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Abnormal Uterine Bleeding in Adolescents

Developed by Sarah Moor and Dr. Amanda Kallen for PedsCases.com.
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Introduction

Hello everyone, my name is Sarah Moor and I am a third-year medical student at Yale School of Medicine. In this podcast we will present an approach to abnormal uterine bleeding (AUB) in the adolescent population. This podcast was developed with Dr. Amanda Kallen who is an Assistant Professor of Obstetrics and Gynecology at Yale School of Medicine and member of the Reproductive Scientist Development Program.

Learning Objectives

The Objectives of this podcast are to:

1) Review the definition of abnormal uterine bleeding.
2) Generate an organized differential diagnosis for abnormal uterine bleeding
3) Review investigations and management for abnormal uterine bleeding in adolescent patients compared to adult patients

The patient case we will be discussing today is that of a 16 y.o. female, G0P0 who presents to the clinic complaining of a heavy period. She describes a two-year history of heavy menstrual bleeding. She has to change her tampon frequently, and often has to leave class to change her tampon or pad. Her period lasts one week. . She decided to come into the clinic today because she says she is fed up with her heavy period.

Definitions

Menarche is defined as the first occurrence of menstruation. The average age for menarche is 12-13 years old with bleeding typically lasting between 3 and 8 days. The normal interv al between menses in adolescents is variable and can range between 21 and 45 days(1).

Abnormal uterine bleeding is commonly reported during adolescence and is defined as bleeding that is abnormal in duration, volume, frequency and/or regularity(2). Some important definitions of AUB are as follows:

- **Acute AUB** is defined as an episode of bleeding that is of sufficient quantity to require immediate intervention to prevent further blood loss.
- **Chronic AUB** means that these symptoms have been present for the majority of at least 6 months.
- **Heavy menstrual bleeding (HMB),** formerly called menorrhagia, is defined as excessive menstrual blood loss that affects the quality of a patient's life, which typically correlates to more than 80 mL per menstrual cycle. Quantifying the blood loss seen in heavy menstrual bleeding is not necessary as the most important piece to assess is the impact the HMB has on a patient's quality of life. Heavy menstrual bleeding is the most common gynecologic complaint in adolescents admitted to the hospital(2).
- **Irregular menstrual bleeding**, formerly referred to as metrorrhagia, is defined as varying lengths in menstrual cycle bleeding-free intervals longer than 20 days within a 90 day period(3).
- **Prolonged menstrual bleeding** is defined as periods that regularly exceed eight days in length (2).
- **Infrequent menstrual bleeding** describes 1-2 episodes of menses over a 90 day period while frequent menstrual bleeding is more than 4 episodes of menses over 90 days(2).
- **Amenorrhea,** or absent menstrual bleeding has been covered in detail in a separate podcast.

History

A detailed history is important in the assessment of abnormal uterine bleeding, particularly if the patient is less comfortable discussing menstruation. In adolescence, a history should be taken with and without the parents. Parents may help provide some details, but it may also be difficult to get a complete history with parents present due to the sensitive nature of taking a sexual and menstrual history. A detailed history should include menstrual history (including age of menarche, regularity, duration, number of pads/tampons per day), sexual history, past medical history, and review of systems, particularly probing for questions related to bleeding, such as easy bruising or bleeding from the gums.

Back to patient case:

So let's return to our patient case to put all of this in context. As a reminder, the patient is a 16 y.o. female, G0P0000 who presents to the clinic complaining of a heavy period.

Menarche was at age 12; menses were sometimes irregular until she was 13 years old. Then menses became heavy - lasting upwards of a week and soaking through heavy pads and tampons every one hour. She complains of fatigue and expresses frustration with her heavy

menstrual bleeding. She has not noticed any clots or felt any gushing sensations. She endorses bruising easily and bleeding from her gums when she brushes her teeth.

You probe her specifically about what she means when she says her periods were irregular for the first year, as this can mean different things to different people. She elaborates that the interval between her periods would often change and she would occasionally skip her periods during this time. Her past medical history only consists of allergic rhinitis, she has no previous surgeries and takes no medications. In terms of social history, she lives with her mother and her younger brother. She has never been sexually active and she denies any alcohol or drug use. She is not aware of any health concerns in her mother's family, but says she does not know the family history on her father's side.

Initial Assessment and Physical Examination

The initial approach to a patient with heavy menstrual bleeding is to determine whether this is an acute problem causing hemodynamic instability that requires immediate intervention. Physical exam should consist of careful assessment for the signs of systemic causes. Assessment of the patient's weight can indicate the likelihood of PCOS. Examining the thyroid can point to hyperthyroidism as a contributing factor. Careful examination of the skin is important to look for signs of anemia such as pallor, signs of coagulopathies such as easy bruising or petechiae, and signs of anovulatory cycles such as hirsutism(3). Additionally, a thorough abdominal exam is essential to assess for the presence of any masses or hepatosplenomegaly(3). A pelvic examination while routinely done in adults, requires more careful consideration in adolescents as this exam tends to be more sensitive for this age group, particularly in sexually inexperienced patients. Structural causes of AUB are very rare in this age group, therefore a pelvic exam may be deferred in these cases until after a trial with medical therapy(2). Transabdominal ultrasound may be helpful in adolescents who have not been sexually active for evaluation of the rare structural causes of AUB in adolescents(3).

Patient Case

General: Well-developed young woman, pale-appearing
Vitals: HR: 65 RR: 12 BP:115/70, 98% O2 sat on RA
Thyroid Exam: Normal sized thyroid, no goiter
Skin: No signs of rashes or petechiae, many bruises on both her upper and lower extremities
CV: RRR, no murmurs, rubs or gallops
Pulmonary: clear to auscultation bilaterally
Abdominal Exam: Soft, nondistended, nontender, no palpable masses or hepatosplenomegaly
Pelvic Exam: deferred

For this patient, her vital signs are within normal range indicating that she is hemodynamically stable so her HMB does not require immediate intervention. You note the pallor of this woman indicating that she may be anemic and bruising on upper and lower extremities pointing towards a bleeding disorder.

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Differential Diagnosis

When developing our differential, we want to first determine if this is pregnancy or non-pregnancy related bleeding, so it is important to obtain a urine pregnancy test. In our patient, the urine pregnancy test is negative, so this represents non-pregnancy related abnormal uterine bleeding.

There is a broad differential for abnormal uterine bleeding in adolescence. International Federation of Gynecology and Obstetrics (FIGO) begins with the classification system 1 to determine if abnormal uterine bleeding is present. When we think in broad categories for a differential diagnosis we can think of infectious causes, bleeding disorders, endocrine disorders, vaginal abnormalities, cervical problems, uterine problems, ovarian problems, endometriosis, trauma, foreign body, medications and systemic disease.

For causes of abnormal uterine bleeding we use the acronym PALM-COEIN – polyps, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified. In adolescents, structural problems are very rarely the cause of abnormal uterine bleeding, this makes the first half of our acronym PALM, move lower down on our differential.

The COEIN part of our acronym then forms the basis for our differential: coagulopathies, such as von Willebrand disease. Ovulatory dysfunction, namely anovulatory cycles, is our O in the acronym and is the most common cause of heavy menstrual bleeding in adolescents as the hypothalamic-pituitary-ovarian axis can still be immature (2). Ovulatory dysfunction is characterized by irregular, prolonged, and heavy menstrual bleeding. In adolescents, anovulatory dysfunction is physiologic as the HPO axis continues to mature, but later in life it can be pathologic and is often associated with endocrine abnormalities associated, such as PCOS. In normal menstruation, the corpus luteum is formed after ovulation and begins releasing progesterone which stabilizes the endometrium. In anovulatory cycles, the corpus luteum is not formed so there is a decrease in progesterone production which leads to continued endometrial proliferation. However, this endometrial tissue is unstable and tends to shed irregularly. In addition without progesterone, estrogen is high and unopposed leading to vascular fragility in the endometrium such that a greater volume of blood is lost (4). Endometrial causes, such as endometrial hyperplasia, are important to keep on the differential, particularly in patients with a personal history of multiple years of untreated anovulatory bleeding and a family history of endometrial, ovarian, breast or colon cancer (5). Iatrogenic in this case is unlikely as the patient is not taking any medications or reporting any previous surgical history. Not otherwise classified keeps us mindful that this acronym is not all-encompassing and to keep our differential open to changes depending on the findings of the workup.

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Investigations

Workup for heavy menstrual bleeding should include human chorionic gonadotropin, complete blood count, peripheral blood smear, iron studies, prothrombin time, activated partial thromboplastin time and fibrinogen(2). If you are concerned about bleeding disorders, such as von Willebrand Disease, then you would also test for plasma von Willebrand factor (vWF) antigen and perform functional tests for vWF and factor VIII activity.

When the labs return, her hemoglobin is mildly decreased, blood smear shows microcytic, hypochromic RBCs. Iron studies reveal low serum iron and ferritin levels and a mildly elevated TIBC. She has a normal PT, but slightly prolonged aPTT. The von Willebrand panel returns positive indicating that this patient has von Willebrand Disease.

Management

Treatment of HMB focuses on treating the underlying etiology, relieving anemia and associated symptoms and achieving regularity in menstrual cycles(2). This patient has signs of iron-deficiency anemia, both clinically with pallor and microcytic anemia with low iron levels on lab results. Therefore, oral iron supplementation should be initiated for this patient(2). Medical therapy must also consider the need for contraception and deliberate counselling should be performed with the patient. The Canadian Pediatrics Society recommends levonorgestrel-releasing intrauterine system as the first line treatment in adolescent patients. It has been shown to be superior to other medical therapies, such as NSAIDs, and has demonstrated to significantly reduce blood loss by causing endometrial atrophy and reducing uterine vascularization(3). Combined hormonal contraceptives and reversible long-acting contraceptives, such as injectable progestin, can also be used for adolescent patients with HMB as they can also reduce blood loss via the same mechanism (3). NSAIDs can also be effective in HMB as they reduce prostaglandin production by inhibiting cyclo-oxygenase, thereby promoting vasoconstriction in the uterus to reduce bleeding. However, they are contraindicated in patients like ours who have coagulation disorders. Lastly, tranexamic acid is an antifibrinolytic agent that prevents fibrin degradation by reversibly binding to plasminogen. Since they do not change blood coagulation parameters, they may be used in patients with bleeding disorders in conjunction with other medical therapies. Tranexamic acid is taken every 6 hours during menstruation and is shown to reduce the amount of blood loss during menstruation. Danazol and GnRH agonists work by disrupting ovarian steroidogenesis to cause endometrial atrophy, however these agents are rarely recommended in adolescents because of their side effects. Danazol typically leads to weight gain, acne and irritability while GnRH agonists result in the low estrogen associated symptoms such as hot flashes, night sweats and vaginal dryness(3). There are a variety of options for management of HMB in adolescents so clinicians can think critically about what would work best for their particular patient.

That concludes our discussion of the approach to diagnosis and management of heavy menstrual bleeding in adolescents.

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The take home points for this discussion are:

1) Abnormal uterine bleeding encompasses bleeding that differs in duration, volume, frequency or regularity from a patient's baseline. The most common presentation of AUB, particularly in adolescents, is heavy menstrual bleeding.
2) The initial approach to AUB in adolescents is similar to that of adults in that you must determine if this bleeding is occurring in pregnancy or not and whether it is an acute presentation causing hemodynamic instability. However, the approach to gathering this information and to examination in adolescents should be taken more carefully as for adolescents the history and physical exam are particularly sensitive.
3) The underlying etiologies for AUB are described by the mnemonic PALM-COIEN, but structural problems are rare in adolescents so COIEN causes should be prioritized during the workup for AUB in adolescents.
4) Management of AUB prioritizes treating the underlying cause in addition to the use of hormonal and non-hormonal medical therapies to lower the risk of continued heavy bleeding.

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