Evaluation and management of abnormal uterine bleeding

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SUMMARY

Abnormal uterine bleeding (AUB) is one of the commonest complaints of women in reproductive age and non-gravid state that brings them to the attention of the primary care doctor or the gynaecologist. Anovulation without any medical illness or pelvic pathology seems to be the common cause. Bleeding due to a wide variation in pathology both inside and outside the reproductive tract can be termed as anovulatory bleeding. Therefore, it is mandatory to elicit a focused menstrual history and appropriate evaluation followed by a pelvic examination. This includes a vaginal speculum examination to differentiate anovulatory bleeding from other causes of bleeding. In contrast, Heavy menstrual bleeding (HMB) is referred to as an ovulatory bleeding exceeding 8 days duration and is often caused by uterine fibroids or adenomyosis, a copper IUD or coagulation disorders. PALM-COEIN classification is a system designed by the Federation Internationale de Gynaecologie et d'Obstetrique to define the precise underlying causes of AUB. Aetiology of AUB can be classified as the following acronym "PALM-COEIN": Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic and Not yet classified. AUB describes a range of symptoms, such as HMB, inter-menstrual bleeding (IMB) and a combination of both heavy and prolonged menstrual bleeding (MB). Dysfunctional uterine bleeding (DUB) and menorrhagia are now better described as AUB. Newborn girls sometimes spot for a few days after birth, due to placental oestrogenic stimulation of the endometrium in utero.

KEYWORDS:
Abnormal uterine bleeding, Historical views of menstruation, Female genital tract pathology, Bleeding disorders (thrombophilia), Pharmacological treatment, Minimally invasive surgical procedures

INTRODUCTION

Abnormal uterine bleeding (AUB), a frequent reason for outpatient and emergency department visits in reproductive-aged, non-gravid women, may substantially affect a woman's physical, social, and mental quality of life. Evaluation and management of AUB incurs high healthcare costs. This predicament may affect 10–30% of women of reproductive age group.[1,2] All clinicians in the field, therefore need to be alert about the causes and keep a well-organised and prudent approach to formulate the management plan.

Formally AUB describes a range of symptoms, such as HMB, IMB, and combination of both heavy and prolonged menstrual bleeding. Menstrual disorders previously portrayed as DUB and menorrhagia are now better described as AUB.[3]

Bleeding due to a wide variation of pathology both inside and outside the reproductive tract can be mimicked as an anovulatory bleeding. Therefore, it is mandatory to elicit a focused menstrual history appropriate for AUB followed by a pelvic examination that includes a vaginal speculum examination, to differentiate anovulatory bleeding from other causes of bleeding. In contrast, HMB is referred to ovulatory bleeding exceeding 8 days duration and is often caused by uterine fibroids, adenomyosis, a copper intrauterine device (IUD), or coagulation disorders. Newborn girls sometimes spot for a few days after birth, due to placental oestrogenic stimulation of the endometrium in utero.

There is no agreement on a structured, universal approach to the diagnosis of AUB with the aide memoires PALM-COEIN as shown in Fig. 1. Once malignancy and pelvic pathology have been ruled out, medical treatment is an effective first-line therapeutic option, with surgery including endometrial ablation or hysterectomy, offered when medical management failed to resolve symptoms and fertility is no longer desired. The acronym PALM-COEIN denotes Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not yet classified as defined by the Federation of Internationale de Gynaecologie et d'Obstetrique.[4]

Learning Objectives:

1. To understand the causes of AUB and its management in non-pregnant, pre-menopausal women.
2. To be able to evaluate various relevant investigations required to evaluate AUB.
3. To recognise the differential diagnosis of AUB in various phases of reproduction.
4. To be aware of both medical and surgical therapies including the newer hysteroscopic and non-hysteroscopic ablative techniques, taking into cognizance the morbidity and mortality

Not Yet Classified:

This group is poorly defined, inadequately studied, and rare. They include arteriovenous malformations, myometrial hypertrophy, and uterine isthmocele secondary to previous caesarean section residual scar defects. Imaging with TVUS and MRI[3] will be able to recognise these defects.

FIGO defines normal uterine bleeding as approximately 37–41 ml of blood loss over the first 5–7 days of the menstrual cycle, FIGO also defines HMB as 100–130 ml of blood loss, over a varying number of days throughout the whole cycle but often within the first 10 days resulting in anaemia.[5] AUB

This article was accepted: 24 February 2022
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can have a significant impact on women's quality of family perspectives and poses embarrassment, because of soiling outer garments with blood.[1] Also, AUB can be as consequences of infections, uterine fibroids, polyps, adenomyosis, or endometriosis. Newborn girls sometimes spot for a few days after birth due to placental oestrogenic stimulation of the endometrium in utero.

The term DUB is synonymous with anovulatory bleeding, in the absence of pregnancy or any obvious pelvic pathology. In anovulatory menstruation, the follicles grow without any selection of a dominant follicle. The oestrogen is secreted in increasing amount. The net effect is unopposed secretion of oestrogen leading to fragile endometrial growth without proper stromal support. When the oestrogen level falls, there is asynchronous shedding of the endometrium resulting in heavy or prolonged and irregular bleeding. The term *menorrhagia* spells out as regular, heavy, or prolonged bleeding. In clinical practice, a wide variety of terms are used to denote this pattern of bleeding.

Historical Views of Menstruation

Throughout early recorded history, many superstitious beliefs have surrounded menstruation, and women were isolated and prevented from handling food. Many considered menstruating women were impure, unclean, and subjected to segregation with special rituals. They were prohibited and shunned at holy places and social functions. These practices were prevalent in rural and remote areas in India and Nepal and other third world countries decades ago.[6,7] Attitudes and ideas about this aspect of female physiology have changed dramatically. The scientific progress in recent years has revealed the dynamic relationships between the pituitary and gonadal hormones and the cyclic pattern of the normal reproductive process. In Malaysia, there are no anecdotal records of such segregation practices.

Recognising these cultural sensitivities, healthcare providers need to be familiar with the existing cultural and social views and attitudes towards menstrual disorders and provide medically appropriate therapies for their menstrual disturbances.

Despite sophistication and modernisation in lifestyle, negative attitudes towards menstruation do persist in modern times in many countries.[8]

Clinical evaluation of AUB

A careful and detailed history of the presenting illness, menstrual health, sexual and contraceptive details inclusive of past obstetric performance, drug history and allergies, family and social history are pertinent. This is followed by a general examination including vital signs, cardio-respiratory assessment, breast examination followed by abdominal and pelvic examination inclusive of speculum and bimanual examination. Requesting relevant laboratory and imaging tests is done when indicated.

Bimanual examination elicits the size and contour of the uterus. An enlarged or lobular uterus suggests leiomyomas or adenomyosis. Cervical or adnexal tenderness is suggestive of *pelvic inflammatory disease* (PID). The presence of hyperandrogenic features, for example, acne, hirsutism, and basal metabolic index (BMI) >25 kg/m^2, suggests polycystic ovarian syndrome (PCOS), whereas galactorrhoea demonstrates possibility of a pituitary hyperprolactinaemia and hypothyroidism.

On the other hand, intermenstrual bleeding IMB may be caused by an endometrial polyp, endometritis, or an IUD, whilst postcoital bleeding suggests presence of cervical disease (cervicitis, polyp, or malignancy as in Fig II). Anticoagulant use can cause HMB whilst medications that may induce hyper-prolactinaemia (e.g., risperidone or haloperidol) can cause AUB. Pregnancy test is prudent in women younger than 55 years. Laboratory testing should include cervical cytology, human papillomavirus along with *Chlamydia trachomatis*, *Neisseria gonorrhoea* and *Trichomonas vaginalis* using nucleic acid amplification testing on vaginal swabs for patients younger than 25 years or when there is vaginal discharge, pelvic pain, new or multiple sexual partners with cervical motion or adnexal tenderness. A complete full blood count (FBC) and serum ferritin levels should be taken from women with HMB because of the risk of iron depletion resulting in an iron deficiency anaemia. Leucocytosis is pathognomonic of PID or postpartum endometritis. Assessment of thyroid and prolactin concentrations is vital. Von Willebrand disease (VWB) is the most common inherited bleeding abnormality affecting women. In adolescent girls, a heavy bleeding pattern since menarche is suspicious. The possibility of *coagulopathy* also should be kept in mind especially in adolescents whose menstrual history is short and not yet well defined. Besides, in adolescents, genital trauma, sexual abuse, cervicitis relating to sexually transmitting infections *(Chlamydia trachomatis)*, and foreign bodies (e.g., retained tampons merit special consideration).

Certain medications can predispose to AUB, by interfering with haemostasis, resulting in menorrhagia by disrupting the hypothalamic-pituitary-ovarian (HPO) axis. Drugs associated with AUB include hormonal contraception, anticonvulsants, anticoagulants, and psychopharmacologic medications. Some common herbs have oestrogenic activity (e.g., ginseng)

Systemic illnesses may predispose to anovulation or coagulation abnormalities; examples include diabetes mellitus, systemic lupus erythematosus, malignancies, and myelodysplasias. Chronic renal disease is associated with both ovulatory and platelet dysfunction. Liver disease too can affect oestrogen metabolism and predispose to anovulation.

The reality of a post-tubal ligation syndrome of menstrual abnormalities has been debated for some time now.[9] The popular theory is that extensive tubal electrocoagulation adversely affects ovarian blood supply and steroidogenesis. This syndrome is seen frequently many years after sterilisation particularly electrocautery but not with rings and clips.

Imaging the transvaginal route is useful in the evaluation of patients with AUB. Imaging is also useful in suspected PCOS and polyps or leiomyoma in the endometrial cavity. Abdominal ultrasound is appropriate in virginal patients and others in whom a vaginal ultrasound is inappropriate.

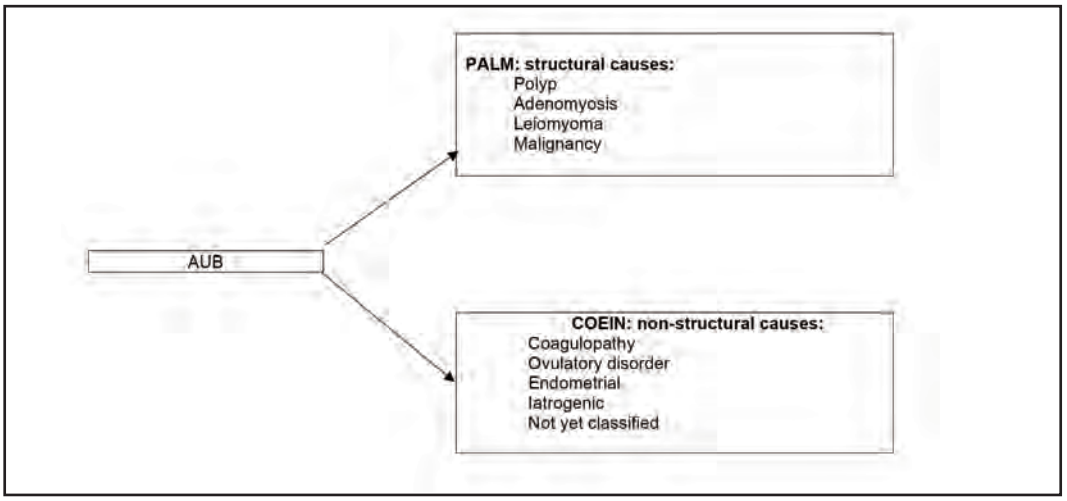

Fig. 1: FIGO AUB System II PALM COEIN (2011)
(Source: British Medical Bulletin 2017, 123: 103-114)

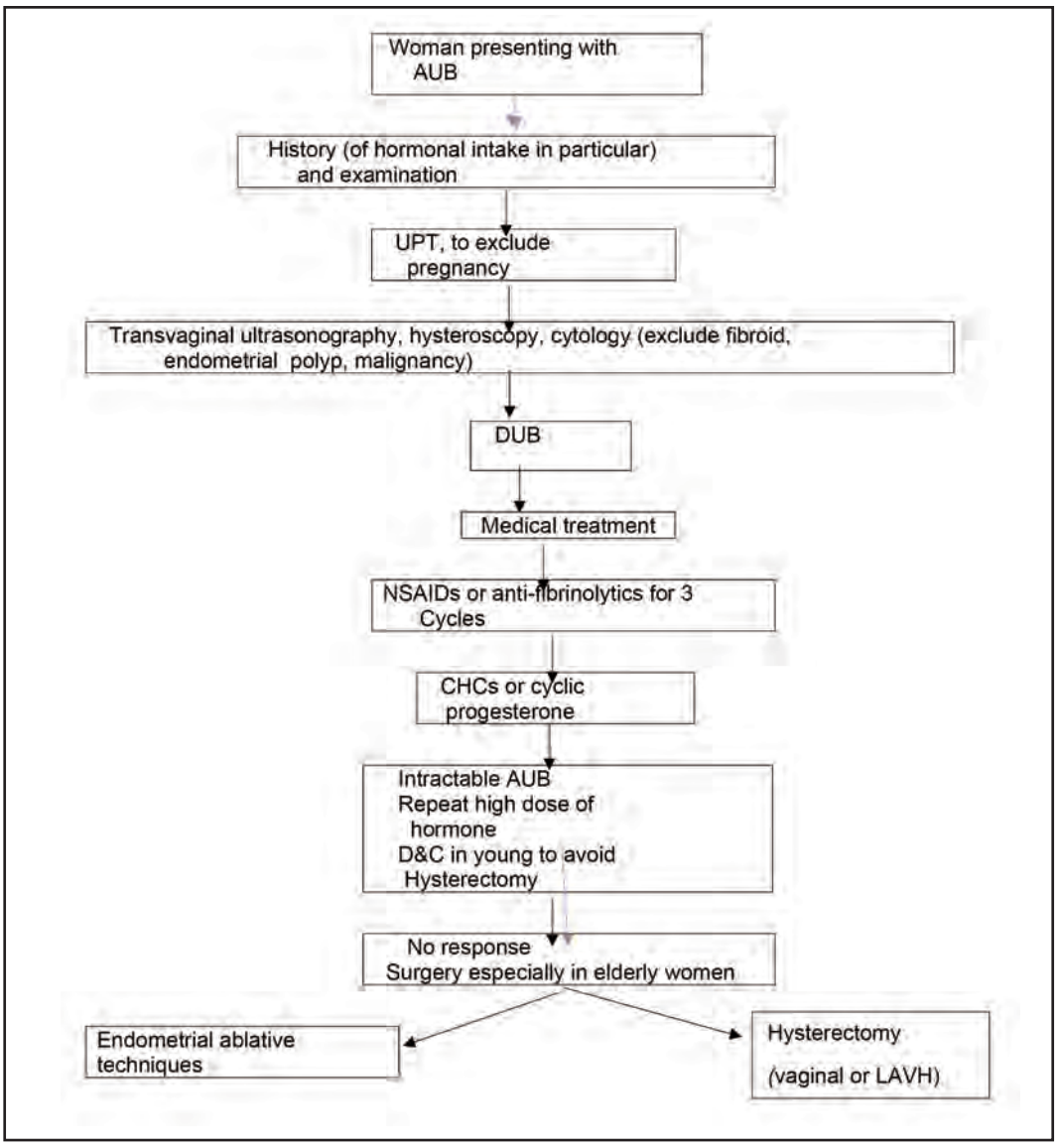

Fig. 2: Algorithm in the clinical evaluation of patient presenting with AUB.

Table I: Laboratory evaluation

Laboratory evaluation	Specific Laboratory Tests
Initial laboratory testing	• Full blood count (FBC) • Blood group and cross match • Pregnancy test • Well-timed serum progesterone
Initial laboratory evaluation for disorders of haemostasis	• Partial thromboplastin time • Prothrombin time (PT) • Activated partial thromboplastin time (aPTT) • Fibrinogen
Initial testing for Von Willebrand disease	• Von Willebrand factor activity (optional) • Factor VIII level (optional)
Other laboratory tests to consider	• Thyroid-stimulating hormone (TSH) • Serum iron/ferritin • Total iron-binding capacity (TIBC) • Liver function tests (LFTs) (optional) • Renal function tests (RFTs) for those with suspected renal disease (optional) • Chlamydia trachomatis N. Gonorrhoea • Wet prep for Trichomonas vaginalis
Ultrasonography as primary diagnostic tool	• Early pregnancy features • Small ovarian cysts
Saline infusion sonography (SIS)(optional) Magnetic resonance imaging (MRI) if ultrasonography information is inadequate (optional)	• Leiomyoma/adenomyosis • Endometrial thickness
Hysteroscopy and endometrial biopsy	• Small polyps • Submucous fibroids • Endometrial hyperplasia • Endometrial carcinoma

Table II: Medical Treatment

Hormonal

- Combined hormonal contraceptives (CHCs)
- Progestins
- Levonorgestrel impregnated intrauterine system (LNG-IUS)
  (Suitable to patients <35 years, non-smokers, no comorbid complications, migraine, and history of VTE)

Non-Hormonal

- Prostaglandin synthetase inhibitors (PGSI)
- Anti-fibrinolytic agents – Tranexamic acid
- Reducers of platelet fragility – Ethamsylate
  (Suitable for women >35 years with hypertension, diabetes)

Others

- Danazol (17-α-ethinyl testosterone)
- GnRH agonists
- Selective oestrogen receptor modulations (SERMs)
- Epsilon amino caproic acid
- Gestrinone (19-Norsteroid derivative)
- Interleukin II
- Vasopressin analogues
- Desmopressin (dDAVP) analogues
  (Suitable in women with HMB in women with Von Willebrand disease, beginning treatment with onset of menstruation)

Other second-line imaging tests are computed tomography (CT) and magnetic resonance imaging (MRI) in exceptional cases. Alternatively, hysteroscopy may facilitate targeted biopsy, resection of intracavitary pathology or both. Endometrial sampling is performed after exclusion of pregnancy in patients with AUB. Biopsy facilitates to exclude endometrial hyperplasia or cancer.

Case study I

Ms. T, an 18-year-old college student came to the primary health centre HMB lasting 6–7 days interfering with her lifestyle. Menstrual history showed she had this problem since her first period at 12. Never been on any hormonal medications. She has history of excessive bleed during dental scaling and few occasions of epistaxis, and both conditions resolved spontaneously. She is not sexually active. There was mild pallor and pelvic ultrasonography was unremarkable. Her vital signs were normal. There were few ecchymosis spots on her abdomen and forearms.

Questions:

1. What could be the possible causes of this problem?
2. List two tests that may confirm her diagnosis.
3. How do you manage and follow-up this case?

Answers:

1. Anovulation and effect of unopposed oestrogen stimulation leading to endometrial hyperplasia
2. i. Pelvic ultrasonography to check endometrial thickening
   ii. Full blood count/evaluation of disorders of haemostasis, e.g., PT and aPTT
3. Progestins for three cycles, prostaglandin synthetase inhibitors (PGSI), rarely surgical interventions at this age

Pathophysiology

The menstrual cycle is an organised string of endocrine signals that gives the menstrual cycle the regularity, predictability, and reliability. The cycles become irregular around extremes of reproductive age (menarche and menopause) mainly due to anovulation and inadequate follicular development.[10] This is due to disturbance in the hypothalamus-pituitary-ovarian (HPO) axis, a phenomenon seen commonly in PCOS and extremes of reproductive age groups as shown in Table I. The term DUB refers to anovulatory bleeding in the absence of pregnancy or any demonstrable pelvic pathology or coagulation disorders.[11]

In ovulatory DUB, the bleeding is regular but heavy with 90% of the bleeding is greater in the first three days.[12] The HPO axis is not involved. Here, the gonadotrophin and steroid hormone profiles are similar as in normal menstrual cycles. The decline in oestrogen and progesterone levels in the late secretary phase leads to disintegration, followed by re-epithelialisation of the functional layer of the endometrium. The main defect appears in the process of vasoconstriction and haemostasis.

HMB refers to ovulatory (cyclic) bleeding exceeding 8 days' duration or heavy enough to soak a pad or tampon more than every 2 hours and during peak flow, large clots are passed and interfere with daily activities of life.[13] About 1 in 20 women aged 10–49 years will consult their primary care physicians. HMB is often caused by uterine fibroids or adenomyosis but may also be caused by a copper intrauterine device (IUD) or coagulation disorders.

The differential diagnosis of AUB includes problems associated with pregnancy, infection, vaginal and cervical abnormalities, benign and malignant uterine neoplasms, coagulopathies, endocrine disorders, trauma, and foreign bodies inserted into the lower genital tract, systemic diseases leading to vaginal bleeding as seen in Table I. The causes may vary with age. In premenarchial girls, foreign bodies, trauma, and infection are more prevalent as in Table I. In post menarche adolescents, anovulatory bleeding, coagulopathies, infections, and pregnancy complications are common. In suspected cases of a coagulopathy, history of heavy menstrual bleeding from menarche, after dental procedures, epistaxis, frequent gum bleeding, skin bruises, and a family history of bleeding symptoms are noted. During the reproduction years, anovulation, hormonal contraception, complications of pregnancy, infection, endocrine disorders, cervical lesions, and fibroids are frequent. In perimenopausal women, anovulation, uterine neoplasia, and endometrial hyperplasia are the principal causative factors. In postmenopausal women, vaginal/endometrial atrophy, and HRT prescriptions are the chief causes.

Laboratory Evaluation

Laboratory tests can be very helpful but not always necessary. A urine pregnancy test quickly excludes the possibility of an early pregnancy abnormal bleeding. A complete FBC excludes anaemia and thrombocytopenia which is useful in women who complaints abnormal bleeding.

A complete Serum progesterone level exceeding 3 ng/ml during the luteal phase between days 22 and 24 of the cycle can help diagnose ovulation. If the menstrual pattern is erratic or poorly documented, then conventional basal body temperature (BBT) measurement may be employed. Endometrial sampling is only reserved for women beyond 40 years or when suspected of endometrial hyperplasia or cancer.

In women who are sexually active, tests for *chlamydia* and *gonorrhoea* and a wet preparation for trichomonas infection merit consideration, particularly in those with evidence of cervicitis/vaginitis. Cervical cultures and a cervical smear are appropriate for the presence of sexually transmitted diseases or cervical dysplasia. In adolescent girls who present heavy menstruation since menarche or a family history, it may be prudent to do coagulation screening. In addition to VWB disease, other factor deficiencies, platelet function abnormalities, screening should also include both PT and aPTT as in Table I. The former demonstrates abnormalities of the extrinsic and common pathway, whilst the latter is the intrinsic and common pathway. With proven abnormalities, consultation with a haematologist is pertinent. Renal and liver function tests are done when there is a suspicion of the particular-organ involvement.

Imaging techniques could shed light on anatomical abnormalities such as fibroids and endometrial polyps. Transvaginal may throw light on the precise size and location of fibroids or may explain bleeding due to other causes.[14] Saline infusion sonography identifies intracavitary lesions such as endometrial polyps or submucous myomas with high accuracy. CT scans and MRIs are done in more obscure cases. MRI can reliably define uterine anatomy, distinguishing between adenomyosis and leiomyomas. The risk of cancer is remote in women who are either perimenopause, or post-menopause with an endometrial thickness less than 5 mm but clinically present with abnormal bleeding.[15] Endometrial hyperplasia and cancer are more commonly detected in older than in younger women. The duration of exposure to unopposed oestrogen stimulation is the most critical risk factor. Endometrial biopsy is almost mandatory.

Hysteroscopy plays a very decisive role in those with intrauterine pathology that requires biopsy or excision. Modern hysteroscopes with an outer diameter of 2–3 mm permit both diagnostic and therapeutic procedures at an office setting.[16]

Case study II

Mrs. R.K., a 36-year-old lady with 2 living children 8 and 10, went to the outpatient clinic in a district hospital for excessive per vaginal bleeding during every cycle using 8–10 pads per day with clots for the past one year. She was on barrier contraception between her 2 children but nil presently.

Her vital signs were normal with pallor. Cardiorespiratory systems were normal. Abdominal palpation showed a firm 16-week size central mass below the umbilicus, soft in consistency, no nodularity, mobile side to side and non-tender and could not feel the lower border. A trans-abdominal ultrasonography revealed a bulky mass measuring 15 x 8 x 5 cm. A pelvic examination confirmed a normal cervix, the size and consistency of the uterine mass with normal adnexa.

Questions:

1. What is the probable diagnosis and why?
2. What further investigations would complement your diagnosis?
3. How would you manage this case?

Answers:

1. Submucous fibroid/adenomyosis presenting with a firm central mass of 16-week size
2. Imaging techniques: pelvic ultrasonography, CT scan, and MRI (optional)
3. Expectant management if one desires further childbearing: myomectomy, endometrial ablation, uterine artery embolisation, otherwise opt for hysterectomy

Medical Treatment

Although AUB can often be managed medically on an outpatient basis as in Table II, discussion pertaining to contraceptive needs, desire for future pregnancies, medical comorbidities, patient preferences, and desire for endometrial ablation or hysterectomy is well discussed. Improving access to care will require multi-level approaches that involve local socio-cultural needs and improved healthcare facilities.

Combined hormonal contraceptives (CHCs)

CHCs reduce the MBL and result in a consistent menstrual cycle interval.[17] The reported MBL or Pictorial blood assessment chart (PBAC) score range from 32–36% at 3 months and 35–68% in 12 months.[18] CHCs could be prescribed for 3 weeks followed by a pill-free week to facilitate withdrawal bleed or be given as hormone free interval to induce amenorrhoea in 80–100% of women.

Rare side effects of CHCs are breast tenderness and mood changes. The contraindications for use of CHCs are for women more than 35 years, who smoke, have hypertension, cardio-vascular disease, migraine, breast cancer, or history of VTE.

Progestin Therapy:

Synthetic progestogens have been used in the treatment of menorrhagia for over 30 years. The drug dosage and the duration of use will influence the effect on the endometrium and consequent pattern of bleeding. Progestins are the mainstay of treatment for anovulatory bleeding. This is commenced after organic pathology is excluded. In oligomenorrhoeic anovulatory patients, an orderly organised withdrawal bleeding can be worked out. Cyclic oral progestins, medroxyprogesterone acetate (MPA) 5–10 mg for 10–12 days each month. MPA inhibits FSH release from the anterior pituitary and prevents ovulation. When the endometrium is either normal or increased in thickness, the regime is continued for 3 weeks and 10 days thereafter, decreased to once a day for 7–10 days.[19]

The progesterone impregnated intrauterine device: relating to 20 µg of levonorgestrel per day has proven to be successful in reducing menstrual blood loss.[20] Progestogens may be safely used for long-term treatment of DUB.

Modern low dose CHCs can be safely prescribed for most young women, provided they do not have any contraindications. The CHC is used frequently for the treatment of menorrhagia. The efficacy has been confirmed objectively.[21] CHCs are unpopular for treatment of menorrhagia, particularly in women over 35 years of age over concerns of thromboembolic diseases.

Non-hormonal medical therapy

Suitable for women beyond 35 years, smokers with comorbid complications and history of VTE.

Iron therapy

Intravenous iron like iron sucrose is given 200 mg intravenous in 200 ml of normal saline over 30 min, thrice a week. Side effects: mainly gastro-intestinal. Contraindications: known hypersensitivity to intravenous iron. Precautions: asthma, eczema, and other atopic allergies.[22]

Prostaglandin Synthetase Inhibitors (PGSIs)

Use of inhibitors of COX enzymes had been shown to reduce MBL implicating impairment of prostaglandin pathways in the aetiology of excessive menstrual bleeding. NSAIDs reduce MBL by (10–51%) inhibiting endometrial prostaglandin synthesis. The endometrium is a rich source of PGE_2 and $PGF_{2\alpha}$. Reductions in MBL in proven menorrhagia range from 22% to 46%.[23,24]

Anti-Fibrinolytic Agents

The endometrium possesses an active fibrinolytic system. Tranexamic acid is an inhibitor of fibrinolysis, is used frequently as first-line therapy in the United Kingdom , despite of a number of trials showed only 50% reduction in MBL.[25,26] It decreases endometrial plasminogen activator activity. Side effects were minimal with no discontinuation on account of adverse drug reactions. A third of women experience gastrointestinal side effects with 3–6 grams daily. As 90% of MBL in the first 3 days of flow, dose-related side effects can be minimised by limiting the number of treatment days to the first 3 or 4 days of the period.

Other Medical Therapies

Danazol is a synthetic androgen (17-α-ethinyl testosterone) with anti-oestrogenic and anti-progestogen activities, leading to endometrial atrophy and reduced blood loss. A high incidence of androgenic side effects such as weight gain, muscle cramps, and skin rashes have limited its treatment option. When prescribed at more than 400 mg daily, as a treatment option for women with gynaecological diseases, it is mainly used as a second-line therapy, especially as a short-term, pre-surgical procedures.[27]

Gonadotrophin-Releasing Hormone Agonists (GnRHa)

GnRH agonists achieve short-term relief from a bleeding problem and has been used as a pre-operative adjunct in women awaiting myomectomy or endometrial ablation or definitive surgery (hysterectomy) for AUB. The resultant shrinkage of myomas and thinning of endometrium promotes less bleeding intra-operatively.[28]

The analogues control menstrual loss by pituitary down regulation and subsequent inhibition of cyclical ovarian activity. Ovarian suppression and amenorrhoea with associated hypo-oestrogenic-state and endometrial atrophy leads to hot flushes, vaginal dryness, and bone mineral depletion. Add-back therapy with oestrogen may alleviate the problem.

The Levonorgestrel-releasing Intrauterine System (LNG-IUS, Mirena®)

Progestogen can be delivered directly to the endometrium using a hormonal intrauterine device. The operation compliance and carry with them additional contraceptive benefits. Potential modes of action of progesterone and progestogen-releasing devices are a reduction of endometrial prostaglandin synthesis and endometrial fibrinolytic activity.[29] The reservoir contains 52 mg of LNG mixed with polydimethylsiloxane and release 20 µg of LNG per day. It is contraindicated in pregnancy and unexplained vaginal bleeding.

Desmopressin (dDAVP)

A synthetic analogue, Desmopressin is used to treat AUB in women with coagulation disorders especially those with VWD. It has been shown to reduce median PBAC score by 24–42% during two cycles of treatment.[30]

Ethamsylate is a haemostatic agent used to treat HMB given at 500 mg 4 times daily during days of menstruation, it reduces MBL by 25% of women during 3 cycles.[31]

Other options include haemostatic agents, SERMs, epsilon aminocaproic acid, gestrinone (19-Norsteroid derivative) and interleukin II.

Case study: III

Madam M, 48-years-old lady with 3 living children age ranging 18–12, delivered normally, was never on any form of contraception. She was amenorrhoeic for 8 months followed by per vaginal spotting and frank bleeding past 6 months. She had gone to see her family physician. She is not a hypertensive or diabetic.

Her BMI was 26, BP 120/70 mm Hg, looked tired and weak. Abdominal examination was unremarkable, pelvic examination showed a pale vaginal mucosa, normal cervix, and bulky uterus, with no adnexal masses. A transvaginal scan essentially showed normal uterus with an endometrial thickening of 11 mm. Her doctor referred her to see the gynaecologist at a tertiary centre.

Questions:

1. What is your provisional and differential diagnosis?
2. What investigations would you perform for the thickened endometrium?
3. What will be your further management of this patient?

Answers:

1. Small polyps, submucous fibroids, endometrial hyperplasia, endometrial carcinoma.
2. Endometrial sampling is performed after exclusion of pregnancy. Biopsy facilitates to exclude endometrial hyperplasia or cancer.
3. Further management depends on investigation results: In view of the age group, surgical extirpation of uterus is more plausible.

Surgical considerations

Surgery is seldom indicated in young women with menstrual disturbances. Hysterectomy, the traditional surgical treatment of menorrhagia, is only suitable for women who have no further wish to conceive. The operation itself is not without risk. Concerns about the "invasiveness" of hysterectomy have led to the development of minimal access approaches including endometrial resection and ablation both as inpatient and as outpatient treatment modality.[32]

Uterine artery embolisation (UAE) is an alternative for uterine fibroids in cases where pregnancy is still desired. Both the uterine arteries are blocked with particles injected through a catheter inserted into them via the femoral artery. This procedure causes shrinkage of the fibroids. UAE is performed by an interventional radiologist. Embolisation may be an appropriate treatment for larger fibroids where the risks from surgery are higher.[33]

Current minimal Access Techniques

Hysteroscopy and visually directed endometrial sampling have replaced blind curettage for the diagnosis of endometrial disease. The development of minimal access techniques has made it possible to therapeutic destruction of endometrium in situ as a day-care operation. The earliest techniques ablated endometrium with ND: YAG LASER,

(hysteroscopic first generation).34 The second-generation of endometrial ablation devices are technically simpler to perform, less invasive, designed to ablate the full thickness of endometrium by application of heat, cold, or microwave. The aim of these new procedures is to remove only the endometrium and leave the myometrium intact. Generally, the technique of endometrial ablation is divided into two groups: Hysteroscopic and Non-Hysteroscopic procedures.

A. Hysteroscopic (First-Generation Devices).
- Transcervical resection of endometrium (TCRE)
- Rollerball endometrial ablation (Endometrial "Rollerball" Electrocoagulation)
- LASER ablation (Nd YAG LASER)

B. Non-Hysteroscopic (Second-Generation Devices) Hot liquid balloons
- Thermal balloon endometrial ablation: Cavaterm, ThermaChoice

Thermablate
- Microwave endometrial ablation (MEA)
- Bipolar radiofrequency induced thermal endometrial ablation (RITEA)

COMPLICATIONS

Both hysteroscopic and non-hysteroscopic techniques for endometrial ablation appear to offer good patient satisfaction and symptom relief. Endometrial ablation generally is more effective when the endometrium is relatively thin.

Complications associated with hysteroscopic techniques primarily involve those resulting from unrecognised uterine perforation and injury to the bladder and bowel and from fluid and electrolyte disturbance relating to excessive absorption of distention media.[35] Fluid overload can result in hyponatremia and pulmonary oedema.[36]

Non-hysteroscopic methods of endometrial ablation requires less technical skill and operative time.

CONCLUSION

Gynaecological health has historically remained a taboo subject, yet this stigmatisation, has meant that many women today are not able to talk about issues such as menstruation. This has resulted in many women normalising symptoms or "suffering in silence". AUB is a disabling condition compelling many women to seek medical help. The literature is replete with drugs recommended for the treatment of menorrhagia throughout the ages. There are a limited number of studies that have explored women's experiences in accessing care for AUB. Improving access to care will require multi-level approaches that include consideration of local socio-cultural needs with improved training for primary healthcare providers.

In addition, consequent to failure of medical therapy, an increasing number of surgical procedures have developed. Although hysterectomy is associated with increasing patient satisfaction, it is beset with unprecedented morbidity and mortality. The last two decades have witnessed development of less invasive minimal access techniques that conserve the uterus facilitating shorter in-patient care and faster recovery. Training in hysteroscopic surgery, knowledge about the indications, contraindications, and limitations are essential prerequisites to ensure the safety and sound care of the patients. Adolescent menstrual disorders are relatively commonly handled by primary care physicians, in many instances reassurance is all that is required. Otherwise, those presenting with protracted bleeding require referral to tertiary centres for further assessment of rare haematological, endocrine, or structural abnormalities.

Conflict of interest
None declared

Ethics approval and consent to participate
Not applicable

Funding
There was no funding for this CME article

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Multiple Choice Questions:

1. Abnormal uterine bleeding (AUB) encompasses cyclic and non-cyclic bleeding.
   A. Anovulatory bleeding is the most common type of non-cyclic uterine bleeding.
   B. Menorrhagia is defined as excessive cyclical uterine bleeding more than 100 ml or above.
   C. In many women, the underlying cause is still unknown.
   D. Polyp, adenomyosis. and coagulopathy are some of the possible causes of AUB.
   E. Treatment mainly involves surgical procedures.

2. Dysfunctional uterine bleeding (DUB)
   A. It is an excessive, prolonged, or erratic endometrial bleeding with no organic, general, or local lesions.
   B. DUB is common in all age groups during the reproductive phase.
   C. It is due to abnormalities of the hypothalamus-pituitary-ovary-endometrial axis.
   D. Gestagen therapy (progestogen) is one of the medical forms of therapy.
   E. Minimal access techniques have no role as alternative therapies.

3. AUB in a 48-year-old woman came with an endometrial biopsy, whose histopathological examination (HPE) revealed as 'endometrial hyperplasia', and she came for counselling.
   A. The knowledge of pathogenesis and type of 'endometrial hyperplasia' is irrelevant in advising modality of further treatment.
   B. Role of informed consent is disregarded.
   C. First- and second-generation ablative techniques as day-care procedures is advised.
   D. Endometrial hyperplasia without atypia could be treated with progestins/medroxyprogesterone acetate (MPA)/LNG-IUS.
   E. Reconsideration for hysterectomy in the presence of persistent or non-regressive symptoms is advisable.

4. AUB in adolescent girls
   A. Anovulation and oestrogen excess secondary to a lack of maturation of the negative feedback in the hypothalamus-pituitary axis.
   B. Coagulation defects is the cause in up to 20% mainly due to ITP and Von Willebrand's disease.
   C. The possibility of a pregnancy must be ruled out.
   D. Thyroid dysfunctions must be excluded.
   E. Close follow-up, iron supplementation, and reassurance are adequate in many instances.

5 Endometrial hyperplasia
   A. In anovulatory type of DUB, the histological changes are described as 'cystic glandular hyperplasia'.
   B. Cystic glandular hyperplasia can be treated by endometrial resection and ablation.
   C. Simple endometrial and adenomatous hyperplasia without atypia are usually precursors of endometrial malignancy.
   D. Cytologic atypia or atypical adenomatous hyperplasia are best treated by hysterectomy.
   E. Dilatation and curettage can be employed when the histological features are unknown.