

Abnormal Uterine Bleeding Can Refer to Serious Health Condition

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Abstract

Normal uterine bleeding is that of the menstrual cycle. In most women, the menstrual cycle lasts about 28 days, with menstrual bleeding 4-7 days. Menstrual cycles shorter than 21 days or longer than 35 days are considered abnormal.

Keywords: menstrual cycle; bleeding; diagnosis; treatment

Introduction

There are many different causes of abnormal uterine bleeding (AUB), and it accounts for majority of gynecological consults with most office visits among peri- and postmenopausal women [1]. Although there is variation within cycles, a normal menstrual cycle typically lasts between 21 and 35 days, lasting an average of 5 days. Traditionally, abnormal uterine bleeding has been described as menorrhagia, metrorrhagia, and menometrorrhagia. These terms are inaccurate because abnormal bleeding patterns are very dependent on a patient's perception of her bleeding.

Causes of abnormal uterine bleeding were categorized to be either due to structural or systemic causes. The acronym "PALM" signifies structural causes. Structural causes include P for polyps, A for adenomyosis, L for leiomyoma, and M for malignancy and hyperplasia. "COEIN" indicates nonstructural or systemic causes. "COEIN" include C for coagulopathy, O for ovulatory disorders, E for endometrial causes, I for iatrogenic, and N for not yet classified.

It can be difficult to assess the extent of the bleeding suffered by an individual woman [2]. Some women who have significant blood loss don't complain of HMB (Heavy Menstrual Bleeding), whereas other women who perceive that they have HMB, do not actually lose all that much blood when assessed quantitatively. For this reason, NICE Clinical Guideline 44 stresses that if the woman feels that her blood loss is excessive, then it is. Measuring the amount of blood lost is regarded as old fashioned and is no longer considered relevant as it has no place in clinical management. Questions which might be helpful when trying to determine the impact of bleeding on the individual woman include enquiring as to whether clots are passed, and whether the patient has to use more than one method of sanitary protection e.g. towels and tampons.

The ultraviolet and the blue components of light have the greatest potential to cause harm [9,10] Using some types of CFLs for long periods of time at close distances may expose users to levels of UV nearing the limits set to protect workers from skin and eye damage. The wavelength of visible light determines its colour, from violet (shorter wavelength) through to red (longer wavelength). The sun emits radiation over the full range of wavelengths, but the earth's atmosphere blocks a lot of UV and infrared radiations [9]. The effect of light on cells depends on the radiation and its wavelength, the type of cell, the chromophore, and the chemical reaction involved [10, 11].

A lifelong history of HMB (since menarche) in association with excessive bleeding during other operations e.g. on tooth extractions, or easy bruising may suggest an



inherited coagulopathy such as von Willebrand's Disease. This is a rare condition, but von Willebrand factor should be checked for if the history is suggestive.

Heavy menstrual bleeding (HMB) is defined as regular cyclic bleeding that is heavy or prolonged and can be caused by any structural abnormality, bleeding disorder, or hyperplasia or malignancy [3]. Intermenstrual bleeding can be caused by endometrial polyps, hormonal contraceptives, endometrial hyperplasia or malignancy, or endometritis. Conditions of the cervix are ruled out prior to endometrial investigations. Irregular bleeding is commonly associated with ovulatory dysfunction secondary to extremes of reproductive age, polycystic ovarian syndrome, and other endocrine disorders.

Menstrual Cycle

Normal menstrual bleeding with ovulatory cycles is spontaneous, regular, cyclic, and predictable and is frequently associated with discomfort (dysmenorrhea) [4]. Deviations from this pattern associated with cycles that are still regular and predictable are most often due to organic disease of the outflow tract. For example, regular but prolonged and excessive bleeding episodes unassociated with bleeding dyscrasias (hypermenorrhea or menorrhagia) can result from abnormalities of the uterus such as submucous leiomyomas, adenomyosis, or endometrial polyps. Regular, cyclic, predictable menstruation characterized by spotting or light bleeding is termed hypomenorrhea and is due to obstruction of the outflow tract as from intrauterine synechiae or scarring of the cervix. Intermenstrual bleeding between episodes of regular, ovulatory menstruation is also often due to cervical or endometrial lesions. An exception to the association between organic disease and abnormal uterine bleeding is the occurrence of regular menstruation more frequently than 21 days apart (polymenorrhea). Such cycles may be a normal variant.

Normal menstrual cycles could last between 21 days and 35 days with a normal duration of 5 days and the first 3 days associated with most blood loss [1]. A normal ovulatory cycle depends on an intact hypothalamus producing gonadotropin-releasing hormone, which then stimulates the anterior pituitary gland to produce follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Estrogen and progesterone production by the ovary depends on the feedback regulation of the gonadotropin hormones. Proliferation of the uterine endometrium and shedding is in response to ovarian production of estrogen and progesterone.

Ovulatory dysfunction typically occurs in adolescents and perimenopausal women causing AUB-O. Physiologic anovulation during puberty due to the immature hypothalamic-pituitary-ovarian axis causes AUB. In the perimenopausal women, anovulation occurs because of abnormal follicular development resulting from reduction of ovarian reserve.

Bleeding

A thorough history and physical examination is essential to evaluate and treat a patient with AUB [1]. Another important question is to determine whether the bleeding episode is acute or chronic. Anovulation or immaturity/dysfunction of the hypothalamic-pituitary-ovarian axis is the most common cause of

AUB in adolescents. Other causes include infection, pregnancy, hormonal contraception, and coagulopathies. It is important to rule out pregnancy in patients who have childbearing capabilities. For patients with risk factors such as obesity and comorbidities associated with endometrial hyperplasia and malignancy, an endometrial biopsy is warranted. Medical conditions such as thyroid disease and prolactinoma require testing in patients with associated medical conditions or symptoms. Laboratory testing needs to be adapted according to the possible cause of AUB in conjunction with a patient's age, acuity of symptoms, and findings on examination.

Abnormal Bleeding

Normal uterine bleeding is the result of cyclic, sequential stimulation of the endometrium by estrogen and progesterone, and occurs after withdrawal of the hormonal effect [5]. This pattern is mimicked pharmacologically by OCs and some HT (hormone therapy) regimens. Abnormal uterine bleeding (AUB) can result from hormonal disturbances such as estrogen withdrawal (estrogen only HT, missed pill) or unopposed estrogen with breakthrough bleeding (anovulatory cycles). Women on progesterone only medications (contraceptive pill, implant, and injections) can have abnormal bleeding patterns due to progesterone withdrawal or breakthrough bleeding.

Anovulatory cycles can be due to many etiologies including PCOS (polycystic ovary syndrome), eating disorders, endocrinopathies (i.e., thyroid disease or prolactinoma), obesity, or the suppression of ovulation from weight loss or excessive exercise. Menstrual abnormalities in women with thyroid disease occur in just under 25% of women with either hyper- or hypothyroidism; the most common complaint in both groups is oligomenorrhea. Anovulation is also seen at the extremes of a woman's reproductive life. In reproductive age women, anovulatory bleeding and hormonal medication use are the most common causes of noncyclic bleeding.

Risk factors for endometrial cancer include age (>40 years), anovulatory cycles, obesity, nulliparity, diabetes, and tamoxifen therapy. Endometrial cancer has been reported in women younger than age 40 years; women with chronic anovulation and obesity who present with AUB should be considered at risk.

Medications such as antipsychotics, anticoagulants, SSRIs, corticosteroids, and tamoxifen have been known to cause AUB, as have certain herbal supplements (e.g., ginseng, ginkgo, soy). Renal, hepatic, adrenal, and thyroid disease and blood dyscrasias may cause AUB. Other causes for AUB include foreign objects, including IUDs, trauma, and congenital (Müllerian) structural abnormalities. Coagulopathies, once thought to be a rare cause of abnormal bleeding, have been shown to be present in 13% of women with heavy uterine bleeding.

Some causes of AUB vary with age. The incidence of structural lesions and endometrial cancer increases with age. Pregnancy-related causes occur during the reproductive years. Anovulation can occur throughout the reproductive years.

Pelvic Exam

The pelvic examination can be a very challenging examination to execute because of associated patient discomfort, anxiety, and embarrassment [6]. The American College of Physicians reported



that 35 percent of surveyed women experience fear, anxiety, discomfort, and/or pain during their pelvic examination. Women who experienced pain with their pelvic examination were found to be less likely to return for their visit than those who did not have a negative experience. Another study sought to address suggestions to improve the examination process from patients that had negative experience. Explaining each step of the examination in advance, providing information about the reproductive organs, warming the instruments, increased gentleness, and maintaining eye contact have been suggested by the patients as ways to improve the overall experience of the basic GYN examination. All of these areas can be addressed with simulation training.

The pelvic examination is conducted to screen for pathology, with the examination made of three elements: inspection of the external genitalia; speculum examination of the vagina and cervix; and bimanual examination of the adnexa, uterus, ovaries, and bladder and sometimes a rectovaginal examination.

Teaching the pelvic examination portion of the basic GYN exam can start with an overview of the necessary materials. Reviewing the various swabs, Pap smear collection devices, bacterial wound culture, viral culture container, review of various specula (pediatric, nulliparous, multiparous speculum), and urine culture collection are some of the many various useful materials that a learner may not have seen before. Becoming familiar with these materials, recognizing what they look like, and indications and uses of collecting samples may be very helpful for the learner and lead to a more efficient and streamlined exam.

Having the opportunity to be instructed by a standardized patient on proper techniques for performing pelvic examinations is ideal as the anatomy is real and the feedback is immediate. Standardized patients are often utilized as both instructors and patients for these sessions. The standardized patient is able to talk the learner through proper bedside manner and work through a pelvic examination and bimanual examination usually with an instructor present to further provide brief lecture to the students prior to the examination. Often, the standardized patient provides the learner with feedback and helpful critiques to allow for improvement in clinical skills as both the content expert and patient.

Diagnosis

AUB is broadly defined as any uterine bleeding that occurs outside the parameters of normal menstruation during the reproductive years [7]. It includes bleeding originating from either the uterine fundus or cervix and does not include bleeding that originates in the lower genital tract (i.e., the vagina or vulva). However, these causes can be difficult to distinguish clinically. Therefore, both of these origins should be considered in all patients presenting with bleeding from the uterus. It can be further characterized in terms of volume, duration, frequency, and regularity. AUB can be classified as acute or chronic. Chronic abnormal uterine bleeding is bleeding that has occurred for at least 6 months.

The terms “menorrhagia” and “metrorrhagia” have now been replaced by more descriptive terms, including “heavy menstrual bleeding” and “intermenstrual bleeding.” A new classification system is also being used to classify AUB according to the etiology. The acronym PALM COEIN classifies the causes of AUB into structural abnormalities and nonstructural abnormalities.

In making the diagnosis, it is important not to assume the obvious [8]. A careful history and pelvic examination are vital. The possibility of pregnancy must be considered, as well as use of oral contraceptives, IUDs, and hormones.

Another important evaluation during the workup of abnormal uterine bleeding is to decide whether the bleeding is associated with ovulatory or anovulatory cycles. In ovulatory cycles, the bleeding might be due to a persistent corpus luteum cyst or short luteal phase. In anovulatory cycles, the endometrium outgrows its blood supply, partially breaks down, and is sloughed in an irregular manner. In these cases, an organic cause of anovulation must be excluded (eg, thyroid or adrenal abnormalities). Conversion from proliferative to secretory endometrium (by combined oral contraceptive pills or progesterone in the luteal phase) corrects most acute and chronic bleeding problems.

Improved diagnostic techniques and treatment have resulted in decreased use of hysterectomy to treat abnormal bleeding patterns. If pathologic causes (eg, submucous myomas, adenomyosis) can be excluded, if there is no significant risk for cancer development (as from atypical endometrial hyperplasia), and if there is no acute life-threatening hemorrhage, most patients can be treated with hormone preparations or minimally invasive procedures, which are considered as alternatives to hysterectomy. Myomectomy (hysteroscopic, laparoscopic, or conservative) can be suggested for treatment of myoma if the patient wishes to retain her childbearing potential. Endometrial ablation and endometrial resection may offer successful outpatient and inoffice alternatives.

In the differential diagnosis of abnormal bleeding, nongynecologic causes of bleeding (eg, rectal or urologic disorders) must be ruled out, because patients may have difficulty differentiating the source of bleeding. Gynecologic and nongynecologic causes of bleeding may coexist. Systemic disease may cause abnormal uterine bleeding. For example, myxedema usually causes amenorrhea, but less severe hypothyroidism is associated with increased uterine bleeding. Liver disease interferes with estrogen metabolism and may cause variable degrees of bleeding. Both of these conditions are usually clinically apparent before gynecologic symptoms appear. Blood dyscrasias and coagulation abnormalities can also produce gynecologic bleeding. Patients receiving anticoagulants or adrenal steroids may expect abnormalities. Extreme weight loss due to eating disorders, exercise, or dieting may be associated with anovulation and amenorrhea.

Exclusion of all possible pathologic causes of abnormal bleeding establishes the diagnosis of dysfunctional uterine bleeding (nearly 60% of cases). Dysfunctional bleeding occurs most commonly at the extremes of reproductive age (20% of cases occur in adolescents and 40% in patients over age 40 years). Management depends on the age of the patient (adolescent, young woman, or premenopausal woman).

Disfunction

Dysfunctional uterine bleeding (DUB) is a term that refers to excessive uterine bleeding in cases in which no uterine pathology can be identified and is therefore a diagnosis of exclusion [7]. Due to the development of a greater understanding of AUB and the availability of more sophisticated diagnostic techniques, this term is less frequently used today.

In many cases that would have been referred to as DUB in the



past, modern diagnostic techniques identify either uterine or systemic pathologies that (1) result in anovulation (e.g., hypothyroidism), (2) result from anovulation (e.g., endometrial hyperplasia or carcinoma), or (3) coexists with anovulatory bleeding but may or may not be causal (e.g., leiomyomata). Bleeding unrelated to uterine pathology can usually be determined to be a result of chronic anovulation (polycystic ovary syndrome [PCOS] and related conditions), exogenous steroid hormones (contraceptives or hormone replacement therapy), or hemostatic disorders (e.g., von Willebrand disease).

Treatment is most likely to be effective when specific causes of AUB can be identified. Since the term “DUB” is used to refer to widely divergent causes of AUB, a national consensus group recently concluded that this term is unlikely to improve diagnosis or treatment and thus no longer has any usefulness in clinical medicine.

Biopsy

As abnormal uterine bleeding may be the result of benign etiologies, including endometrial polyp, fibroid uterus, or dysregulation of the hypothalamic pituitary axis, the extent of a work up should be dictated by clinical suspicion [9]. This may include biopsy of the endometrial cavity especially in those patients with increased risk for hyperplasia or malignancy (increasing age, postmenopausal status, use of hormone replacement therapy). The American College of Obstetricians and Gynecologists (ACOG) recommends performing endometrial sampling in patients younger than 45 with a history of unopposed estrogen exposure, such as in the obese population or patients with PCOS (polycystic ovary syndrome). Other prompts for sampling may include abnormal endometrial glands seen on routine cervical cancer screening with Pap smear.

Endometrial sampling is typically performed via pipelle biopsy or dilation and curettage. Pipelle biopsy offers an outpatient method of detection of endometrial cancer that may be performed without anesthesia in the office setting, compared with a dilation and curettage which is typically performed in the operating room. There is some evidence that dilation and curettage may be more likely to diagnose those concurrent cancers only subsequently discovered on hysterectomy specimen. Suh-Bermann et al. found those patients who received a diagnosis of atypical endometrial hyperplasia by dilation and curettage preoperatively were less likely to be subsequently diagnosed with endometrial cancer compared with those who received a preoperative diagnosis of atypical endometrial hyperplasia by pipelle biopsy.

Treatment

Effective treatment of heavy bleeding requires determining the cause [10]. A urine pregnancy test should be performed in all reproductive-aged patients with unexplained bleeding as pregnancy-related bleeding is managed completely differently from other causes, and undiagnosed ectopic pregnancy is life threatening. The timing of the bleeding episodes must be determined, as it can help differentiate bleeding from the different causes. The PALM-COEIN system classifies uterine bleeding abnormalities by their pattern and etiology. In this instance, a clinical picture of irregular, unpredictable bleeding episodes is present. Based on the history and clinical findings obtained during

examination of the patient, a picture of abnormal uterine bleeding with ovulatory dysfunction (AUB-O) is most likely. The patient is obese and has clinical signs of androgen excess with hirsutism and acne, making PCOS (polycystic ovarian syndrome) the probable cause of her chronic anovulation. Her history suggests that the problem is longstanding, which is typical for PCOS. Given her uterus was felt to be normal on palpation, a structural problem such as a large myoma is less likely. However, her anovulatory bleeding could be compounded by a small submucosal myoma or endometrial polyp.

Patients with anovulation can have significant bleeding leading to life-threatening volume loss and hemodynamic instability. Patients with heavy bleeding and hypovolemia should have intravenous access for fluid administration and if need be, transfusion. Assessment of blood loss and hemodynamic status of the patient will dictate the need for surgical or medical management. Hemoglobin and hematocrit status should be obtained. Blood products should be cross-matched for patients who have symptomatic hypovolemia or lifethreatening acute bleeding. Patients with lesser bleeding but where transfusion may be necessary should have a type and screen sent. The patient should be hemodynamically stabilized while completing the evaluation and initiating therapy.

Medical management of most nonneoplastic causes of abnormal uterine bleeding is generally prescribed before considering surgery because many symptoms will resolve or managed without surgical intervention [11]. Chronic blood loss due to hypermenorrhea produced by leiomyoma or hyperplasia, can be reduced by the administration of a progestin. A gonadotropin-releasing hormone (GnRH) agonist will result in amenorrhea and is sometimes prescribed prior to planned surgery for leiomyomata. The antiprogestin mifepristone may significantly shrink leiomyomata, but a side effect includes increased risk of endometrial hyperplasia. Dysfunctional bleeding due to chronic anovulation is treated with cyclic progestin therapy, or oral contraceptives. For women who wish to conceive, ovulation induction with drugs such as with clomiphene are prescribed. Control of acute heavy bleeding may be achieved through the use of higher doses of combination oral contraceptives prescribed as one pill four times a day for 3 or 4 days, tapered to one pill a day over one week. Alternatively, intravenous conjugated estrogen, 25 mg every 4 hours, has been used also to control acute bleeding. Such a regimen must be followed by a progestin to prevent additional irregular bleeding at a later time. Following control of acute bleeding, maintenance therapy with an oral contraceptive is recommended. Another strategy for maintenance includes placement of an intrauterine device (IUD) containing levonorgestrel resulting in amenorrhea in about 25% of women and light menses in the remainder. In the absence of identified intrauterine pathology, hypermenorrhea associated with ovulatory cycles can be ameliorated with nonsteroidal antiinflammatory drugs.

Conclusion

Normal uterine bleeding is that of the menstrual cycle. Any other vaginal bleeding is abnormal. Physician advice should be sought whenever abnormal vaginal bleeding occurs, especially if pregnancy is in progress. Some minor problems can be solved on their own. If this problem persists for a long time, neglect can lead to worsening of the condition. If the bleeding is accompanied by



pain, nausea, dizziness, fever, it may mean a more serious health condition and require urgent medical intervention.

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