

ABNORMAL UTERINE BLEEDING IN ADOLESCENT FEMALES

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Abstract

Abnormal uterine bleeding is a possibly severe condition which appears in the first years of reproductive activity. The etiology is very complex, with anovulation being the most frequent cause. The diagnosis is difficult and has to be very thorough and quick. The therapy must commence during the diagnosis and must be in relationship with the etiology, with the severity of the case and sometimes requires interdisciplinary work.

Key words: abnormal uterine bleeding, adolescence, hormonal treatment

Introduction

Abnormal uterine bleeding, which is heavy, prolonged or frequent bleeding of uterine origin causing various degrees of anemia, is a condition that appears relative often in adolescence, being sometimes a very severe disease even a life threatening condition. In the first years after the menarche the menstrual cycle is characterized by a high grade of irregularity. This is due to the immaturity of the hypothalamus-hypophyse axis and its instable connections with the ovaries. So most of the cycles in this period are anovulatory – monophasic. In the anovulatory cycles the progesterone secretion in the second part of the cycle (the luteal phase) is lacking. Without progesterone the endometrium is only under estrogen influence. Even if the estrogen level is not elevated, being sometimes at the level of the mid follicular phase or even lower, the stimulation of the endometrium by the sole estrogens causes a hyperproliferation. Being under estrogen stimulation a longer period of time, the endometrium overgrows its blood supply and so parts of it shed from the uterine wall. This causes bleeding from those portions of the uterine cavity. The healing of the desquamated parts of the endometrial cavity will be irregular as is the shedding. When some parts of the endometrium are healed other parts are sloughing. The bleeding was compared with a chess board. The bleeding is also favoured by the weak contractility of the insufficient developed uterus. In the first 2 years after the menarche only 7-8% of the cycles are ovulatory, this proportion rising to 40% in the next 2 years. Therefore it can be stated that in this period of the female life there is a relative functional infertility.

The menstrual bleeding is pathologic if the amount of blood loss is over 80mL or if it lasts more than 7 days.

The excessive menstrual bleeding can be the first symptom of a hemathologic disease.

Diagnosis – anamnesis

Establishing a good communication with the patient is very important but sometimes also difficult. In collecting a good history of the disease the physician must speak with the adult part of the patient's family and be careful of the fact that the young girl can hide some parts of the history because of her parents being there. The doctor must carefully interrogate the patient and the family and sometimes, being very cautious, must speak with the young girl alone and try to win her confidence. A good psychological background of the gynecologist is of great advantage.

For the therapy of the bleeding we must exclude the organic causes of bleeding. One of the algorithms of etiologic diagnosis of the bleeding is the PALM - COEIN classification, P - polyps (endometrial), A - adenomyosis, L- leiomyoma, M – malignancy and hyperplasia, these being the structural causes and C – coagulopathy, O – ovulatory disorders, E – endometrial, I – iatrogenic, N – not classified. But this classification is for women in reproductive age and for adolescents needs some adjustments. Practically, adenomyosis and leiomyoma don't appear in adolescents. Polyps and malignancy are very seldom - one case of endometrial polyp at a 13 year old girl [1] and one case of endometrial cancer at a 15-year old girl found in the literature [2]. So we must concentrate in the second part of the classification, most of the cases being due to the ovulatory disorders. At this subject the diagnosis must go further in revealing endocrine pathology as a cause of the ovulatory dysfunction or the cause of the anovulation being the immaturity of the nervous-endocrine-genital system.

One of the traps in the management is the exaggeration of the symptoms in some cases and the slighting of the clinical signs in other cases. We encountered both in our practice.

The second one is more dangerous because can lead to a late presentation at the gynecologist with all the possible complications even life threatening. This is also the result of insufficient information about the menstrual cycle between adolescents [3].

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The history must reveal the age of the onset of the menses, how were the first cycles (frequency, duration, intensity, regularity of the menses).

Then we must seek symptoms of coagulopathies (von Willebrand disease, idiopathic thrombocytopenia, leukemia). History of coagulopathies in the family must be carefully interrogated. Furthermore the patient is asked about heavy bleeding by little wounds, epistaxis, slight bruising, purpura or petechiae. Sometimes the abnormal uterine bleeding is the first symptom of the existing coagulopathy [4]. Also, one fifth of the adolescent with heavy uterine bleeding have been found to have a coagulopathy [3].

It is important to try to reveal anatomic causes of the bleeding, like visible abdominal masses and the sexual history of the patient, a most delicate issue.

Next, the patient and the family are questioned about medication used in the last period, like contraceptives, anticoagulants, aspirin and other nonsteroidal antiinflammatory drugs.

Also the history must continue with the search of symptoms of eat disorders, symptoms of PCOS, thyroid diseases, diabetes, hyperprolactinemia, hepatic diseases, renal failure, neurologic diseases (10-24% of girls with epilepsy have PCOS and by girls with valproic acid treatment 40% have PCOS and 30% menstrual disorders), rheumatologic diseases (chronic juvenile arthritis, lupus), gastrointestinal diseases (inflammatory) and cyanotic cardiac diseases [5].

The history will be completed with the actual disease, by reviewing the last normal menstruation, the onset of the actual bleeding and its evolution – the intensity of the bleeding is sometimes difficult to evaluate by the patient or the parents. Our opinion is that scores like the pictorial bleeding assessment calendar (PBAC) are not very useful especially in emergency situations. The use of more than 8 pads in 24 hours or change of the pad more often than hourly or clots larger than 3 cm signify an abnormal menstrual bleeding [6].

Even if we are dealing with a very young patient, we must not forget to ask about normal and complicated pregnancy symptoms, like nausea, breast tenderness, pelvic pain or discharge of soft tissue through the vagina. It is very possible that young patients will hide or deny these symptoms if the parents are there.

Diagnosis – physical examination

The examination of the patient begins with the inspection of the skin, revealing pallor (sign of anemia), petechiae (sign of coagulopathy), or hirsutism (sign of hyperandrogenic disorders including PCOS). Next the blood pressure, pulse, temperature, weight and height are measured, and BMI is calculated.

Briefly we must palpate the thyroid and the breasts. Then an abdominal palpation is carefully done focusing on abdominal or pelvic masses (one must remember that ovarian cysts and benign or malignant tumors are possible even at this age). Hepatomegaly or splenomegaly must also be excluded.

Then it comes to the difficult issue of pelvic examination. This is possible in non virgin adolescents, with a speculum examination and digital palpation through the vagina. The source of the bleeding is clarified, the intensity of the actual bleeding is evaluated, enlarged uterus, signs of pelvic inflammatory disease or parauterine tumors are being diagnosed. Attention to foreign bodies, injuries of the vulva, vagina or hymenal ring. By virgin girls the examination will be the inspection of outer genitals and eventually rectal examination (we didn't use it).

Diagnosis – laboratory

Start with a complete blood count, fibrinogen, coagulation time, prothrombin time, partial thromboplastin time and blood type. By non virgin girls, pregnancy test is mandatory. During the speculum examination the gynecologist must take probes for cultures and Chlamydia trachomatis (DNA probes are preferred if available). Depending on the history of the patient other analysis are required: TSH, fT4, prolactin, dehydroepiandrosterone sulphate, testosterone, 17-hydroxyprogesterone, von Willebrand factor antigen, ristocetin C cofactor, factor VIII, glucose and glucose tolerance test.

Diagnosis – ultrasound examination

The best examination is the transvaginal ultrasound. Because it is not possible in all cases (by virgin girls), we are obliged to examine the girls transabdominally. If we do so then the examination is better with full bladder. The ultrasound examination is very valuable in excluding organic causes of uterine bleeding, like pregnancy complications, uterine fibroids, endometrial polyps, endometrial cancer, ovarian cysts, ovarian benign or malignant tumors. Also through ultrasound polycystic ovarian syndrome is identified (together with specific history and laboratory findings). Ultrasound is also very important in evaluating the endometrium, with consequences in the therapy. A thick endometrium is the sign of a hyperproliferation through relative hyperestrogenemia or intrauterine clots. A thin endometrium indicates a hypoestrogenemia.

Therapy

The therapy must begin during the diagnostic procedures. We must obtain quickly intravenous access and administer crystalloids, the volume depending on the gravity of the anemia (tachycardia, pallor, orthostatic hypotension). When a gynecologist has to handle such a case, he must always think that a young organism is a system with a lower stability, so sometimes quick intervention is required. After the first results of the emergency complete blood count, in collaboration with the intensive therapy unit, we decide and administer blood products. This is the case when hemoglobin is under 7 g/dL or in symptomatic severe anemia or shock.

Another principle of treatment is avoiding surgical procedures or perform a minimum invasive one. Of course the decision of a surgical procedure is very difficult at a virgin young girl where preservation of the hymenal ring in

some families is important and the preservation of the fertility is always a very important issue.

If the organic, systemic, endocrine and hemathologic causes are excluded then the hormonal therapy is initiated. In our opinion, the therapy must be guided after the results of the ultrasound examination of the endometrium.

By cases with thick endometrium we prefer the oral combined contraceptive pill with 30 mcg ethinyl estradiol, 1 pill every 6 hours until the bleeding stops, then, after one day, 3 pills daily 3 days, then 2 pills daily 3 days and finally 1 pill in 24 hours for 10-15 days. In our experience pills with 30 mcg ethinyl estradiol and dienogest as a progestative was very good in acute cases and also for long term therapy in preventing recurrent menorrhagia. Unfortunately this pill is out of the market in Romania. The good efficacy of dienogest containing tablets was also studied by other authors which found that it was highly effective- the combination was with estradiol valerate, not with ethinylestradiol as in the pill we used [7]. Actually this combination of estradiol valerate and dienogest (Natazia) is the only one approved by the FDA for the treatment of heavy menstrual bleeding [8].

As an alternative, we can use injectable progesterone 100-200 mg intramuscular, then oral therapy with 200 – 400 mg micronized progesterone daily for 10-14 days. Another progesterone acute therapy is the administration of norethisterone 10 mg three times a day [9]. Another progesterone only therapy, whose efficacy has been demonstrated in a well conducted study is the administration of 150 mg depo-medroxyprogesterone acetate intramuscular, followed by the oral administration of 20 mg medroxyprogesterone acetate every 8 hours for three days. But the study was not for adolescents only and hemodynamically unstable patients and those with hemoglobin less than 8 g/dL were excluded [10]. So, the treatment can be very good in moderate form of uterine bleedings.

By cases with thin endometrium we use the same scheme with oral combined contraceptive (4, 3, 2, 1) or Premarin 25 mg intravenous every 4 - 6 hours for maximum 24 hours, then a combination of oral contraceptives or progesterone only, 10 – 14 days. The bleeding usually ceases with this therapy during the first day. If not, reevaluation is needed.

When we use a treatment with estrogen containing products we must take care of the contraindications to estrogen, like lupus erythematosus, personal or close family history of venous thromboembolism – how important is a

good anamnesis! – and in those cases we use therapies with progestin-containing products [9].

As a associated therapy, we used injectable ergometrin or misoprostol orally. As an uterotonic is used also oral antiprogestone. Also, nausea being a frequent secondary effect of the estrogene therapy, we use antiemethics. And by prolonged bleeding, especially when there is a liquid in pelvis (identified at ultrasound) we recommend antibiotics.

Antifibrinolytic drugs, like tranexamic acid or aminocaproic acid, have been used in the treatment of menorrhagia alone or in combination with a non-steroidal-antiinflammatory drug or with hormonal therapy [11]. They are indicated especially at patients with bleeding disorders, interdisciplinary aproach (with the hematology unit) being necessary. We have no experience with these treatments, anyway this drugs have been removed from the market in Romania.

Desmopressin is indicated for the treatment of uterine bleeding in patients with von Willebrand disease. In such cases we recommend collaboration with a hematologist.

The levonorgestrel intrauterine device was also used as a therapy for bleeding in adolescents [12], but is a difficult decision in virgin girls and in non virgin but nuliparous adolescents there is the possible late complication of infertility. We have not used this therapy.

Other treatments in patients with coagulopathies are platelet transfusions, factors 7, 8, 9, 10, 13, fibrinogen, fresh frozen plasma, cryoprecipitate or prothrombin complex concentrates. These are reserved only at patients where the coagulopathy has been investigated and only in consultation with a hematologist [13].

Exceptional therapies, used only in very severe cases which do not respond to medical therapy and there is a life threatening condition, are: vaginal examination under general anesthesia and evacuation of the intrauterine clots, dilatation and curetage, histeroscopy, Foley catheter intrauterine, uterine artery embolisation, endometrium ablation and hysterectomy. Fortunately, in our activity we have not been obliged to use such therapies.

From these treatmens we would choose the intrauterine insertion of a Foley catheter with the help of a rigid instrument fittet into the tip of the catheter, after a small dilatation of the cervix [14].

In conclusion we state that abnormal uterine bleeding in adolescent girls is a condition with possible severe complications, which requires a rapid but thorough diagnosis and a quick, exact and sometimes curageous therapy.

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