Abnormal Uterine Bleeding in the Adolescent Patient

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Common Clinical Scenario: *A 14-year-old female presents to your office with the complaint of menses "every 2 weeks" for the past few months. She states that her periods started at age 13, and after her first period she did not have another menses for 3 months. After her second menstrual cycle, her periods started "happening all the time." She notes that menses sometimes come once a month, sometimes "skip a month," and lately have been coming twice a month. Her menses last for 5 days, during which she changes 3 pads per day. She is in good health, with no medical problems or history of surgeries. Urine pregnancy test is negative.*

Menstrual disorders are among the most common complaints of adolescents. This is in part because adolescents and their families often have difficulty understanding what normal cycles or patterns of bleeding are and in part because there is considerable menstrual cycle variability in the adolescent years.[1] Regular ovulatory menstrual cycles occur every 21 to 35 days and last up to 7 days, with an average blood loss of 25 to 69 mL.[2] Many patients complain of menstrual problems that actually fall within normal variations. In the first year after menarche, 50% of cycles are anovulatory, but 80% still fall in the normal range for duration. By the third year of menarche, 95% of menstrual cycles fall into this range.[3] Charting the menstrual flow on a calendar can be helpful to clarify normal versus abnormal cycles. Cycles that fall outside of the norm should be evaluated for underlying pathology.

While there are multiple causes for abnormal uterine bleeding in adolescents, the most likely cause is dysfunctional uterine bleeding (DUB) due to an immature hypothalamic-pituitary-ovarian (HPO) axis, causing anovulatory cycles and irregular bleeding.[4] Before the diagnosis of immature HPO axis can be assumed, more serious disorders must be ruled out (Table).[5,6] While there are numerous etiologies for abnormal uterine bleeding in the adolescent, this article will concentrate on the evaluation and management of DUB in the adolescent female.

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FOCUSPOINT

Many patients complain of menstrual problems that actually fall within normal variations.

EVALUATION

When an adolescent presents with the complaint of DUB, she should be asked detailed questions about her menstrual history, including the age at menarche and the timing, duration, and quantity of her uterine bleeding. The presence of cramping and/or clots can be useful information as well.

Review of systems should address psychosocial stressors, weight changes, eating and exercise habits, medications, and symptoms of hyperandrogenism. Family history of bleeding disorders and menstrual history is imperative, as is a sexual history.[7]

Physical examination should include vital signs and evaluate for signs of hyperandrogenism and bleeding. The Sexual Maturity Rating scale should be determined to be at the appropriate stage for the patient's age. The nipples should be assessed for discharge. In most patients, especially those who are not sexually active, an internal pelvic exam is not necessary to evaluate the pelvic anatomy. In such patients, an ultrasound may be sufficient to evaluate for pelvic pathology. If a pelvic exam is absolutely needed in cases of massive bleeding, trauma, or suspected congenital anomolies, one can be performed under anesthesia. Sexually active

TABLE. Causes of Abnormal Uterine Bleeding in the Adolescent[5,6]

Anovulation

Bleeding associated with pregnancy
- Abortion (threatened or incomplete)
- Ectopic
- Retained products of conception

Coagulation defects

Congenital malformation of the uterus

Endometriosis

Exercise-induced amenorrhea

Hyperprolactinemia

Infections
- Condyloma of the cervix/vagina
- Pelvic inflammatory disease
- Vaginitis/cervicitis (trichomonas/gonorrhea)

Medications
- Anticoagulants
- Chemotherapy drugs
- Danazol
- Exogenous steroids
- Oral contraception (eg, midcycle bleeding or continuous use)
- Progestins (eg, Depo-Provera)
- Spironolactone

Ovarian failure

Pathology involving the reproductive tract
- Endometrial hyperplasia/carcinoma
- Endometrial polyp

Systemic diseases
- Adrenal insufficiency
- Chronic renal disease
- Cushing syndrome
- Diabetes mellitus
- Late-onset congenital adrenal hyperplasia
- Liver disease
- Polycystic ovary syndrome
- Systemic lupus erythematosis
- Thyroid abnormalities

Trauma

Tumor
- Ovarian cyst or tumor
- Sarcoma botryoides

females should receive testing for sexually transmitted infections.

Laboratory work-up of adolescents with abnormal uterine bleeding should include a pregnancy test, regardless of whether the history reveals sexual activity. Once pregnancy has been ruled out, the practitioner should consider additional lab work to rule on other diagnoses in the differential based on the presenting signs and symptoms. A complete blood count may be helpful to evaluate for anemia. ACOG recommends that all patients younger than 18 who present with abnormal uterine bleeding be screened for coagulation disorders, particularly von Willebrand disease, as this disorder has a prevalence of 1% and is the most common disorder that causes menorrhagia at menarche.[1,6] Screening for such disorders should include a partial thromboplastin time, prothrombin time, and assessment of platelet function, plasma von Willebrand factor (VWF) antigen, and plasma VWF activity (ristocetin cofactor activity).

As well, in any patient with abnormal uterine bleeding, thyroid function tests should be considered, as this can be a common cause of abnormal uterine bleeding. In patients with headaches or nipple discharge, prolactin testing is warranted. In those with signs of polycystic ovary syndrome or insulin resistance, the practitioner should consider appropriate lab testing, including testosterone, insulin, and glucose levels. Evaluating the adrenal glands to look for abnormalities in suspected cases may be warranted as well.

MANAGEMENT

After other diagnoses have been ruled out, the management of DUB can occur as an outpatient in the majority of cases. Occasionally, however, hospitalization is required due to hemodynamic instability.

Mild Uterine Bleeding (Hgb >12 mg/dL)
Management of mild abnormal bleeding consists of observation and reassurance. If hemoglobin (Hgb) concentration is normal (>12 mg/dL), girls with mild DUB should be asked to keep a menstrual calendar and can be given the option to avoid treatment with hormonal therapy. They should follow up in 3 to 6 months, unless bleeding becomes more severe, in which case they should be seen acutely.

Moderate Uterine Bleeding (Hgb 10-12 mg/dL)
Moderate DUB is characterized by moderately prolonged or frequent menses every 1 to 3 weeks.[8] Menstrual flow is moderate to heavy. Mild anemia (Hgb 10-12 mg/dL) is often present but without signs of hypovolemia or hemodynamic instability. Moderate DUB can usually be managed in the outpatient setting. The treatment typically involves hormonal therapy to stabilize endometrial proliferation and shedding. The choice of agent(s) depends, to some extent, upon how heavily the patient is bleeding.[9] Girls with moderate DUB should be provided with iron supplementation.

There is a paucity of data from randomized trials regarding the treatment of DUB in adolescents. Nonetheless, there are a variety of regimens that appear to be equally effective. Patients who have complaints of heavier bleeding may have a better response to oral contraceptives (OCs) that have a combination of estrogen and progestin rather than to progestin-only preparations, as estrogen provides hemostasis. Thus, one option is to use monophasic contraceptive pills in the traditional fashion of 1 per day. Another regimen states that OC pills be taken 3 times per day until the bleeding ceases (usually within 48 hours), then tapered to twice daily for 5 days, and then decreased to once daily to complete 21 days of hormone therapy.[9]

Once the 21-day course is finished, patients start another pack and take 1 pill per day in the typical fashion. If bleeding recurs when the dose is decreased to once per day, twice-per-day dosing may be necessary for an extended period of time. Close follow-up is essential during twice-per-day dosing. High-dose estrogen therapy can cause nausea, which may result in noncompliance. Antiemetic therapy (ie, promethazine or ondansetron) is often required before each dose of the pill.[8] Progestin-only therapy is an alternative for girls with moderate DUB who cannot tolerate, dislike, or have a contraindication to estrogen therapy.

Severe Uterine Bleeding/Menorrhagia (Hgb <10 mg/dL)
Excessive menstrual bleeding is diagnosed as menses more often than every 21 days or bleeding resulting in a loss of more than 80 mL of blood.[2] Menstrual flow requiring changes of menstrual products every 1 to 2 hours is considered excessive, especially if the flow lasts longer than 7 days.[1] While it may be due to anovulation, this type of bleeding may be associated with a bleeding disorder, and work-up for this should ensue.

FOCUSPOINT

Menstrual flow requiring changes of menstrual products every 1 to 2 hours is considered excessive, especially if the flow lasts longer than 7 days.

Hospitalization is necessary for patients who are hemodynamically unstable, who have low Hgb concentration (<7 mg/dL), or who have symptomatic anemia.[8] Heavy active bleeding and Hgb lower than 10 mg/dL are also considered by some to be an indication for hospitalization. If the Hgb is between 8 and 10 mg/dL, *and* the patient is hemodynamically stable, *and* the patient and family are reliable *and* can maintain close telephone contact, home management may be possible with daily monitoring.

The need for blood transfusion should be individualized, and it should be administered as deemed necessary by the clinician based on the patient's initial blood count, amount of bleeding, and any other comorbidities.

Girls who require hospitalization for DUB should undergo evaluation for a bleeding disorder. Coagulation disorders are the second most common cause of menorrhagia in adolescents and have been noted in 20% of adolescents hospitalized with menorrhagia.[10] Blood for evaluation of bleeding disorders should be obtained before administration of blood products or estrogen (exogenous estrogen may elevate VWF into the normal range).[8] Assessment should include a complete blood count with platelets, platelet function analyzer, examination of the peripheral blood smear, prothrombin time, activated partial thromboplastin time, plasma VWF antigen, plasma VWF activity (ristocetin cofactor activity), factor VIII activity, blood group typing (blood group O is associated with lower levels of VWF), and thyroid stimulating hormone. Any underlying disorder noted should be promptly treated. Consultation with a hematologist is recommended.

FOCUSPOINT

Long-term management depends on the anemia and the desire for contraception.

For patients who can tolerate oral intake, therapy typically includes a monophasic combination OC pill with 50 µg estradiol and 0.5 mg norgestrel (eg, Ovral, Ogestrel) or 50 µg estradiol and 1 mg norethindrone (eg, Ovcon 50), administered according to various schedules. A common schedule is to take it 4 times a day until bleeding is controlled, then wean to 3 times daily for 3 days, and then to twice daily to complete a 21-day course of pills.[8] Then the patient starts a new pack of pills (without using the placebo pills).

For patients who can take oral medications but in whom estrogen is contraindicated (eg, those with thromboembolic disease, estrogen-dependent tumors, or hepatic disease), a progestin such as norethindrone acetate (5 to 10 mg daily) or micronized progesterone (200 mg before bedtime) can be used.

In patients who need intravenous treatment, conjugated equine estrogen (Premarin) may be used. In cases of severe menorrhagia unresponsive to 24 hours of hormonal therapy or in those with platelet dysfunction, nonhormonal hemostatic drugs may be used. These include the antifibrinolytic compounds, aminocaproic acid or tranexamic acid, or desmopressin, which is classically used for the treatment of von Willebrand disease.[11] Treatment is continued for approximately 8 hours or until the bleeding has been controlled. Once the bleeding has been controlled and the patient can tolerate oral intake, she should be transitioned to oral hormonal therapy for maintenance.

FOLLOW-UP AND LONG-TERM CARE

After treatment is initiated, patients should be seen at regular intervals to ensure that their bleeding profile has improved to their satisfaction and that they are tolerating any medicines that may have been started. Long-term management depends on the anemia and the desire for contraception. Most experts recommend continuing hormonal therapy for at least 6 months. After therapy is discontinued, the patient should still be followed to ensure regulation of menstruation.

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