk. In 1976, Kosseff et al described a 1-year-old female BWS patient who died of cardiopulmonary arrest after a protracted course of diarrhea and urinary tract infection.[7] At autopsy, she was found to have multiple visceral hyperplasia along with streak-like, elongated ovaries filled with multiple cortical cysts.

To our knowledge, there are no previous reports of ovarian hyperplasia presenting during adolescence with torsion. Our case highlights a potentially important aspect of visceral organ hyperplasia in patients with BWS that could remain indolent until presenting in an emergency fashion such as our patient. Ovarian torsion should be considered an important potential cause of abrupt-onset abdominopelvic pain in female BWS patients.

Consent

Appropriate consent was obtained from parents before preparation of this report. All patient identifying information has been removed.

References

1. Weksberg R, Shuman C, Beckwith JB: Beckwith-Wiedemann syndrome. Eur J Hum Genet 2010; 137:12
2. Choufani S, Shuman C, Weksberg R: Beckwith-Wiedemann syndrome. Am J Med Genet C Semin Med Genet 2010; 154C:343
3. Rump P, Zeegers MP, van Essen AJ: Tumor risk in Beckwith-Wiedemann syndrome: a review and meta-analysis. Am J Med Genet A 2005; 136:95
4. Lapunzina P: Risk of tumorigenesis in overgrowth syndromes: a comprehensive review. Am J Med Genet C Semin Med Genet 2005; 137C:53
5. Beckwith JB: Macroglossia, omphalocele, adrenal cytomegaly, gigantism, and hyperplastic visceromegaly. Birth Defects 1969; 5:188
6. Irving IM: Exomphalos with macroglossia: a study of eleven cases. J Pediatr Surg 1967; 2:499
7. Kosseff AL, Herrmann J, Gilbert EF, et al: Studies of malformation syndromes of man XXIX: the Wiedemann-Beckwith syndrome. Clinical, genetic and pathogenetic studies of 12 cases. Eur J Pediatr 1976; 123:139