Abnormal Uterine Bleeding in Adolescents

Anna Cohen*, Joseph S Sanfilippo2,4 and Serena H Chan2,3

1University of Pittsburgh School of Medicine, USA
2Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh School of Medicine, USA
3Division of Pediatric and Adolescent Gynecology, UPMC Children’s Hospital of Pittsburgh, USA
4Division of Reproductive Endocrinology and Infertility, UPMC Magee-Women’s Hospital, USA

Introduction

Abnormal Uterine Bleeding (AUB), defined as any deviation from the normal menstrual pattern, accounts for approximately half of gynecologic visits by adolescents. It is a broad term that encompasses the changes in blood loss, regularity, frequency, and duration of menses. The PALM-COEIN classification, developed by the FIGO Menstrual Disorders Working Group, summarizes the possible etiologies of AUB to include structural (polyp, adenomyosis, leiomyoma, malignancy/hyperplasia) and non-structural (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not yet classified) causes [1]. Other important causes of AUB in adolescents include Sexually Transmitted Infections (STI) and pregnancy complications, such as ectopic pregnancy or first trimester miscarriage [1].

Structural etiologies only account for 1.3% to 1.7% of AUB in adolescents [1]. Rather, AUB in this population is most commonly due to anovulatory cycles owing to an immature Hypothalamic-Pituitary-Ovarian (HPO) axis [1]. The HPO axis operates using hormonal regulation and feedback loops, thus creating cyclic and orderly regulation of menstruation. The pulsatile secretion of Gonadotropin-Releasing Hormone (GnRH) from the hypothalamus stimulates the gonadotrophs in the anterior pituitary, which synthesize, store, and secrete Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH) in response. These trophic hormones then go on to stimulate the gonads to synthesize and secrete sex steroids. Hormone release at each level in the HPO axis is delicately regulated by negative feedback. As such, disruption in this axis may result in amenorrhea or menstrual cycle disturbances [2]. It is typical for otherwise healthy females in the first 2 years of menarche to have approximately 55% to 82% anovulatory cycles. With time, the percentage of ovulatory cycle’s increases [1]. However, regardless of age of menarche, amenorrhea for greater than 3 months should be considered abnormal [2].

The menstrual cycle is an important biological marker of general health in adolescents. As such, thorough evaluation of menstrual cycle disorders permits an opportunity for early diagnosis and treatment of potential health concerns affecting the HPO axis and lifelong health [2].

Basics in adolescent gynecologic history and physical

Before performing the exam, obtain the history while the patient is clothed to facilitate rapport building. Providers should set the expectation with the family that the adolescent will be interviewed alone at some point during the visit. Establish the identity of the adult(s) accompanying the patient. If they are not the patient’s parent or guardian, the relationship should be noted [3]. The gynecologic history should include age at menarche, frequency and duration of menses, last and previous menstrual periods, and a sexual history. A careful review of symptoms should also be obtained, with particular emphasis on symptoms of hematologic and endocrinologic conditions. Medications should also be documented as some, such as atypical anti-psychotic drugs, can be associated with anovulatory bleeding or amenorrhea. Many providers find it helpful to structure the discussion of psychosocial history using the HEADSS (Home, Education/employment, peer group Activities, Drugs, Sexuality, and Suicide/depression) assessment for adolescents (Table 1). The provider should also ensure confidentiality for minors of all matters stated above unless there is suspicion for abuse, neglect, or suicidality [3].

As the gynecologic exam is accompanied by anxiety for many adolescents, approach the exam with explanations of the purpose, method, and expected outcomes of all exam components. Seek the approval of the patient and caregiver and inquire whether the patient would like a caregiver present.
during the exam. Important aspects of the exam are assessment of development and confirmation of normal anatomy. Begin the exam with evaluation of the mons and labia majora. Note the Tanner stage of pubic hair as well as shaving practices, including evidence of folliculitis or poor hygiene. Assess the appearance of the clitoral hood and clitoral size, particularly in an adolescent with concern for androgen excess. Also assess the appearance of the hymen, including possible anomalies, such as a hymenal septum or micro perforate opening. Screen for chlamydia and gonorrhea routinely in sexually-active adolescents using nucleic acid amplification techniques with a urine sample or vaginal swab [3]. A speculum exam is not required at each visit, and asymptomatic patients who are not sexually active can delay this aspect of the exam until age 21. If speculum exam is indicated, patient positioning using stirrups is ideal. Place the speculum horizontally rather than at 45-degree angle as it may decrease traction on the hymen. Water-based lubricant may also be helpful. Open the speculum only once fully inserted in the vagina to visualize the cervix and note any lesions. If a bimanual exam is clinically indicated, single digit exam is preferred. Office vaginoscopy, preferably with irrigating endoscope or exam under anesthesia may be required when an office exam and ultrasonography do not provide adequate diagnostic information.

**Ovulatory Dysfunction: Androgen Excess States, Endocrinopathies, Immature HPO**

A 16-year-old patient complains of secondary amenorrhea and 20 lb weight gain over 6 months. Menarche occurred at 11 years of age. She reports her menses have never been regular. She also has a past medical history of seizure disorder, for which she is on anti-epileptic drugs. Her BMI is 34 (>95% tile for age). Her exam is positive for cystic/inflammatory acne and hirsutism (coarse terminal hairs on upper lip, jawline, chest, midline lower abdomen). Lab values are notable for an HbA1c of 6.0%.

**Differential diagnosis**

Hyperandrogenism, as evidenced by this patient’s exam, is a sign that suggests several possible endocrinopathies. These include Polycystic Ovary Syndrome (PCOS), Cushing’s syndrome and disease, and Non-Classic Congenital Adrenal Hyperplasia (NCAH). Other endocrinopathies associated with AUB include hyper or hypothyroidism and hyperprolactinemia.

Most common among the endocrinopathies, PCOS affects 6% to 15% of women of reproductive age. PCOS is thought to be due to rapid GnRH pulses causing hormonal dysregulation, excessive androgen production, and ovulatory dysfunction [4]. It is associated with several metabolic abnormalities including obesity, hyperinsulinism, and increased risk of type 2 diabetes, hypertension, Cardiovascular Disease (CVD), and endometrial hyperplasia. Current guidelines recommended all women with PCOS should be screened for individual CVD risk factors with particular attention to excess body weight [5]. PCOS and obesity frequently co-occur [5]. In fact, obesity alone, without PCOS, commonly leads to anovulatory cycles. This is owing to the hyperestrogenic state of obesity, leading to excess conversion to androgens.

In adult women, diagnostic criteria for PCOS have been set forth by the National Institutes of Health, the Rotterdam consensus, and the Androgen Excess and PCOS Societies. Two of three of the following criteria must be met-oligo-anovulatory cycles (cycle length >35 days), biochemical or clinical hyperandrogenism (must be present in the Androgen Excess Society criteria), and polycystic ovaries (ovarian volume >10 mL, or ≥ 12 to 25 follicles in one ovary (increased follicle count threshold recommended by Androgen Excess Society due to improved ultrasound resolution)) [6,7].

In adults, phenotypes of PCOS can be categorized into four categories: A) hyperandrogenism (biochemical or clinical), ovulatory dysfunction, and polycystic ovaries; B) hyperandrogenisms and ovulatory dysfunction; C) hyperandrogenism and polycystic ovaries; and D) ovulatory dysfunction with polycystic ovaries. Overall, 75% to 85% of those with phenotypes A and B demonstrate insulin resistance and carry an increased risk of glucose intolerance and diabetes. Alternatively, women with phenotype D, who do not demonstrate overt evidence of androgen excess, show little evidence of metabolic dysfunction and are at low risk of developing disorders of glucose intolerance. Patients with phenotype C have levels of metabolic dysfunction and risk that are less than that of phenotypes A and B, but are still measurably higher than those of phenotype D and women without PCOS. Furthermore, women with phenotypes including ovulatory dysfunction are at higher risk of endometrial hyperplasia and endometrial cancer, in addition to infertility [8].

The diagnosis of PCOS in adolescence can be more challenging for several reasons. Anovulatory cycles in the first couple of years after menarche may be physiologic in the setting of an immature HPO axis. Acne (particularly comedonal acne) is also a common finding in adolescence, even in girls without biochemical hyperandrogenism. Testosterone levels also increase with the lengthening of anovulatory adolescent cycles, in both symptomatic and asymptomatic patients. Approximately half of girls evaluated for abnormal menstrual patterns without clinical signs of hyperandrogenism may have mildly elevated androgen levels. However, the hyperandrogenemia in approximately half of these adolescents will resolve over time. In addition, ovarian volume peaks post-menarche, during adolescence. Therefore, an ovarian volume of >10 mL may actually be physiologic in an adolescent. Transvaginal ultrasound is also performed less frequently in virginal adolescents, and a follicle count cannot be accurately accessed via a transabdominal sonographic approach. Because of these challenges, the Pediatric Endocrine Society worked with the Androgen Excess-PCOS Society and international pediatric and adolescent gynecology societies to publish consensus guidelines in 2015 on diagnostic criteria for adolescent PCOS. They concluded that patients must demonstrate persistent oligo-anovulation >2 years post-menarche. Signs of clinical hyperandrogenism in an adolescent may include moderate to severe comedonal acne (particularly if resistant to treatment) or inflammatory acne (rare in adolescents), and moderate to significant hirsutism. Biochemical hyperandrogenemia should persist. Patients <2 years post-menarche with evidence of
hyperandrogenic oligo-anovulation should be considered “at risk for PCOS” (after ruling out other causes of hyperandrogenism). Given that ovarian volumes peak in adolescence, a multi-follicular pattern can be normal in adolescence, and many ultrasounds are done via a transabdominal approach in adolescents, the conclusion was that sonographic follicle count should not be used as diagnostic criteria. Furthermore, in girls with regular menses and no clinical evidence of hyperandrogenism, polycystic ovarian morphology should not be used to diagnose PCOS. The guidelines recommended that, pending additional data regarding normal adolescent ovarian volumes, an ovarian volume >12 mL could be used to support the diagnosis of PCOS [9].

In an adolescent reporting AUB with signs of androgen excess, non-classical CAH should also be considered. In fact, the most common presenting signs of NCAH are menstrual irregularities and primary amenorrhea. They may also complain of acne, hirsutism, and alopecia. Clitoromegaly can be found in 11% of patients. NCAH, similar to the classic form, is most commonly associated with defects of 21-hydroxylase (21-OH) activity and resultant elevations in 17-hydroxyprogesterone (17-OHP) levels. In the classic form, the resulting reduction of circulating cortisol leads to increased Adrenocorticotropic Hormone (ACTH) production and subsequently to adrenal hyperplasia. However, in NCAH, the majority of patients have normal ACTH production. Interestingly, despite the normal circulating levels of ACTH, adrenal androgen secretion and its response to ACTH are increased in NCAH. As a result, there is increased peripheral conversion of steroid metabolites to androgens. Dehydroepiandrosterone sulfate (DHEA-S) serum levels are generally normal while androstenedione, testosterone and Dihydrotestosterone (DHT) are similar to the levels found in PCOS [10].

Amenorrhea and elevated androgen levels are also a common finding in women with ACTH-secreting adenosas (Cushing’s disease), though this condition is rare in adolescents. Cushing’s disease is associated with elevated serum cortisol levels leading to suppression of GnRH, and subsequent amenorrhea [11].

Other common endocrinopathies causing pathologic AUB include thyroid dysfunction and hyperprolactinemia. Both hyperand hypothyroidism may result in menstrual irregularities and anovulatory cycles. In hyperthyroidism, two of the most common manifestations in the adolescent population are oligomenorrhea and delayed menarche. Heavy menstrual bleeding may occur with hyperthyroidism, but is rare. In contrast, hypothyroidism is more often associated with increased menstrual bleeding. These changes are due to the fact that Thyroid Stimulating Hormone (TSH) biochemically mimics LH and FSH. Galactorrhea may also be present in hypothyroidism, possibly because Thyrotropin-Releasing Hormone (TRH) increases the secretion of both TSH and prolactin (PRL) [12].

Hyperprolactinemia, which has several physiologic, pathologic, and iatrogenic causes, often leads to secondary amenorrhea. The exact mechanism by which this occurs is not well known. However, studies of hyperprolactinemic women have shown reduced LH-pulse frequency and reduced LH responsiveness to estrogen, suggesting that GnRH suppression is a key factor. Increased prolactin may inhibit GnRH through down regulation of kisspeptin (a potent stimulator of GnRH) and/or through up regulation of Corticotropin-Releasing Hormone (CRH) at the level of the hypothalamus [13].

Finally, Functional Hypothalamic Amenorrhea (FHA), or stress-induced anovulation, is one of the most common causes of secondary amenorrhea. FHA accounts for the reproductive dysfunction seen in under nutrition, excessive exercise, severe emotional stress, and chronic disease. In such states, the activated Hypothalamic-Pituitary-Adrenal (HPA) axis may inhibit the HPO axis at multiple levels: at the level of the hypothalamus, CRH suppresses GnRH secretion, leading to decreased FSH/LH. At the level of the pituitary, ACTH also has a suppressive effect leading to decreased secretion of FSH/LH [13]. Decreased levels of leptin and insulin in the context of chronic malnutrition have also been shown in FHA. Similarly, FGF-21, which is a liver-derived hormone whose production is up-regulated in response to starvation, has been shown to be a potential mediator of starvation-induced amenorrhea [13].

**Evaluation**

Evaluation should first include a thorough menstrual, past medical, and family history. In addition to general review of symptoms, care should be taken to ask about symptoms of androgen excess. It is also pertinent to ask about headaches, visual changes, or galactorrhea, as these may be symptoms of a pituitary adenoma leading to excess prolactin production. If hyperprolactinemia is suspected, a careful review of current medications may also be warranted. On exam, assess for signs of hyperinsulinism such as alopecia and acanthosis nigricans, along with signs of androgen excess such as hirsutism or acne. Assess the thyroid for any nodules, tenderness, or goiter; the abdomen for any masses; and the genital area for clitoromegaly or other signs of virilization. Lab tests for PCOS are provided in Table 2.

An LH: FSH ratio of 2:1 is commonly seen with PCOS, but it is not used as diagnostic criteria for PCOS. Both total and free testosterone may be elevated, and Sex Hormone Binding Globulin (SHBG) is often low. Evidence suggests using a 2 ng/ml (6 nmol/l) cut-off value of basal 17-OHP concentrations to screen for NCAH (followed by confirmatory ACTH stimulation testing). The 17-OHP value should be obtained early in the morning as 17-OHP levels peak in the morning and decrease throughout the day. A pre-pubertal patient with this condition may show signs of early pubarche on exam. In this context, a bone age study may also be beneficial, as

---

**Table 1: Adolescent Psychosocial History - HEADSS Assessment.**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>History Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Home (co-habitants, living situation)</td>
</tr>
<tr>
<td>E</td>
<td>Education/employment</td>
</tr>
<tr>
<td>A</td>
<td>Activities (school, extracurricular)</td>
</tr>
<tr>
<td>D</td>
<td>Drugs</td>
</tr>
<tr>
<td>S</td>
<td>Sexuality (sexual activity [type, past/present/plans], sexual orientation, gender identity)</td>
</tr>
<tr>
<td>S</td>
<td>Suicideality (mood stability, suicidal/homicidal ideation, thoughts of self-harm)</td>
</tr>
</tbody>
</table>
NCAH is frequently associated with advanced bone age [14]. A total testosterone level greater than 200 ng/dL and a DHEA-S level greater than 700 mcg/dL are suggestive of androgen-secreting tumors, and warrant prompt imaging of the ovaries and adrenal glands, respectively (ultrasound or MRI).

In the case of hyperthyroidism, laboratory evaluation of the thyroid may show increased Sex Hormone-Binding Globulin (SHBG). As such, serum levels of total estradiol and testosterone may be elevated out of proportion to the free levels. In addition, LH and FSH may also be elevated [11]. As previously stated, an elevated prolactin may accompany an elevated TSH in a patient with hyperprolactinemia. Elevations in prolactin in the absence of pregnancy should prompt a review of medications as well as an MRI depending on level of prolactin. Ideally, the prolactin level should be obtained in the morning, when the patient is in a steady state, without any preceding breast manipulation.

Management

Definitive therapy is directed towards the diagnosis. Weight loss is the primary therapy in PCOS-reduction in weight of as little as 5% can restore regular menstrual cycles [10]. The management of women with PCOS is also focused on providing endometrial protection, and minimizing signs of hirsutism, alopecia, and acne. Combined Hormonal Contraceptives (CHC) are first line, as they suppress ovarian androgen production and increase sex hormone-binding globulin, effectively blocking the effect of androgens [6]. If symptoms persist, anti-androgens, such as spironolactone or finasteride, may be used. Providers, however, must be aware that many features of PCOS, including acne, menstrual irregularities, and hyperinsulinemia, are also common in normal puberty [6]. A concern regarding the use of anti-androgens is the risk of impaired virilization of the external genitalia of a male fetus in the event of an unplanned pregnancy [14]. It is important to counsel adolescent girls and young women with PCOS that while some women may have difficulty conceiving, spontaneous pregnancy is possible, so reliable contraception is still recommended in sexually active patients with PCOS who wish to avoid pregnancy.

Education on the long-term metabolic sequelae of PCOS is essential. Hemoglobin A1C is often obtained to screen for diabetes or prediabetes, and warrants prompt imaging of the ovaries and adrenal glands, respectively (ultrasound or MRI).

For NCAH, treatment with glucocorticoids is recommended for pre and peripubertal patients with significantly advanced bone age. Otherwise, treatment should be reserved for those who demonstrate important or clinically significant hyperandrogenism. The treatment for hyperandrogenism in this context is the same as that for PCOS. Although the anti-mineralocorticoid action of spironolactone is a theoretical concern in patients with NCAH, this risk has not been documented to date [14].

Irregular thyroid and prolactin levels should prompt treatment directed towards the underlying cause. In the case of hyperprolactinemia, evaluation of any current medications, such as atypical anti-psychotic drugs, should be obtained. In addition, a brain MRI should be conducted to rule out a pituitary microadenoma adenoma or other CNS pathology.

Heavy Menstrual Bleeding: Coagulopathies and Uterine Abnormalities

15-year-old patient presents with heavy menstrual bleeding since menarche at age 13. Her past medical history is only significant for anemia.

Differential diagnosis

Heavy Menstrual Bleeding (HMB) is defined as menses lasting longer than seven days or loss of more than 80 mL of blood per cycle [15]. As previously stated, prolonged and irregular bleeding should prompt an investigation into both structural and systemic etiologies according to the PALM-COEIN classification. Though rare in the adolescent population, possible structural etiologies include leiomyomas, endometrial polyps, and adenomyosis. Other rare causes include endometrial hyperplasia and uterine arteriovenous malformations.

Although most adolescent girls have prolonged menses due to ovulation, there is an accompanying bleeding disorder in almost 20% of patients with HMB and, thus, HMB may be the first presenting sign of an underlying bleeding disorder [15]. The most common bleeding disorders in adolescent girls who present with HMB are von Willebrand disease, Immune/I idiopathic Thrombocytopenic Purpura (ITP), disorders of platelet aggregation, and clotting factor deficiencies. Hypothyroidism can also cause heavy menstrual bleeding, although it is more commonly associated with heavy, irregular menses. Defects in hemostasis, such as decreased levels of factors VII, VIII, IX, and XI, have been reported with hypothyroidism, and may contribute to heavier menstrual flow [12].

Approximately one half of adolescent girls with bleeding disorders present with heavy menstrual bleeding at menarche; others may not present until cycles become ovulatory. Among adolescent girls and women with an inherited bleeding disorder, 75% to 80% report heavy menses as the most common clinical manifestation of their disorder, and 70% report passage of clots and bleeding through clothing. Anemia that results from bleeding can cause associated symptoms of headaches and fatigue. Low iron stores, reflected by a low ferritin level, even without anemia, are associated with fatigue and decreased cognition. Adolescents with heavy bleeding may have impaired school attendance and performance, decreased participation in sports, and may present with symptoms of depressed mood or anxiety [12].

Evaluation

When obtaining a medical history, it is important to identify risk factors for bleeding disorders, as well as medical conditions that would alter management. The provider should inquire about age of menarche, Last Menstrual Period (LMP), cycle length, number of pads/tampons on heaviest days, menstrual staining of clothes, and missed days of school/work due to HMB. Care should be taken to inquire about both personal and family history of prolonged bleeding after procedures such as tooth extraction, need for surgical intervention for uterine bleeding, or treatment for anemia. To

<table>
<thead>
<tr>
<th>Table 2: Laboratory tests to evaluate for PCOS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH, LH, Estradiol</td>
</tr>
<tr>
<td>TSH</td>
</tr>
<tr>
<td>Prolactin</td>
</tr>
<tr>
<td>DHEA-S</td>
</tr>
<tr>
<td>Total/Free testosterone</td>
</tr>
<tr>
<td>17-hydroxyprogesterone (early morning value)</td>
</tr>
</tbody>
</table>

Irregular thyroid and prolactin levels should prompt treatment directed towards the underlying cause. In the case of hyperprolactinemia, evaluation of any current medications, such as atypical anti-psychotic drugs, should be obtained. In addition, a brain MRI should be conducted to rule out a pituitary microadenoma/adenoma or other CNS pathology.
better quantify heaviness of menstrual bleeding, it may be helpful to clarify frequency of pad/tampon changes (also note size/absorbency of sanitary products), whether sanitary products are saturated, and whether clothing or sheets are frequently soiled. Physical examination should include an evaluation for signs of anemia. An assessment of hemodynamic stability may include orthostatic blood pressure and pulse measurements. Skin examination for purpura, petechiae, conjunctival pallor may also guide differential diagnosis. An abdominal examination should be done to assess for distention, hepatosplenomegaly, or masses. The uterus may be palpable uterus on abdominal examination in the setting of large leiomyomas. Trauma should be ruled out as a cause of acute bleeding. Speculum examination may not be required for most cases of heavy menstrual bleeding in adolescents [17].

Laboratory evaluation should include a urine pregnancy test, Complete Blood Count (CBC) with platelet count, and ferritin level. Coagulation labs, such as Prothrombin Time (PT), Partial Thromboplastin Time (PTT), international Normalized Ratio (INR), and fibrinogen levels, should be considered. If there is suspicion for a bleeding disorder, a von Willebrand (vW) screen or panel may also be obtained (this includes a measure of vW factor activity and antigen, and Factor VIII). A type and screen can also be considered in the event of severe anemia and/or hemodynamic instability. Other labs should be obtained based on clinical signs or symptoms of other conditions (such as thyroid dysfunction, PCOS) [15]. Routine sonographic imaging to evaluate for structural etiologies of heavy menstrual bleeding is not recommended unless the patient does not respond to initial management.

Management

Choice of acute management is dependent on clinical stability and suspected etiology. If there is profuse bleeding, vital signs show evidence of hypovolemia, or Hgb<8/Hct<25, inpatient admission may be warranted for blood transfusion. Rapid cessation of heavy bleeding can be achieved with estrogen containing therapies or progestin-only therapies. Estrogen-containing therapies may include high-dose monophasic combined Oral Contraceptive Pills (OCP) or intravenous conjugated estrogen, followed by a combined OCP taper once bleeding has stopped. High dose oral progestin-only therapies, such as medroxyprogesterone or norethindrone acetate, have also been shown to be effective for acute cessation of bleeding. Some patients may require additional hemostatic agents, such as intravenous or oral anti-fibrinolytics (tranexamic acid or aminocaproic acid) [16]. Continued iron supplementation is recommended on an outpatient basis for patients with iron-deficiency anemia due to blood loss.

If the patient is clinically stable but has active bleeding, she could be treated on an outpatient basis with initial combined OCP taper, followed by maintenance therapy. Oral progestin-only therapy can also be used for acute cessation of bleeding. Long-term maintenance therapies for heavy menstrual bleeding include combined hormonal contraceptives (oral pill, transdermal patch, vaginal ring) and progestin-only therapies (oral pill, depot medroxyprogesterone acetate injections, levonorgestrel intra-uterine device). Again, iron-deficiency anemia due to blood loss should also be treated with iron supplementation until the hemoglobin has normalized [15].

Surgical management should be reserved for those who do not respond to medical therapy [15]. Intra-uterine balloon tamponade may be considered under ultrasound guidance (to minimize the risk of uterine rupture). Therapeutic curettage is reserved as a last resort if bleeding continues, and the patient’s clinical status continues to decline. Endometrial ablation is typically avoided in adolescents due to risks to future fertility [17].

Ovarian Tumors

14-year-old female presents with acute, severe unilateral pelvic pain with nausea/vomiting, and a 5-month history of irregular menstrual bleeding. Patient is not sexually active. Pelvic US demonstrate a large right ovarian mass and decreased Doppler flow to the right ovary.

Differential diagnosis

Ovarian tumors account for approximately 1% of all malignancies in patients aged 0 to 17 years. These include both neoplastic and non-neoplastic processes. Non-neoplastic conditions include follicular cysts, corpus luteal cysts, and endometriomas. Neoplastic processes include both benign tumors, such as mature cystic teratomas, as well as malignant tumors, with a predominance of germ cell tumors (such as dysgerminomas), which have the potential to metastasize. The most common sites for metastasis are the lungs, liver, lymph nodes, and central nervous system. Children and adolescents may also present with sex cord-stromal tumors (thecoma, Sertoli-Leydig, granulosa cell) and epithelial tumors (cystadenomas). Juvenile granulosa cell tumors follow a very different clinical course than granulosa cell tumors in adult women and, although they have malignant potential, they commonly follow a benign clinical course. Epithelial tumors occur in benign, borderline, and malignant forms. Epithelial ovarian malignancies are rare in children and adolescents. Of note, mature ovarian teratomas are seen more commonly in adolescents than adults [18].

In the absence of adnexal torsion, ovarian neoplasms do not typically cause pain. Abdominal distention and pressure symptoms (urinary frequency, constipation, early satiety) may occur in the setting of a large mass [19]. Some ovarian cysts/masses may be first diagnosed when the patient presents with adnexal torsion. Precocious puberty or abnormal uterine bleeding is common presenting signs of juvenile granulosa cell tumors, due to the excess estrogen produced by the tumor. With Sertoli-leydig cell tumors and other androgen secreting ovarian tumors, virilization can be seen in girls. Overall, many patients with ovarian tumors are asymptomatic and are diagnosed incidentally [18].

Evaluation

When an ovarian mass is suspected, evaluation should include a detailed menstrual, sexual, and medical history, physical examination, and imaging (pelvic ultrasonography is first-line). Pregnancy test and complete blood count with differential may also be indicated [19].

Sonography is used routinely to determine the overall size of the mass and to identify whether it is a simple or complex cyst, has solid components, is seen bilaterally, or associated with free fluid. The resistive index of an ovarian mass can also be evaluated by sonographic Doppler flow. This information can be used along with sonographic characteristics of mass and elevated tumor markers, to increase suspicion for ovarian malignancy [19]. To better characterize an ovarian mass (and to assess for extra-ovarian disease), an MRI pelvis with and with IV contrast be beneficial. Soasm’s secreted protein tumor markers, which can be helpful in making a diagnosis, as well as following the clinical response to treatment [20].
Management

Management is directed toward acuity and presumed diagnosis. Follicular cysts found on routine examination in adolescents resolve spontaneously in two to eight weeks. Asymptomatic simple cysts <6 cm on ultrasound examination can be observed with or without administration of oral contraceptive pills [21]. If a simple fluid-filled cyst persists, increases in size, is greater than 4 cm to 6 cm, or causes symptoms, then laparoscopic ovarian cystectomy may be considered. It is possible that cysts larger than 6 cm will regress spontaneously, and, thus, observation is the initial preferred option. If ovarian cystectomy is performed, the cyst wall should be sent for pathologic examination. Ovarian cystectomy is preferred to cyst aspiration due to the high rate of recurrence after aspiration. Asymptomatic simple cysts of 6 cm to ≤ 10 cm may also spontaneously resolve and can be safely observed. The signs and symptoms of adnexal torsion should be reviewed with the patient and guardians in this setting (acute, severe, lateralized pelvic pain associated with nausea and vomiting).

Functional cysts are common physiologic ovarian cysts in adolescents. They result from the failed involution of the normal corpus luteum and can reach 5 cm to 12 cm in diameter [19]. Bleeding into the cyst or rupture with intraperitoneal hemorrhage may occur [16]. In the absence of pain or intraperitoneal bleeding, observation for a time period between two weeks and three months is appropriate. Combined OCPs may also be used, as they prevent new physiologic cysts from forming (they do not result in quicker resolution of an existing cyst). Though observation is preferred, it is important to recognize that large functional cysts pose an increased risk for ovarian torsion [21].

Surgical intervention for other ovarian masses is directed toward preservation of reproductive and sexual function. Unless a malignancy is suspected, an ovarian-sparing cystectomy is preferred, if possible. If serum tumor markers are abnormal and sonographic malignancy is suspected, an ovarian-sparing cystectomy is preferred, toward preservation of reproductive and sexual function. Unless a risk for ovarian torsion [21].

Resolution of an existing cyst). Though observation is preferred, it is new physiologic cysts from forming (they do not result in quicker resolution of an existing cyst). Though observation is preferred, it is important to recognize that large functional cysts pose an increased risk for ovarian torsion [21].

References