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Diagnosis, surgical treatment, and management of borderline ovarian surface epithelial neoplasms: Report of 2 cases and review of literature☆

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ABSTRACT

Ovarian borderline surface epithelial neoplasms occur infrequently in the pediatric population. Preoperative diagnostic criteria include ultrasound and serum tumor markers with definitive diagnosis made on pathologic examinations intraoperatively. Treatment typically involves resection of the tumor with an emphasis on preserving fertility. Patients diagnosed with borderline tumors generally have a good prognosis; however the possibility of recurrence remains. Two cases of 15 year-old females with borderline ovarian tumors are presented that add to the current literature by highlighting the diagnosis, clinical management, and follow-up postoperatively.

Ovarian neoplasms are rare in the pediatric population, accounting for approximately 1% of all childhood malignancies [1]. Of these, 20% are epithelial in origin with a significant portion classified as borderline ovarian tumors (BOTs), otherwise known as tumors of low malignant potential, according to the World Health Organization [2]. Given the rarity of pediatric BOTs, there are limited studies available that characterize the diagnosis, clinical management, and outcomes in these patients. The currently recommended standard of care is aimed to preserve fertility by resecting all visible disease [3]. In this report, we describe two cases of ovarian borderline surface epithelial neoplasms, one of mucinous and one of serous histological subtype, with subsequent surgical treatment and management.

1. Case report

1.1. Case 1

A 15-year-old female presented with a 1 year history of intermittent abdominal pain, distension, and constipation. Abdominal pain worsened and increased in frequency, localized to the periumbilical and left lower quadrant region 1 week prior to presentation. Patient reported normal menses without nausea or vomiting. Ultrasound of the pelvis and abdomen revealed a large cystic mass to be approximately 34 × 23 × 12 cm (Fig. 1A and B) in size with internal septations, nodularity, and most likely ovarian in etiology. Serum concentration of cancer antigen 125 was elevated (CA 125, 41 U/mL; normal, <34 U/mL) and alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and beta-hCG were within the normal range. On laparotomy, a large cystic structure occupying most of the abdominal cavity was apparent originating from the right ovary (Fig. 1C). Left ovary appeared to be within normal limits. An ultrasound bag with Dermabond was placed on the dried right ovarian wall to produce a water-tight barrier through which a Veress needle was inserted and clear cystic fluid was suctioned [4]. Once the ovary was decompressed it was brought through the umbilical incision (Fig. 1D) and the rest of the

Abbreviations: BOT, borderline ovarian tumor; CA 125, cancer antigen 125; AFP, alpha-fetoprotein; LDH, lactate dehydrogenase; FIGO, International Federation of Gynecology and Obstetrics; AMH, anti-mullerian hormone; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

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cystic structure was separated from the fallopian tube with a Harmonic scalpel. The fallopian tube was returned into the abdomen before incision closure. Pathological examination of the right ovarian cyst confirmed a mucinous borderline tumor classified by the International Federation of Gynecology and Obstetrics (FIGO) as stage IA with foci of epithelial proliferation, stratification, and mild to moderate cytologic atypia without intraepithelial carcinoma or stromal invasion (Fig. 2). An omental biopsy was not performed as the cystic fluid appeared to be simple and serous consistent with a benign ovarian cyst. Peritoneal washings were acellular and negative for malignant cells.

The patient was discharged from the hospital on the 2nd day postoperatively without any complications. Anti-mullerian hormone (AMH) was normal 2 weeks postoperatively and by 1 month serum concentrations of CA 125 normalized with the 3 month follow-up ultrasound showing no residual mass or acute intra-abdominal or intra-pelvic processes.

1.2. Case 2

A 15-year-old female presented with 6–8 weeks of abdominal distension and discomfort. Last menstrual period was reported to have heavier flow with more cramping pain than usual. No nausea, vomiting, constipation, or fever. Abdominal and pelvic ultrasound revealed a large cystic mass superior to the bladder measuring approximately 23 × 18.3 × 8.8 cm presumably arising from the right ovary (Fig. 3A and B). The left ovary was visualized posterior to the uterus with a cyst measuring 5 cm at the maximal diameter (Fig. 3C). Mild bilateral hydronephrosis was noted. CA 125, AFP, and beta-hCG were within normal limits. On laparoscopy, bilateral ovarian masses were noted with the right significantly larger than the left. At this time, a decision was made to proceed to an open procedure through a Pfannestiel incision and a bilateral ovarian tissue sparing oophorectomy was performed. Remaining ovarian tissue was confirmed by frozen section to be negative for tumor. Peritoneal washings showed a few groups of atypical cells and omental biopsy was negative for tumor. Pathological examination of the cystically dilated ovaries revealed bilateral serous borderline tumors, each of similar histology, classified as FIGO stage IB (Fig. 4A and B).

2. Discussion

Although BOTs are rare in the pediatric population, it is important to be included in the differential diagnosis while evaluating cystic masses in adolescent females. An algorithm outlining the diagnosis, treatment, and management is provided (Fig. 5) and subsequently discussed.

As we report 2 cases of BOTs with different histologic subtypes, it is important to recognize geographic discrepancies in the discussion of incidence rates in certain populations. In a recent large systematic review of adult BOTs, serous subtypes were more common in North America, Europe, and the Middle East, whereas mucinous were more common in Eastern Asia [5]. The trend appears to be similar in children with 40–70% characterized as serous BOTs in North America [1,6,7] and in one of the largest series to date, 89.7% were mucinous in a single center study in Korea [3]. However, further large series studies will be necessary to make significant inferences as literature regarding pediatric BOTs is limited. It is also relevant to note that the serous subtype is more commonly bilateral in adults (29.8% of serous and 7% of mucinous) [8] with a similar incidence reported in the pediatric population (30% of serous and 10% of mucinous) [9]. Albeit a small sample, our report has some correlation with a unilateral mucinous BOT (case 1) and a synchronous bilateral serous BOT (case 2).

Clinical presentation in patients with ovarian masses typically includes abdominal pain, distension, nausea, vomiting, and urinary urgency. Although definitive diagnosis of a BOT is made intraoperatively by pathological examination, serum tumor markers and imaging modalities can be of diagnostic use preoperatively. Many ovarian tumors secrete markers that can be readily assayed in the serum, such as AFP, beta-hCG, LDH, and CA 125. Of all markers, CA

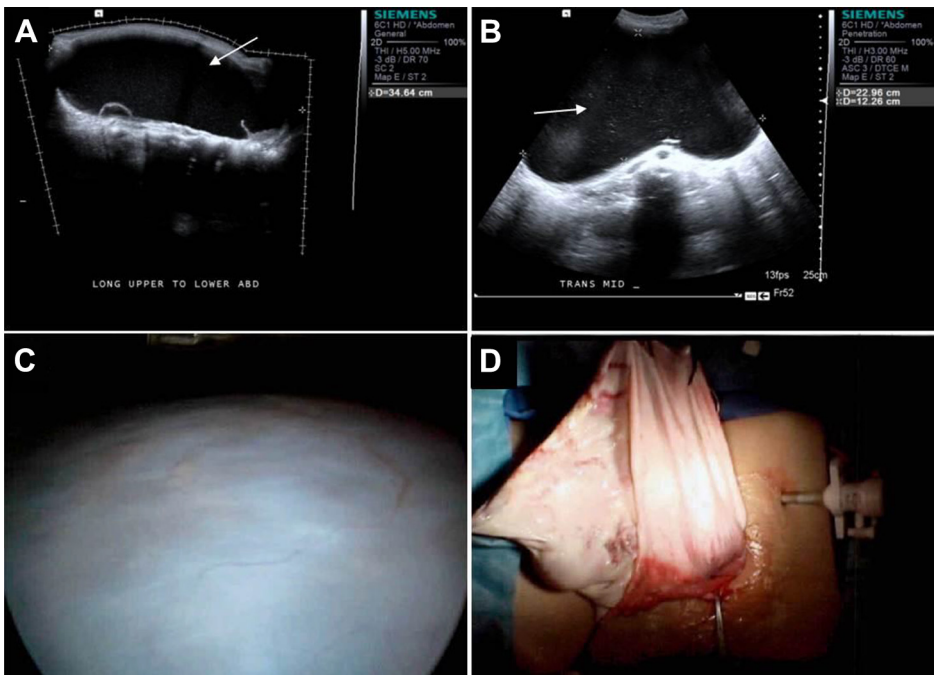

Fig. 1. (A) Longitudinal and (B) transverse ultrasound shows a large cystic mass to be approximately 34 × 23 × 12 cm (C) visualized on laparotomy which was subsequently (D) decompressed and pulled through the umbilical incision site. White arrows indicate cystic mass.

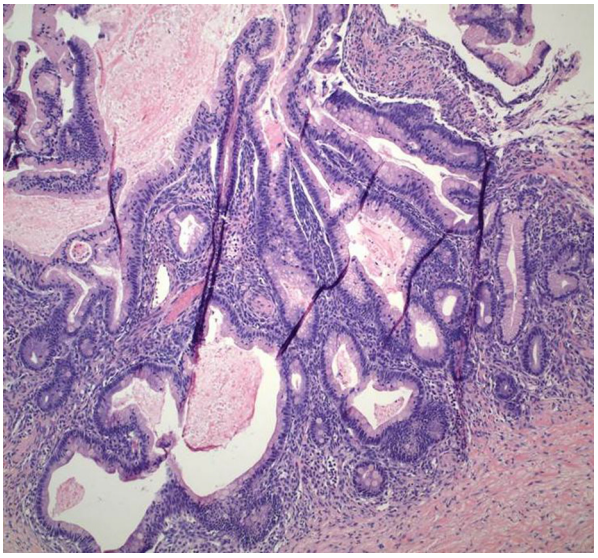

Fig. 2. Pathological examination of case 1 shows a stage IA mucinous borderline ovarian tumor characterized by foci of epithelial proliferation, stratification, and mild to moderate cytologic atypia without intraepithelial carcinoma or stromal invasion (H&E, 100×).

125 is the best diagnostic value in the detection of epithelial ovarian neoplasms. Although it has a low specificity for early ovarian tumors and sensitivity for stage I disease, values greater than 35 U/mL are generally good indicators of BOTs and malignancies. Only one of the patients reported had elevated levels of CA 125 and previous literature has shown that these levels are elevated in 24–61% of BOTs [10]. Serum LDH levels have been suggested as a non-specific marker for malignancy [11], beta-hCG in the detection of neoplastic processes associated with syncytiotrophoblasts, and elevated levels of AFP associated with yolk sac tumors [12]. However, none of these markers were elevated in either of the patients reported.

Along with tumor markers, the imaging technique of choice to evaluate ovarian pathology is ultrasound. Benign tumors are typically characterized by smooth thin walls and few thin septations, whereas malignancies are generally larger soft tissue masses with papillary projections and thick septations [13–16]. Furthermore, evidence has suggested that a morphologic scoring system may be used to help differentiate benign from malignant adnexal masses preoperatively in the pediatric population [15,17]. Computed tomography (CT) or magnetic resonance imaging (MRI) may be useful when the origin of the mass is not readily seen by US. Recent studies have also shown that positron emission tomography (PET) may be beneficial in the differentiation of borderline from malignant tumors along with identification of recurrent ovarian cancer in the absence of a large mass with rising tumor marker levels [18].

As the incidence of BOTs in the pediatric population is low, guidelines are currently lacking and treatment plans tend to be oriented toward adults, which involve surgical resection of the tumor by either cystectomy or oophorectomy with the objective of preserving childbearing potential [2,3,6]. Recurrence rates following cystectomy have been shown to be higher than in patients that undergo oophorectomy (12–58% and 0–20% respectively) [19], suggesting that tumors involving the resection margin may not be fully removed. However, studies in adults have shown that contralateral relapse can occur at a similar rate following conservative surgery, suggesting that tumor localization to the other ovary may account for some cases of recurrence [20]. Despite the higher recurrence rates with cystectomy, conservative treatment is still suggested since there is no significant difference in survival outcomes, as future recurrences can be treated surgically [20]. When considering surgical approach, most cases are performed by laparotomy as there is concern for spillage in the laparoscopic removal of adnexal masses suspicious for malignancy [21]. However, studies have shown that there is no significant difference in the rate of cystic rupture between techniques [22,23]. Full staging of the disease requires tissue histology, cytologic analysis of peritoneal washings, and an omental biopsy in accordance with the International Federation of Gynecologists and Obstetrics (FIGO), which have been updated as of the beginning of 2014 [24]. A biopsy of the omentum was not performed in case 1 as the fluid appeared

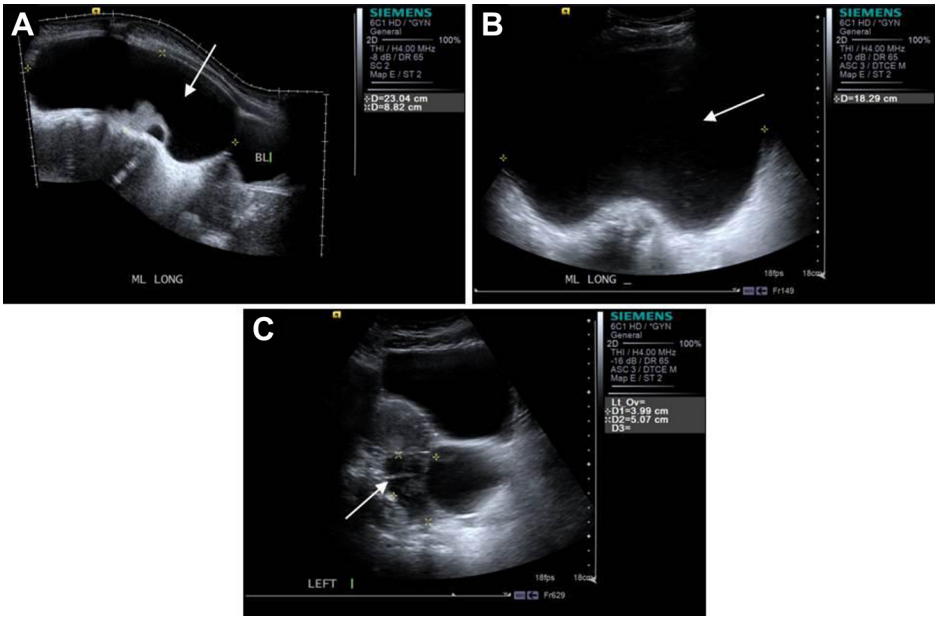

Fig. 3. (A) Longitudinal and (B) transverse ultrasound shows a large cystic mass approximately 23 × 18.3 × 8.8 cm in size most likely originating from the right ovary. (C) Left ovary located posterior to the uterus with a cyst measuring 5 cm in maximal diameter. White arrows indicate cystic masses.

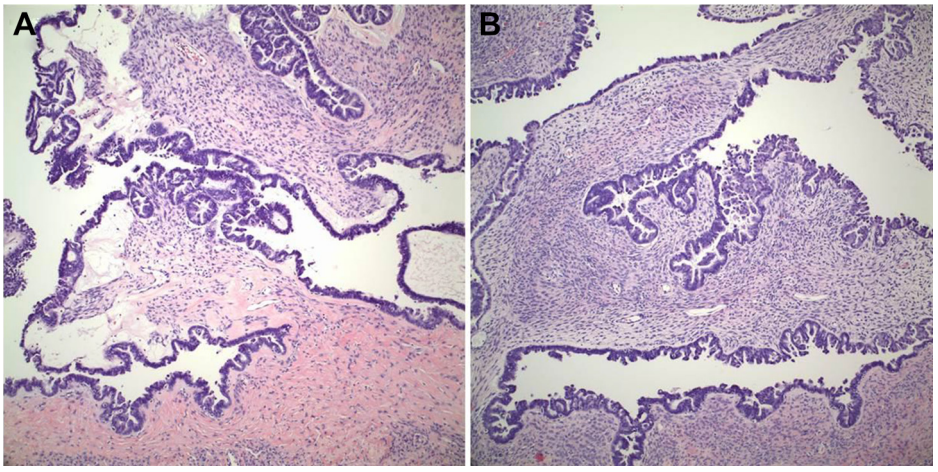

Fig. 4. Pathological examination of case 2 shows histologically similar stage IB serous borderline tumor of the (A) left and (B) right ovary without microinvasion (H&E, 100x).

to be simple and serous consistent with a benign ovarian cyst. In future cases, given the lack of grossly discerning characteristics of BOTs, we recommend omental biopsy even in cases with simple fluid. In mucinous BOTs, an appendectomy is also recommended because of the possibility of a synchronous appendiceal lesion. In case 1, after being diagnosed with a mucinous BOT, an appendectomy was offered to the family as an additional treatment option but they decided not to undergo further surgery. Other treatments such as adjuvant chemotherapy have been used for advanced stage disease with mixed results but have been shown not to be beneficial in early stage BOTs [19].

The prognosis in these patients is considered to be very good, however, with few studies available outlining the long-term outcomes in pediatric BOTs; most data is extrapolated from adults. An extensive review by Massad et al. showed that most adults present with stage I disease with a survival rate of nearly 100% [25]. In a small study of children, Morris et al. showed similar results with 75% presenting with stage I disease with an overall survival of 100% [26]. In a more recent study, Hazard et al. reported 83% of BOTs in children presented with stage I disease with a 100% survival rate [1]. As literature regarding outcomes in pediatric BOTs is limited, there are currently no guidelines for follow-up. However, in consideration of recurrence in adults and children [3,6], we recommend at least 10 years of monitoring with ultrasound and serum CA 125 levels every 3 months for the first year, every 6 months for the second year, and annually thereafter [1,2].

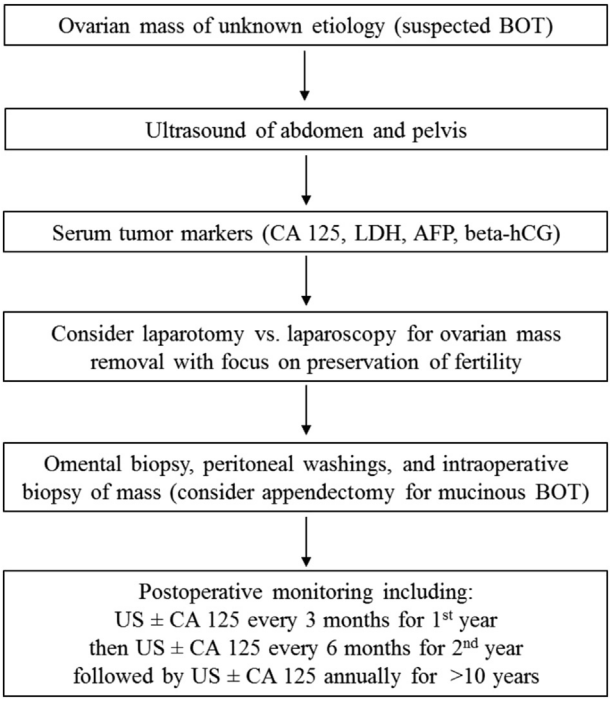

Fig. 5. Algorithm for the management of pediatric borderline ovarian tumors. BOT, borderline ovarian tumor; CA 125, cancer antigen 125; LDH, lactate dehydrogenase; AFP, alpha-fetoprotein.

3. Conclusion

Herein, we report the diagnosis, treatment, and management of 2 adolescents with BOTs. These are rare tumors in the pediatric population that generally have a good prognosis when diagnosed in the early stages of disease but have a high rate of recurrence as treatment involves surgical resection with the goal of preserving fertility. Subsequently, long term follow-up of these patients is important.

Conflict of interest statement

The authors declare that there are no financial or personal conflicts of interest associated with this manuscript.

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