



# Application of International Endometrial Tumor Analysis in Abnormal Uterine Bleeding: A Case Report

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## Abstract

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**BACKGROUND:** Abnormal uterine bleeding (AUB) is one of the clinical symptoms found in malignant conditions where the incidence of newly diagnosed cancers reached 100,000 cases in Europe in 2012 with an incidence of around 14.7/100,000 women. The International Endometrial Tumor Analysis (IETA) group, formed in Chicago in 2008, published a consensus stating how to examine and measure the endometrium.

**CASE REPORT:** Mrs. M, 49 years old, came to Gynecology Clinic of USU Hospital on February 22, 2021, at 13.00 WIB with the complaints of prolonged menstruation for 2 months with a volume of >10 times changing pads. Menstrual pain was found. Low back pain was found. A history of bleeding between menstrual cycles was found. On ultrasound examination, anteфлекed uterus was found with size of 6.95 × 4.2 × 3.85 cm, thickness of the endometrium: 1.64 cm and concluded as AUB-M (thickening of the endometrium). Then, the patient is diagnosed with AUB-M (thickening of the endometrium) and is planned to undergo a diagnostic curettage. Anatomical pathology results showed a complex hyperplasia endometrium without atypia cells. Acute AUB is defined as bleeding profusely so that prompt treatment is needed to prevent blood loss. Ultrasound examination is performed to assess the size, shape of the uterus, the presence of fibroids, polyps, adenomyosis, and uterine anomalies such as uterine didelphys, sometimes polycystic ovaries are also found. Endometrial biopsy can detect more than 90% of cancers. The pathology of the endometrium can diagnose endometrial cancer or determine the likelihood of cancer. These investigative modalities can assist in the diagnosis of endometrial polyps, adenomyosis, leiomyomas, uterine anomalies, and endometrial thickening associated with hyperplasia and malignancy. Curettage is considered to relieve ongoing menorrhagia. According to the SOGC, administration of nonsteroidal anti-inflammatory drugs can inhibit cyclo-oxygenase and reduce levels of endometrial prostaglandins.

**DISCUSSION:** Acute AUB is defined as bleeding profusely so that prompt treatment is needed to prevent blood loss. Ultrasound examination is performed to assess the size, shape of the uterus, the presence of fibroids, polyps, adenomyosis, and uterine anomalies such as uterine didelphys, sometimes polycystic ovaries are also found. Endometrial biopsy can detect more than 90% of cancers. The pathology of the endometrium can diagnose endometrial cancer or determine the likelihood of cancer. These investigative modalities can assist in the diagnosis of endometrial polyps, adenomyosis, leiomyomas, uterine anomalies, and endometrial thickening associated with hyperplasia and malignancy. Curettage is considered to relieve ongoing menorrhagia. According to the SOGC, administration of nonsteroidal anti-inflammatory drugs can inhibit cyclo-oxygenase and reduce levels of endometrial prostaglandins.

**CONCLUSION:** According to IETA, the vascular pattern in the endometrium is reported to be associated with the presence or absence of a "dominant vessel" or other specific pattern. Endometrial thickness is the maximum measurement in the sagittal plane. The accompanying ultrasound provides the measurement of endometrial thickness in the absence of intracavity fluid; the endometrium should be measured where it appears thickest. If intracavity pathology is present, total thickness of endometrium including the lesion should be recorded. Anatomic pathology by curettage is required in women with abnormal bleeding; histological evaluation of the endometrium may identify infectious or neoplastic lesions such as endometrial hyperplasia or cancer.

## Introduction

Abnormal uterine bleeding (AUB) is one of the patient's reasons for seeing a gynecologist and is one of the clinical symptoms found in malignant conditions. Due to the lethal potential of endometrial cancer, most published case studies have focused on its diagnosis. The International Endometrial Tumor Analysis (IETA) group, formed in Chicago in 2008, published a consensus stating how to examine and measure the

endometrium and what terminology is used to describe the sonographic features of the endometrium and intracavity lesions [1], [2], [3], [4].

Several ultrasound studies in women with AUB have evaluated exclusively endometrial thickness measurements to exclude endometrial cancer, thin endometrial walls are associated with a lower incidence of malignancy, and thick walls are associated with an increased risk. However, measurement of endometrial thickness is limited, especially in postmenopausal women. In women of reproductive age, the endometrium

grows rapidly after menstruation, so measuring endometrial thickness is not only associated with cancer but is also associated with benign pathologies such as endometrial polyps or hyperplasia without atypia [2], [4].

AUB which includes bleeding disorders originating from the uterus caused by hormonal disturbances, organic genetic disorders, and bleeding contacts. According to the International Federation of Gynecology and Obstetrics (FIGO), there are nine main categories arranged according to the acronym PALM COEIN, namely, polyps, adenomyosis, leiomyomas, malignancy and hyperplasia, coagulopathy, ovular dysfunction, endometrial, iatrogenic, and not yet classified [5], [6].

Hyperplastic growths or malignant growths of the lining of the endometrium may present symptoms include AUB. Symptoms include AUB. Although rare, atypical hyperplasia and malignancy are important causes of AUB. Classification of malignancy and hyperplasia uses the FIGO and WHO classification systems. Definitive diagnosis based on histopathological examination [2], [5], [6], [7], [8].

There is mild and highly reversible proliferation with slightly crammed and dilated endometrial glands, characteristic of a response to mild estrogenic stimulation or anovulation. Most of these are suspected direct precursors of endometrial carcinoma, which contain glands that are nearly backward from each other and a very abnormal nucleus. These lesions are indistinguishable from well-differentiated endometrioid carcinoma and are frequently found adjacent to it [9].

Simple hyperplasia refers to glands that are diffuse and vary in size with the normal ratio of the gland to the stroma. Complex hyperplasia consists of architecturally unregistered glands and an increased gland-to-stromal ratio. When nuclear atypia (enlargement of the nucleus with uniformly dispersed or clumped chromatin) is present, the former becomes simple atypical hyperplasia (SAH) and the latter becomes complex atypical hyperplasia (CAH). The diagnosis of SAH is so rare that atypical hyperplasia (AH) is often used to indicate any hyperplasia with atypia; AH mainly consists of CAH. Various clinical management options for patients with endometrial hyperplasia include hysterectomy, progestin-based hormonal treatment, and/or recurrent endometrial assessment. Older or postmenopausal women are more likely to undergo hysterectomy, whereas younger patients may be more likely to choose hormones without hysterectomy [9].

## Case Report

Mrs. M, 49 years old, P3A0, Protestant Christian, high school, housewife, the youngest child is

6 years old, married 25 years ago to Mr. R, 50 years old, high school, entrepreneur, came to the Gynecology Clinic of USU Hospital on February 22, 2021, at 1:00 p.m. WIB with the complaints of prolonged menstruation for 2 months with a volume of >10 times changing pads. Menstrual pain was found. Low back pain was found. A history of bleeding between menstrual cycles was found. There was no history of palpable abdominal mass. A history of reduction in body weight, decreased appetite was not found. Micturition and defecation was within normal limits.

There was no history of surgery, previous illness, drug use, and contraception. The patient had menarche at the age of 14 years, irregular menstrual cycles, volume 2–3 × changing pads/day, duration 5 days, pain during menstruation (-), and last menstruation February 19, 2021. Childbirth history of P3A0 with last child aged 12 years and all the child are healthy.

On the examination of vital signs, the results obtained blood pressure 130/80 mmHg, respiration 20×/min, pulse 82×/min, temperature 36.8°C, body height 150 cm, and body weight 52 kg. General examination from head to extremities was within normal limits. Localized status examination found vaginal bleeding due to menstruation on the 3rd day. On gynecological examination, there was an anteflexed uterus with a regular size, smooth portio, no mass palpable, right and left adnexa within normal limits, right and left parametrium found no abnormalities, cavum Douglas was not prominent.

On laboratory examination, the results obtained Hb, 8.2 g/dL, leukocytes 7450/mm<sup>3</sup>, hematocrit 27.8%, platelet 374 × 10<sup>3</sup>/mm<sup>3</sup>, mean corpuscular volume (MCV) 63.5 fL, mean corpuscular hemoglobin (MCH) 18.7 pg, mean corpuscular hemoglobin concentration (MCHC) 29.5 g/dL, ureum/creatinine 32/0.74 mg/dL, blood sugar levels 81 mg/dL, and Na/K/Cl 137/3.6/106 mmol/L. On ultrasound examination, an anteflexed uterus was found with a size of 6.95 × 4.2 × 3.85 cm, endometrial thickness: 1.64 cm, right ovary with a size of 2.88 × 1.34 cm, and left ovary measuring 2.49 × 2.33 cm with the impression: AUB-M (thickening of the endometrium). Then, the patient was diagnosed with AUB-M (endometrial thickening) and given therapy of Primolut 2 × 5 mg tab, mefenamic acid 3 × 500 mg, tranexamic acid 3 × 500 mg, and ferrous sulfate 2 × 1. The patient is planned to undergo diagnostic curettage.

Curettage is performed with a sharp curette starting from 12 o'clock clockwise to take endometrial tissue for examination in the PA laboratory. Microscopically, the tissue preparations of the endometrium, which mostly consist of massive bleeding masses, appear, among others, fragmented endometrial tissue with epithelial coatings of columnar cells forming a polypoid image. The endometrial gland is proliferating, with tubular lumen, and partially dilated. The glandular epithelial lining consists of basophilic

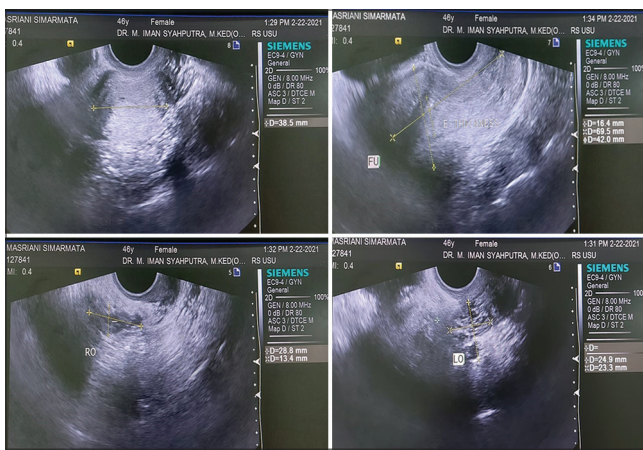


Figure 1: Patient ultrasonography transabdominal examination results

chromatin, eosinophilic cytoplasm. The loose stroma consists of round and oval cells accompanied by a moderate mononucleic inflammatory cell. Proliferation of blood vessels was also found. Then, it is concluded as complex hyperplasia endometrium without atypia cells.

## Discussion

AUB includes all menstrual abnormalities both in terms of number and duration. Clinical manifestations may include profuse, slight bleeding, prolonged, or irregular menstrual cycles. The term menorrhagia is currently replaced by heavy menstrual bleeding while AUB caused by coagulopathy, local endometrial hemostasis disorders, and ovulation disorders are disorders previously included as dysfunctional uterine bleeding. In Mrs. M, there are clinical manifestations in the form of prolonged menstruation with a history of bleeding between menstrual cycles, pain during menstruation, and low back pain. Mrs. M also admitted to changing sanitary napkins >10 times a day. Hence, it can be diagnosed with AUB or AUB. Patients are said to experience pain during menstruation and low back pain so that AUB-A complaints can be excluded. According to FIGO, acute AUB is defined as profuse bleeding so that prompt treatment is needed to prevent blood loss. Acute AUB can occur in chronic AUB conditions or without a previous history.

General examinations should focus on excluding systemic disorders such as thyroid disease, hyperandrogenism, or Cushing's. Abdominal and pelvic examinations are usually recommended to assess pelvic tumors and other specific pathologies. For example, petechiae, purpura, ecchymosis, or bleeding gums may indicate bleeding disorders. When the history was taken, the predisposing factors were denied so that the possibility of AUB due to systemic

conditions was excluded. The patient's physical examination also did not reveal any other systemic complaints so that AUB-C could be excluded. The patient is also not medically intervened by hormonal drugs such as hormonal contraception so that AUB-I can be excluded. According to Tommaso *et al.*, it is said that the history and physical examination are the main keys in assessing the patient's diagnosis. Anamnesis is performed to assess the possibility of uterine abnormalities, risk factors for thyroid disorders, drastic weight gain and loss, as well as a history of hemostatic abnormalities in the patient and his family. It is necessary to inquire about previous menstrual cycles and the time when AUB began. For women using the contraceptive pill, it is necessary to ask about the level of adherence and other drugs that are thought to interfere with coagulation. Physical examination is first performed to assess the stability of the hemodynamic state. Ensure that bleeding originates from the cervical canal and is not associated with pregnancy. Body mass index examination, signs of hyperandrogenism, enlarged thyroid gland or hypothyroid/hyperthyroid manifestations, galactorrhea, visual field disorders (pituitary adenoma), purpura, and ecchymosis should be examined. Careful gynecological examination is necessary for the possibility of uterine myomas, polyps, endometrial hyperplasia, or malignancy.

In the patient, there was no sign of an abnormal mass so that he could exclude any mass such as uterine myoma, polyp, and malignancy so that AUB-L could be excluded. Blood tests especially need to be done to assess the indicators of anemia. Patients with AUB often experience anemia due to excessive bleeding. In patients HB 8.2 g/dL, hematocrit 27.8%, MCV 63.5 fl, MCH 18.7 pg, and MCHC 29.5 g/dL which indicate a decrease of blood components so Mrs. M interpreted with anemia and this finding in according to Tommaso *et al.* said in women with AUB, a complete blood count can identify anemia and the degree of blood loss. Screening for coagulation disorders is also necessary if a clear cause cannot be found. These include a complete blood count with a platelet count partial thromboplastin time and a prothrombin time and possibly also checking for special tests for von Willebrand's disease.

Ultrasound examination is performed to assess the size, shape of the uterus, the presence of fibroids, polyps, adenomyosis, and uterine anomalies such as uterine didelphys, sometimes polycystic ovaries are also found. Endometrial pathologies such as polyps and/or malignancies were excluded. Hysteroscopy was confirmed as the gold standard in AUB assessment. At the time of ultrasound, the patient did not find any significant abnormalities in the ovaries so that he could exclude AUB-O. In patients, there is a thickening of the endometrial wall so that AUB-M can be diagnosed. According to Goldstein, sonography allows evaluation of anatomical abnormalities of the uterus and endometrium. These investigative modalities can assist

in the diagnosis of endometrial polyps, adenomyosis, leiomyomas, uterine anomalies, and endometrial thickening associated with hyperplasia and malignancy.

Age, desire to maintain fertility, coexisting medical conditions, and patient preferences are important considerations. For each method suggested, the patient must be aware of the risks and contraindications, to allow for the correct choice. Patient satisfaction level can be influenced by efficacy, expectations, cost, inconvenience, and side effects. Hence, management must be considered. Patients were given therapy in the form of progesterone, Primolut 2 × 5 mg tabs, administration of nonsteroidal anti-inflammatory drugs (NSAIDs) in the form of 3 × 500 mg tranexamic acid and 3 × 500 mg mefenamic acid, and iron supplementation in the form of 2 × 1 ferrous sulfate (SF) was in accordance with the clinical manifestations of patients with the AUB-M diagnosis. Curettage is considered to relieve ongoing menorrhagia. According to the SOGC, administration of NSAIDs can inhibit cyclo-oxygenase and reduce levels of endometrial prostaglandins. Progestin administration may be useful for women with irregular cycles and with anovulatory cycles if it is given for 21 days every month. Moreover, according to Gibson also said, someone with AUB has anemia due to excessive bleeding so that giving SF also needs to be considered to improve bleeding. In patients, so that worsening due to abnormal circulation can be avoided.

The IETA group was formed in Chicago at the World Congress of Ultrasound in Obstetrics and Gynecology in 2008 with the aim of agreeing on terms and definitions to describe ultrasound findings in the uterine cavity. In most women, the endometrium and uterine cavity should be scanned transvaginally. A transabdominal scan may be needed if there are large fibroids or an enlarged uterus globally. In the IETA agreement, it was adjusted to a category in the form of grayscale ultrasound which was assessed for endometrial echogenicity, whether regular or not, whether heterogeneous, homogeneous, hyperechoic, hypoechoic, or isoechoic. It also assessed for irregular, linear, non-linear or unidentified endometrial diameter, bright edge or not. The endometrial-myometrial junction was assessed whether intermittent, regular, irregular or unidentifiable. In the Doppler feature, the warrants value is 4, namely, colorless, minimal color, medium number of colors, and abundant colors. A single dominant vessel with or without branching, multiple dominant vessels of focal origin, multiple dominal vessels of multifocal origin, scattered vessels, circular flow, or no detectable color Doppler signal were determined. It was assessed whether the blood vessels branched irregularly. It also assessed how the color pattern.

On the transvaginal ultrasound examination, the results were obtained. The bladder is filled, the uterus is anteflexed with a size of 6.95 × 4.2 × 3.85 cm, the thickness of the endometrium: 1.64 cm, the right ovary with a size of 2.88 × 1.34 cm, the left ovary with

a size of 2.49 × 2.33 cm, and free fluid is not found (Figure 1). So that, the impression of TAS ultrasound examination is AUB-M (thickening of the endometrium). According to the IETA, a quantitative assessment of endometrial thickness, intrauterine lesions, and intracavitary fluid is performed. Endometrial thickness is the maximum measurement in the sagittal plane. The accompanying ultrasound provides measurement of endometrial thickness in the absence of intracavity fluid; the endometrium should be measured where it appears thickest. If intracavity pathology is present, the total thickness of the endometrium including the lesion should be recorded. However, if intracavity myomas are clearly identified, they should not be included in the endometrial thickness measurement. The amount of intracavity fluid is determined by its largest measurement in the sagittal plane. The results obtained by this patient were 1.64 cm thick endometrium. The patient was assessed in the form of free fluid which was not found.

In assessing the quality of the endometrium, the echogenicity of the endometrium was seen. The echogenicity was described as hyperechogenic, isoechoic, or hypoechoic as compared to the echogenicity of the myometrium. Endometrial echogenicity should be defined as "uniform," if the endometrium is homogeneous with symmetrical anterior and posterior sides. This patient was not assessed for echogenicity and thus did not meet the appropriate analysis defined by IETA.

Nor patient assessed and the Doppler power assesses the endometrial-myometrial junction and vascular pattern in the endometrium. The entire tumor should be examined with color Doppler imaging. For tumors with multiple sample areas, a series of results with a maximum mean maximum velocity (TAMXV) of  $3 \pm 10$  and corresponding values for the pulsatility index, resistance index, and peak systolic velocity were selected. If a semi-quantitative subjective flow assessment is made, the following terms can be used to describe the amount of blood flow (area and color scale) within the septa, cyst wall, or solid tumor area. This color score refers only to the color Doppler image and not to the Doppler shift spectrum. It is only given once (for the whole tumor).

The patient also did not undergo hystero-graphy examination. Sonohysterography is the infusion of fluid into the uterine cavity to act as a negative contrast agent. Saline-stepped sonohysterography or gel stepped sonohysterography may be used. According to the IETA, the vascular pattern in the endometrium is reported to be associated with the presence or absence of a "dominant vessel" or other specific pattern. "Dominant vessel" is defined as one or more distinct blood vessels (arteries and/or veins) passing through the endomyometrial junction. Echogenicity is acceptable, and the higher the proportion of tumors with multiple vessels of focal or multifocal origin and

the higher the color score. The strongest differentiators between high- and low-grade cancer are larger tumor size (endometrial thickness and volume), irregular endometrial/myometrial border, and high color score.

Anatomic pathology by curettage is required in women with abnormal bleeding, histological evaluation of the endometrium may identify infectious or neoplastic lesions such as endometrial hyperplasia or cancer. On histological evaluation, it appears, among others, fragmented endometrial tissue with epithelial lining of columnar cells forming a polypoid image. The endometrial gland is proliferating, with the lumen tubular, partially dilated. The glandular epithelial lining consists of basophilic chromatin and eosinophilic cytoplasm. The loose stroma consists of round and oval cells accompanied by a moderate mononucleic inflammatory cell and proliferation of blood vessels. It can be concluded that the abnormality is complex hyperplasia endometrium without atypia cells. According to Vand den Bosch T said, endometrial biopsy can be performed easily in premenopausal women with previous vaginal delivery. A biopsy is more difficult in women with a history of previous cesarean delivery, women who are nulliparous or who have had previous cervical surgery. Endometrial biopsy can detect more than 90% of cancers. The pathology of the endometrium can diagnose endometrial cancer or determine the likelihood of cancer.

## Conclusion

According to IETA, the vascular pattern in the endometrium is reported to be associated with the presence or absence of a "dominant vessel" or other specific pattern. "Dominant vessel" is defined as one or more distinct blood vessels (arteries and/or veins) that pass through the endomyometrial passage. The quality of the endometrium is seen from the endometrial echogenicity. The echogenicity was described as hyperechogenic, isoechogenic, or hypoechogenic as compared to the echogenicity of the myometrium. According to the IETA, quantitative measurements was

performed to measure the endometrium, intrauterine lesions and intracavitary fluid. Anatomical pathology examination by means of curettage is required in women with abnormal bleeding, histological evaluation of the endometrium which can identify infectious or neoplastic lesions such as endometrial hyperplasia or cancer. Curettage is prohibited to relieve ongoing menorrhagia.

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