—Case Reports—

Paraovarian Cyst Torsion in a Patient with Rubinstein-Taybi Syndrome: A Case Report

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Rubinstein-Taybi syndrome is an extremely rare autosomal dominant genetic disorder that occurs in 1/125,000 and is characterized by distinctive facial appearance, short stature, mild to severe mental retardation, and higher risk for cancer. In addition, variable organ anomalies had been reported. Paraovarian cyst causing torsion of the ipsilateral fallopian tube is less common, with an estimated incidence of 1/1,500,000, but it can adversely affect tubal function. It occurs mainly in women in the reproductive age and is very rare in prepubescent girls. Here, we described the successful treatment of an extremely rare case of paraovarian cyst causing torsion of the ipsilateral fallopian tube in a patient with Rubinstein-Taybi syndrome. A 14-year-old girl with Rubinstein-Taybi syndrome was referred to our hospital for abdominal pain. Her medical history was unremarkable, except for moderate hirsutism and keloid scar. Physical examination revealed tenderness in the lower abdominal midline. The preoperative diagnosis was torsion of a left ovarian cyst. An exploratory laparoscopy was performed because of acute abdominal pain and revealed a left fallopian tube that was twisted twice due to an ipsilateral paraovarian cyst. The huge paraovarian cyst required laparotomy cystectomy, and the left ovary was preserved. Her postoperative course was uncomplicated. Preoperative diagnosis of paraovarian cysts can be difficult. The moderate hirsutism seen in our patient suggested the presence of a large paraovarian cyst due to androgen receptor-mediated effects. Therefore, Rubinstein-Taybi syndrome patients with hirsutism should be screened and assessed by pediatric surgeons for the presence of paraovarian cysts.
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Key words: paraovarian cyst torsion, Rubinstein-Taybi syndrome, androgen, hirsutism

Introduction

Rubinstein-Taybi syndrome (RSTS, OMIN #180849, #613684) is an extremely rare autosomal dominant genetic disorder that occurs in 1/125,000 and is characterized by distinctive facial appearance, broad/angulated thumbs and/or great toes, short stature, mild to severe mental retardation, and higher risk for cancer[1,2]. In addition, variable anomalies in organs, such as the genitals, kidneys, and eyes, had been reported[3].

Paraovarian cysts account for approximately 10% of adnexal masses and are generally difficult to diagnose preoperatively[4]. They are not frequently seen during teenage years and are commonly benign and asymptomatic. Most cysts are small, with reported diameters of 3-28 cm (mean, 8 cm)[5]. Cysts larger than 20 cm can exert pressure on the lower abdomen and can undergo torsion of the adnexa, thereby, causing acute pain[6,7]. Paraovarian cysts rarely have complication rupture, torsion, or hemorrhage. Cysts larger than 10 cm and clinical suspicion of torsion require surgical treatment[8].

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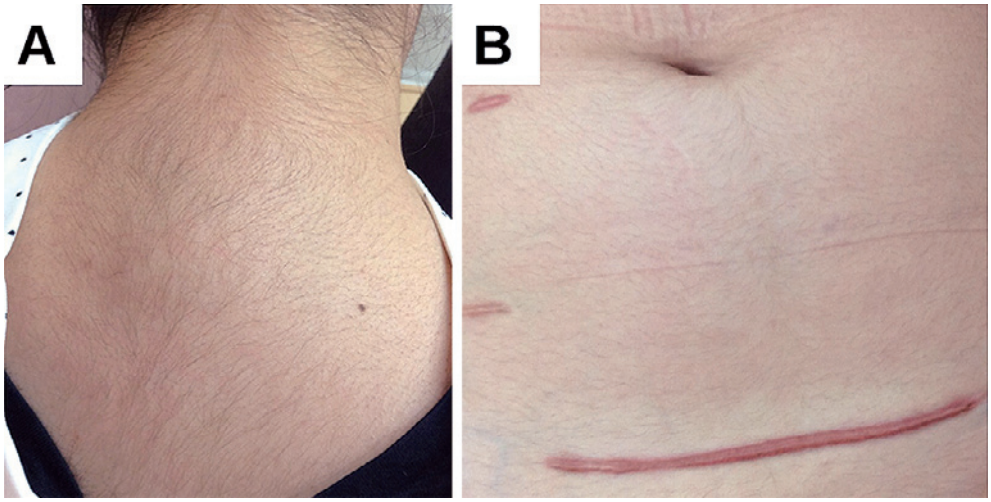

Fig. 1 Physical examination findings.
The patient had moderate hirsutism (A) and keloid scars on the abdomen (B).

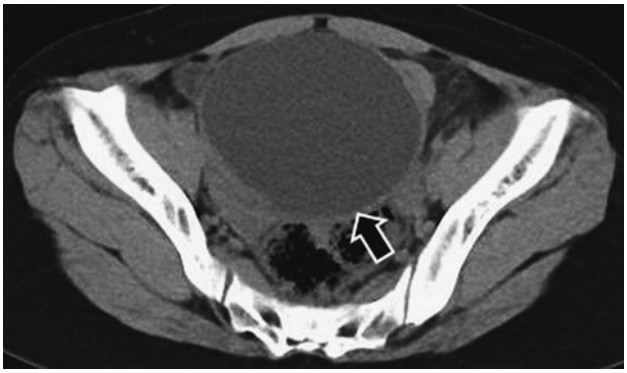

Fig. 2 Abdominal contrast-enhanced computed tomography findings.
There is a huge cystic mass, measuring>9 cm, in the pelvic midline (arrow).

Paraovarian cyst causing torsion of the ipsilateral fallopian tube is less common, with an estimated incidence of 1/1,500,000 women, but it can adversely affect tubal function[9]. It occurs mainly in women in the reproductive age and is very rare in prepubescent girls. It can be difficult to diagnose preoperatively because of the lack of pathognomic symptoms and imaging findings. In this report, we described the successful treatment of an extremely rare case of paraovarian cyst causing torsion of the ipsilateral fallopian tube in a patient with RSTS.

Case Report

A 14-year-old girl with RSTS was referred to our hospital for abdominal pain with vomiting 4 days before admission. At 4 years of age, she had been diagnosed as RSTS. Her medical history was unremarkable, except for glaucoma, moderate hirsutism, and keloid scar (**Fig. 1**). At the time of admission, she was 147-cm tall and weighed 45 kg (body mass index: 20.6 kg/m^2) and had severe mental retardation, with developmental quotient of 27 (normal developmental quotient is considered to be above 85). On physical examination, her blood pressure was 110/76 mmHg, pulse rate was 110/min, and temperature was 38.4°C. There was abdominal tenderness on the midline lower abdomen but no muscle guarding. The patient had no pain at rest. The laboratory results showed white blood cell count of 17.9 × 10^3 cells/mm^3, with 80% segmented neutrophils; total testosterone level of 15.6 ng/dL(normal: 10.8-56.9 ng/dL), free testosterone level of 0.6 pg/mL (normal: 0.4-2.3 pg/mL), and dehydroepiandrosterone level of 1.66 ng/mL (normal: 2-8 ng/mL); and C-reactive protein of 11.0 mg/dL. Transvaginal ultrasonography appears to be the primary diagnostic tool in most gynecological examination, but it is contraindicated in virgin patients. The patient was a 14-year-old girl. Abdominal contrast-enhanced computed tomography was performed. Abdominal contrast-enhanced computed tomography demonstrated a weakly enhancing huge cystic mass, which was larger than 9 cm, in the pelvic midline (**Fig. 2**) and moderate amount of ascites in the pouch of Douglas. The preoperative diagnosis was torsion of left ovarian cyst.

An exploratory laparoscopy was performed because of acute abdominal pain and revealed a left fallopian tube that was twisted at 2 points due to an ipsilateral paraovarian cyst; no abnormal findings were noted for the right ovary. The cyst had no attachments to the ovary and uterus. Thereafter, a lower laparotomy was performed for excision of the cyst and fallopian tube lesion

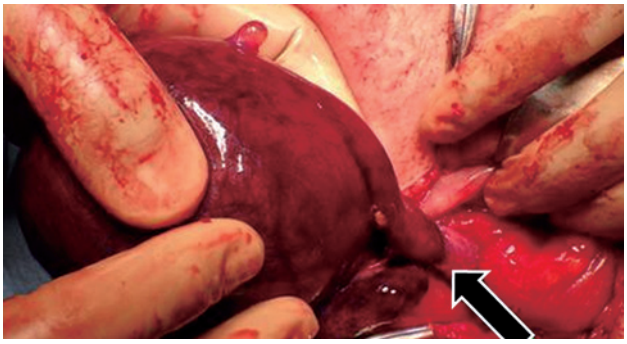

Fig. 3 Intraoperative findings.
There is torsion of the paraovarian cyst (arrow).

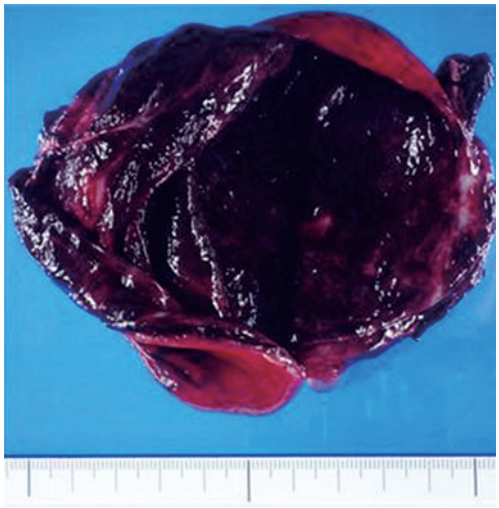

Fig. 4 Resected specimen.
The surgical specimen shows a giant cyst measuring 13.5-cm long.

(**Fig. 3**). The huge paraovarian cyst required laparotomy cystectomy, and the left ovary was preserved. On laparotomy, hemoperitoneum of approximately 220 mL was present.

The histopathologic study revealed a surgical specimen measuring 13.5-cm long and a paraovarian cyst with gangrenous and hemorrhagic necrosis (**Fig. 4**). The cyst fluid was serous not viscous. Microscopic findings revealed that the cyst wall consisted of low cuboidal epithelium, and was diagnosed as left paraovarian cyst. The final pathologic diagnosis was benign paraovarian serous cystadenoma. Her postoperative course was uncomplicated, and she was discharged from our hospital 4 days after the operation.

Written informed consent was obtained from the parents of the patient for the publication of this case report and any accompanying images.

Discussion

RSTS was originally reported by Michail et al in 1957 as the Broad Thumb-Hallux syndrome[10], but it was first formally described by Rubinstein and Taybi in 1963[1]. The incidence of RSTS is not different between men and women[11]. Due to the rarity of the syndrome, only 250 cases had been reported in medical literature worldwide[12]. Torsion of a paraovarian cyst is extremely rare; therefore, its diagnosis may be delayed. In this article, we reported an extremely rare case of paraovarian cyst torsion in a patient with RSTS. To the best of our knowledge, no such cases had been reported.

The underlying cause of RSTS is still not fully understood, but it has been associated with either microdeletions and mutations in the cyclic adenosine monophosphate response element binding protein binding protein gene (*CREBBP*, 16p13.3) or mutations in the E1A binding protein p300 gene (*EP300*, 22q13.2)[13,14]. Approximately 50% to 60% of cases were due to mutations in the *CREBBP* gene; 3% to 5% of cases were due to *EP300*; and the remaining 40% of cases were associated with other genes or had no identifiable gene mutation[15]. RSTS is due to a haploinsufficiency. The two genes *CREBBP* and *EP 300*, which encode histone acetyltransferases, show extensive homology, with amino acid sequence identity of 61%[16], which enables these genes to play important roles as global transcriptional coactivators in various signal transduction pathways. *CREBBP* and *EP300* acetylate the H3 (K14, K18, and K23) and H4 (K5, K8, and K12) histones[17]. Histone acetylation is an epigenetic event that regulates the transcription of various genes, including oncogenes, such as *MYB*, *JUN*, and *FOS*, and tumor suppressor genes, such as *TP53*, *E2F*, *RB*, *SMADs*, *RUNX*, and *BRCA1*[18,19]. Histone lysine acetylation loosens the chromatin structure and exposes the DNA to transcription factors[20]. *CREBBP* and *EP300* are involved in the regulation of both *TP53* and transforming growth factor-beta proteins, which might function as tumor suppressors[21].

RSTS had been characterized by typical facial features and many other features, and there may be involvement of multiple organ systems[16,22]. The dermatologic findings are keloid scars, capillary angioma, and hirsutism[16]. Moreover, patients with RSTS have an increased incidence of benign and malignant tumors[23,24]. Given the tumor suppressor roles of *CREBBP* and *EP300*[21], the propensity of RSTS patients to develop various benign and malignant tumors is not surprising. However, there had been no clear relationship between the incidence of be-

nign and malignant tumors and the *CREBBP/EP300* mutation status. Until now, there had been no meaningful evidence to link *CREBBP/EP300* mutations with paraovarian cysts.

Paraovarian cysts usually occur in the broad ligament and may be simply nonneoplastic or neoplastic. Although paraovarian cysts vary in size from small to large, they are usually small. Paraovarian cysts are of mesothelial origin and comprise male-type embryologic cells that would commonly differentiate into the Wolffian ducts in male fetuses[25–27]. Muolokwu et al proposed that hyperandrogenism was associated with a trend towards development of large paraovarian cysts[28]. Androgen excess can provoke hirsutism, acne, and ovulatory dysfunction. Because Wolffian ducts are androgen-sensitive, paraovarian cysts and the vestigial remnants of these ducts might also be androgen-sensitive; therefore, growth of paraovarian cysts might be caused by androgen excess[27]. Our patient had moderate hirsutism and keloid scar, which had been often observed in cases of RSTS[16,29]. Hirsutism is attributed either to increased androgen production or enhanced sensitivity of the hair follicles to androgen[30]. Our patient's androgen levels were within the normal range. Accordingly, the androgen receptor-mediated sensitivity of the hair follicles may have been a major contributor to her moderate hirsutism, which, consequently, might reflect the presence of a large paraovarian cyst. The preoperative diagnosis of paraovarian cysts is very difficult, and complications of torsion in such cases should be watched out for. Therefore, more attention should be paid to screening of RSTS patients with hirsutism for the presence of paraovarian cysts.

To our best knowledge, this is the first report on torsion of a paraovarian cyst in a patient with RSTS. This case suggested a correlation between hirsutism and torsion as a complication of paraovarian cysts. Pediatric surgeons should keep in mind the need to identify the presence of paraovarian cysts when assessing patients with RSTS. This report can help pediatric surgeons become more aware of paraovarian cysts in RSTS. A study on a larger population is needed to confirm the correlation between androgen and torsion of a paraovarian cyst.

Conflict of Interest: The authors declare no conflict of interests.

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