Detection and management of dysfunctional uterine bleeding

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ABSTRACT

Dysfunctional uterine bleeding is best defined as vaginal bleeding without an apparent organic cause in a patient who is not taking the oral contraceptive pill. It is important to exclude the abnormal bleeding associated with contraceptive pill ingestion as the evaluation and treatment of this is different from that of patients with DUB. Dysfunctional uterine bleeding is a very common problem during the two extremes of a female's reproductive life. This is due to the frequent anovulatory cycles during this time. Dysfunctional uterine bleeding is a diagnosis by exclusion. It may present with any abnormal pattern of uterine bleeding although most commonly it is bleeding which is excessive, either in amount, duration or frequency. Finland had demonstrated that in the first 2 years after menarche, 55-82% of cycles was anovulatory. However, some of these girls may still have regular menstrual bleeding. It has been postulated that the group of adolescents with DUB may be due to a delayed maturation of normal negative feedback cyclically. The underlying etiology of this problem in the adolescent age group is thought to be anovulation secondary to hypothalamic-pituitary dysfunction. Unopposed fluctuating levels of estrogen result in unregulated endometrial growth with irregular shedding leading to bleeding episodes of varying severity. The bleeding pattern is heavy, prolonged and irregular bleeding. The management of DUB depends on the severity of the bleeding and the gynecological age of the girl.

Key words: Dysfunctional uterine bleeding, detection, management

INTRODUCTION

During active reproductive life, the normal monthly cyclic shedding and regrowth of the endometrium is a finely balanced mechanism. It is controlled by the rise and ebb of pituitary and ovarian hormones, not only in regulated, absolute amounts, but also in carefully integrated, relative
levels. This finely adjusted proliferation of a new endometrial mucosa each month is subject to many aberrations that cause either hyperplasia or atrophy of the endometrium.\(^{1,2,3}\)

By far the most common problem is the occurrence of excessive bleeding during or between menstrual periods. The causes of abnormal bleeding from the uterus are many and vary among women of different age groups. In some instances, bleeding is the result of a well-defined organic lesion such as leiomyoma, carcinoma, or polyp, but the largest single group is so-called dysfunctional uterine bleeding (DUB). This is defined as abnormal bleeding in the absence of an organic lesion of the endometrium or uterus.\(^{1,2,4,5,6,7}\)

In most instances, dysfunctional bleeding is due to the development of the progestational phase that regularly follows ovulation.

**ETIOLOGY**

DUB is defined as abnormal bleeding in the presence of a functional disturbance rather than an organic lesion of the endometrium.\(^{1,3,4}\)

In most instances, dysfunctional bleeding is due to the occurrence of an anovulatory cycle, which results in excessive and prolonged estrogenic stimulation without the development of the progestational phase that regularly follow ovulation.

Less commonly, lack of ovulation is the result of an endocrine disorder, such as thyroid disease, adrenal disease, or pituitary tumors, a primary lesion of the ovary, such as a functioning ovarian-tumor or polycystic ovaries.

Generalized metabolic conditions, such as marked obesity, severe malnutrition, or any chronic systemic disease in most female patients may show signs of DUB, however anovulatory cycles are unexplainable, probably occurring because of subtle hormonal unbalancing. Anovulatory cycles are most common at menarche and premenopausal period.\(^{1,2,3,8,9}\)

**DETECTION**

In the first few days directly following cessation of menstruation, the early proliferative phase is characterized by a thin, relatively homogeneous endometrium. Under low power magnification it is evident that the glands are simple and straight, leading directly from the base to the surface. In cross section, therefore, it is unusual to cut one gland in more than one plane, so that the round isolated circles of glandular epithelium are scattered widely in a dense stroma. Under high-power magnification an occasional mitosis may be seen in the low columnar epithelial cells. A similar picture is found in prepuberal or postmenopausal endometrium, except that the endometrium is even thinner, consisting only of the basal layer resting on the myometrium, and the glands are whole inactive, the shrunken nuclei are pyknotic and no mitoses appear to be present.\(^{2,10}\)

The late proliferative stage is much thicker, giving evidence of marked growth in glands and stroma. A low-power view discloses the tortuosity of the glands, and their corkscrew convolutions are sectioned many times in the midportion of the endometrium, providing the explanation of the term “spongiose layer”. The stroma cells of the superficial layer may be separated by edemic fluid. Mitoses are frequently seen under high power. The epithelium is higher and more columnar, and the nuclei are at different levels in the cells. This is a period of maximum regenerative activity corresponding to the 12 to 14th day of the cycle.

Within 2 or 3 days after ovulation, the early signs of the secretory phase induced by progesterone are clearly visible. The endometrium shrinks slightly in thickness, as the edema of the superficial is lost. In the epithelial glands the nuclei are now rounded and arranged more or less in line in the middle of the cell. The cytoplasm of these cells is condensed toward the lumen by the accumulation of glycogen rich secretion basally, but in vacuoles. Mitoses are less common and disappear entirely about day 20th of the cycle (midsecretory phase).\(^{2,10}\)

From day 21 through day 25 the endometrium is normally in active secretion. Under low-power magnification edema is now grossly apparent in the spongiose layer, so that the uterine mucosa reaches a maximum. The glands take on a distinctive jagged or saw-toothed appearance.

Higher magnification reveals that the round nuclei have now sunk to a basal location, while secretions form bubbles at the luminal margin which
were disgorged into the glands lumen and leave the impression of a frayed and shaggy cellular edge.\(^\text{(3,5)}\) Arterioles are found to be cut in several places, exhibiting a major increase in growth and tortuosity. Capillaries are prominent in the superficial and contiguous stromal cells are first noted to become swollen and contiguous by pale staining.

Through the last 2 or 3 day (late secretory phase) of the cycle before the onset of menses, regressive changes are found to coincide with decrease and, finally cessation of function of the corpus luteum. Endometrial intracellular edema is for the most part resorbed, causing shrinkage in total thickness of the endometrium. Superficially, the stroma cells accumulate cytoplasm in a dense layer called predecidue. The sectioned glands are widely dilated and filled with secretion and cellular debris. The glandular epithelium appears inactive, the cells are low columnar or cuboidal and the nuclei are often pyknotic. Venules and sinusoidal spaces engorged with blood cells become common, and with impending menstruation an extensive diapedesis of red and white blood cell is seen in the stroma.

DUB and failure of ovulation result in prolong, excessive endometrial stimulation by estrogens, under these circumstances, the endometrial glands undergo mild architectural changes, including cystic dilatation. Unscheduled break down of the stroma may also occur (anovulatory menstruation), with no evidence of the endometrial secretory activity.\(^\text{(2,3)}\)

**HISTOPATHOLOGICAL CHANGES**

The cyclic changes of the endometrium are regulated and controlled by the hormonal secretions of the ovary. When ovulation fails to occur an inadequate amount of progesterone is secreted, while estrogen continues unabated. Consequently, the endometrial changes recognized as the prostetional or secretory phase of the cycle do not take place. Under the constant stimulus of estrogen, the proliferative phase persists, and this growth phase sometimes but not always becomes exaggerated to develop into endometrial hyperplasia.

The characteristic microscopic changes of such endometrial hyperplasia are recognizable in the epithelial glands, the endometrial stroma and the vascular architecture. The glands often show irregular cystic dilatation, and these areas are lined with low cuboidal epithelium. In long-standing cases the size of the glands and their lumene varies to a great extent. This causes a characteristic pattern of tissue and holes, which has been called Swiss cheese type. In other regions or cases, adenomatous buds or pockets with heaped-up epithelial lining may appear. The overgrowth in both glands and stroma and the mitotic activity in the hyperplastic endometrium are explainable by persistent estrogen stimulation. The capillary network is prominent; venous lakes are evident and spiral arterioles are thick-walled and numerous. These adenomatous changes may, at times, be so extensive and may differ from the normal or hyperplastic endometrium by such enormous proliferation that it becomes difficult to differentiate.

Endometrial hyperplasia is, however, by no means the only cause of abnormal regular or irregular uterine bleeding, which can occur in any stage of the mucosa, even from an atrophic organ. Lacking the knowledge acquired in the past two decades, and faced with this most frequent symptom of gynecological practice, the term functional uterine bleeding had been coined to cover the variety of hemorrhages observed when no organic lesions were detectable.

**DIAGNOSIS**

DUB is a diagnosis by exclusion. The adolescent is not likely to volunteer because of the possibility of pregnancy in most instances. Clinically there are three common types of DUB encountered by the practicing gynecologist. There is regular bleeding in excess of the norm, occurring at the time of the menstrual period, which itself may be regular in timing. This is the commonest form of dysfunctional uterine bleeding and the cycle are usually found to be anovulatory.

There are recurrent episodes of bleeding at other times in the menstrual cycle, but occurring in repeated cycle. This bleeding can occur at mid cycle, or in the premenstrual phase, and the cycle is usually anovulatory when assessed biochemically. The least common form of dysfunctional uterine bleeding is that where an isolated episode of heavy bleeding occurs at any time during the menstrual cycle. These
cycles are usually found to be anovulatory on biochemical assessment. It is only possible to say that an organic cause is not present if clinical assessment, and special investigations have been performed to rule out one and another.

**MANAGEMENT**

The management of DUB in this age group depends on the severity of bleeding and the gynecological age of the girl. It is common to have minor frequent irregular bleeding within the first 2-3 gynecological years (number of years after menarche). If the hemoglobin is normal, explanation to the adolescent and her parents is usually all that is required. She can be instructed to chart a menstrual diary and return for review. However, most times some form of medical treatment with hormones are necessary. Surgical evaluation with dilatation or curettage with or without Hysteroscopy is only necessary in those rare cases where the girl did not respond to medical treatment. In a multicenter retrospective study of adolescent admitted to Canadian hospitals with a primary diagnosis of dysfunctional uterine bleeding only 5 out of 61 patients (8.2%) required dilatation and curettage.\(^{(1,3)}\)

**Improvement of general well-being**

Disturbed general well being is commonly found in these adolescents. Among 234 girls who presented with a problem of DUB in the clinic, 15% weighed 80% or less than their ideal body weight for height. One third of the girls had hemoglobin of less than 11%.\(^{(1)}\) Oral haematinics can be given to build up the hemoglobin level. Adequate rest, sleep and recreation are advised. Reassurance should be given to reduce their stress level about the menstrual irregularity.

**Arrest of acute bleeding**

Most acute bleeding can be managed as outpatient. However, when the severe bleeding is associated with a low hemoglobin (e.g. < 7g%), admission to hospital is required. As the bleeding is anovulatory in nature in most times, an intramuscular injection of pure progesterone or an androgenic gestrogen is required.

The anovulatory cycle is likely to persist for a period of time. Preventive therapy should be continued for another 2-3 months. If contraception is required, the oral contraceptive pill is the best option.\(^{(1,3,9,10,11,12,13)}\) However, in our Asian society where sexual activity is not the social norm among teenagers, cyclical progestogens can be used. This has the added advantage of not suppressing the hypohalamic-pituitary-gonadal axis. Many different regimes have been tried. These include cyclical use from day 5 to day 25, from day 14 to day 28 and from day 16 to day 21. The last two regimes are preferred. The 14 days regime from day 14 to day 28 mimics that of the physiological situation. In the option of using progestogens form day 16 to day 21, no withdrawal bleeding would occur a few days after stopping the progestogen on day 21 if anovulatory cycle have returned, the endometrium would be sustained on the endogenous progesterone that has been produced. This gives some indication on the return of anovulatory cycles so hormonal therapy can be stopped.

**CONCLUSION**

DUB is the most common problem for which women seek medical attention in menstrual function. The probable cause of abnormal uterine bleeding depends somewhat on the age of the patient and the common types of DUB such as failure of ovulation and inadequate luteal phase. The type of anovulatory bleeding is commonly seen soon after the menarche and premenopausal period.

The management of DUB depends on the severity of the bleeding and the gynecological age of the girl. Sometimes medical treatments with hormones are necessary. Oral haematinics can be given to build up the hemoglobin level. Adequate rest, sleep and recreation are advised. Psychological counseling may be required to address adolescent problems such as child-parents relationship, peer pressure, sexuality and teenage pregnancy. As the bleeding is anovulatory an intra muscular injection of pure progesterone or an androgenic can be given.

Abnormalities of menstruation are only symptoms and do not describe pathological condition. Before any treatment is considered, the pathological cause must be determined.
References


