

Three cases of heavy menstrual bleeding with uniform thickening of the junctional zone endometrium

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Abstract

Heavy menstrual bleeding is a type of abnormal uterine bleeding. Abnormal uterine bleeding includes the poorly characterized “not otherwise classified” category. Here, we report three abnormal uterine bleeding-not otherwise classified cases with uniform thickening of the junctional zone endometrium. Case 1: A 33-year-old nullipara with heavy menstrual bleeding presented with severe anemia (hemoglobin: 4.7 g/dL) and an 8.4-mm junctional zone endometrium on magnetic resonance imaging. Her condition improved with iron and low-dose estradiol-progestins. Case 2: A 36-year-old nulligravida had heavy menstrual bleeding, anemia (hemoglobin: 9.5 g/dL), and a 9.4-mm junctional zone endometrium; her anemia improved with iron supplementation. Case 3: A 39-year-old multipara had heavy menstrual bleeding, anemia (hemoglobin: 9.6 g/dL), and a 12.3-mm junctional zone endometrium, and was managed with a levonorgestrel-releasing intrauterine system. Pelvic examination, transvaginal sonography, and uterine size on magnetic resonance imaging were normal in all cases. In those without uterine abnormalities, uniform thickening of the junctional zone endometrium (≥ 8 mm) may trigger heavy menstrual bleeding; hence, magnetic resonance imaging may be warranted in abnormal uterine bleeding-not otherwise classified cases.

Keywords

Heavy menstrual bleeding, abnormal uterine bleeding, PALM-COEIN, junctional zone endometrium, magnetic resonance imaging

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Introduction

Heavy menstrual bleeding (HMB) is a type of abnormal uterine bleeding (AUB), traditionally described as bleeding for >7 days or blood loss of >80 mL per menses.¹ However, it can also be defined as an increase in menstrual blood flow that interferes with quality of life.² AUB cases may be classified as polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia (PALM), which are related to structural abnormalities, or coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic causes, and not otherwise classified (COEIN), which are related to nonstructural causes.³ In the COEIN group, not otherwise classified (AUB-N) refers to cases in which the cause of HMB cannot be identified³ and no standard treatment strategy has been determined.

In the uterus, the junctional zone endometrium (JZE) is a thin layer between the myometrium and endometrium containing very little extracellular matrix, with increased nuclear

size and number.⁴ T2-weighted magnetic resonance imaging (MRI) is one of the most suitable tools for visualization and evaluation of the JZE.⁴ The function of the JZE may be related to uterine contraction and sperm transport, but this has not yet been properly clarified.⁴ In addition, JZE thickening is associated with various uterine pathologies, particularly in the diagnosis of adenomyosis, in which the JZE grows to >12 mm.⁵

Here, we report three cases of AUB-N in which JZE was uniformly thickened without any structural abnormalities.

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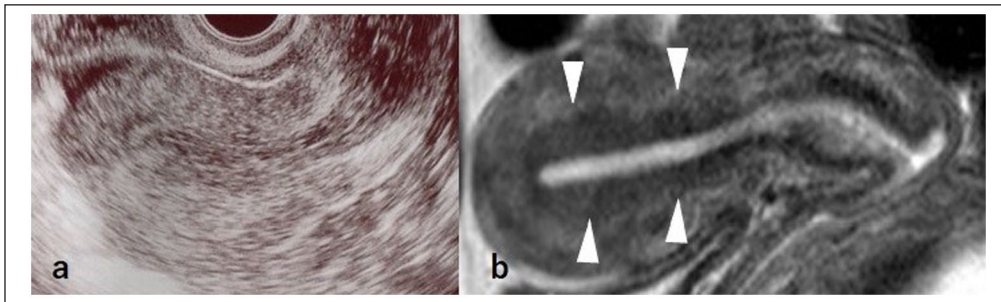


Figure 1. The uterus of case 1: (a) transvaginal ultrasonography and (b) magnetic resonance imaging T2-weighted image. Arrowheads: junctional zone endometrium.

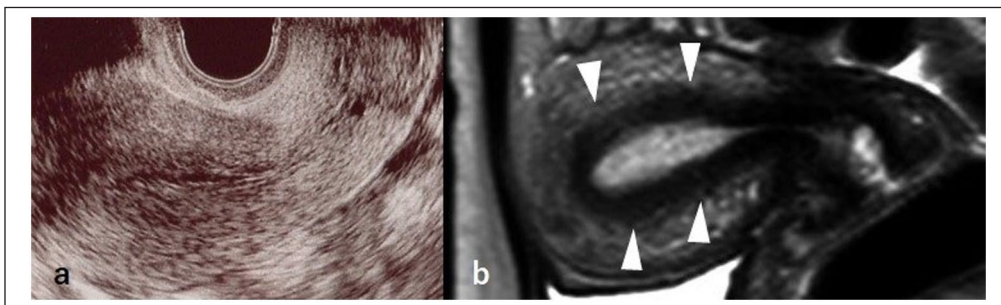


Figure 2. The uterus of case 2: (a) transvaginal ultrasonography and (b) magnetic resonance imaging T2-weighted image. Arrowheads: junctional zone endometrium.

Case

Case 1

A 33-year-old nulliparous woman visited another doctor with a chief complaint of HMB. She was referred to our hospital for severe anemia (hemoglobin: 4.7 g/dL). The patient had a regular menstrual cycle with normal duration and very mild dysmenorrhea. No other abnormalities related to HMB were found in the blood examination results. Pelvic examination and transvaginal ultrasonography were normal (Figure 1(a)), while color Doppler showed normal blood flow. MRI revealed normal uterine size, with a long axis of 80.6 mm, a short axis of 41.0 mm, and a width of 51.6 mm; however, the JZE thickness was 8.4 mm (Figure 1(b)). No uterine fibroma or adenomyosis was observed. Cervical and endometrial cytopathological results were repeatedly negative, and serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), and estradiol (E2) levels were normal. We therefore classified this case as AUB-N. Blood transfusion was recommended, but the patient did not provide consent; therefore, iron preparations (saccharated ferric oxide 80 mg/day intravenously during admission, dry iron sulfate 0.035 mg/day orally after discharge) and low-dose estradiol-progestin (norethisterone 1 mg, ethinylestradiol 0.035 mg/day orally) were administered instead. Two months later, the patient's anemia was cured.

Case 2

A 36-year-old nulligravid woman visited our hospital for HMB. She had a history of leiomyoma prior to 4 years managed with hysteroscopic myomectomy. Her HMB resolved after surgery but had recurred shortly before her visit; consequently, she revisited our hospital. She had no dysmenorrhea or menstrual cycle irregularities. She had anemia with a hemoglobin level of 9.5 g/dL; however, her blood examination results revealed no other abnormalities associated with HMB. Serum LH, FSH, PRL, and E2 levels were normal. Pelvic examination or ultrasonography likewise showed a normal uterus (Figure 2(a)), and color Doppler revealed normal blood flow. HMB did not improve even after dilatation and curettage, and pathological examination of the excised endometrial tissue revealed normal findings. MRI also revealed normal uterine size, with a long axis of 84.4 mm, short axis of 50.4 mm, and width of 65.2 mm; however, the JZE thickness was 9.4 mm (Figure 2(b)). JZE thickening was not evident on MRI before surgery for submucosal fibroids, and no uterine fibroma or adenomyosis was observed. We therefore classified this case as AUB-N. Her anemia was alleviated only by administration of iron preparations (two tablets of 50-mg sodium ferrous citrate/day orally). The patient is currently under observation without signs of anemia.

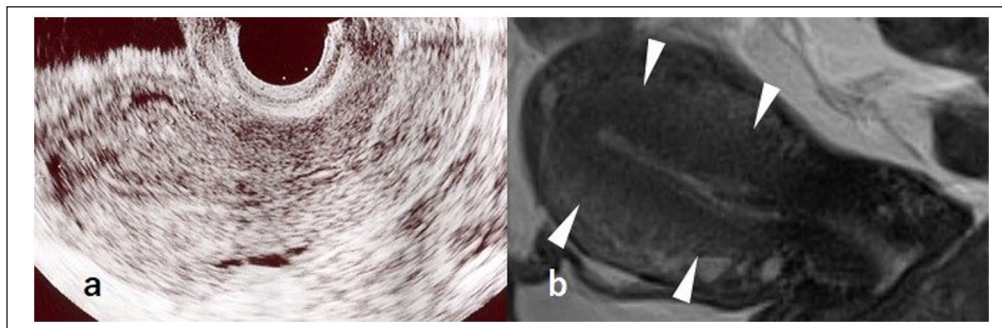


Figure 3. The uterus of case 3: (a) transvaginal ultrasonography and (b) magnetic resonance imaging T2-weighted image. Arrowheads: junctional zone endometrium.

Case 3

A 39-year-old multiparous woman visited our hospital for HMB without dysmenorrhea. Her menstrual cycle was irregular, occurring approximately every 32–36 days, but the duration of her menstruation was normal, lasting for 6 days. Serum LH, FSH, PRL, and E2 levels were normal. She had anemia with a hemoglobin level of 9.6 g/dL; no other abnormalities indicating significant HMB were observed in her blood examination results. Pelvic examination and ultrasonography showed a normal uterus (Figure 3(a)), and color Doppler showed normal blood flow. MRI also revealed a normal uterus, with a long axis of 86.8 mm, short axis of 51.3 mm, and width of 52.5 mm; however, the JZE thickness was 12.3 mm (Figure 3(b)). No uterine fibroma or adenomyosis was observed. Cervical and endometrial cytopathological results were repeatedly negative. We therefore classified this case as AUB-N. The patient's anemia and HMB were alleviated through placement of a levonorgestrel-releasing intrauterine system. Currently, no recurrence of HMB has been observed and the patient is under observation.

Discussion

In the PALM-COEIN classification, cases classified as AUB-N have an unclear cause. In the present study, the three cases of AUB-N were characterized by uniform thickening of the JZE rather than partial thickening, such as in typical adenomyosis. Furthermore, this thickening was characterized by the absence of high-intensity regions on T2-weighted MRI, which indicate endometrial glands and are usually present in adenomyosis. In addition, unlike adenomyosis, these cases had no uterine wall thickening or uterine body swelling.

JZE thickening appears to be one of the causes of HMB. The two-dimensional ultrasonography used in general gynecological examinations makes it difficult to visualize the JZE even with a high-frequency probe (5–10 MHz); hence, it is not suitable for JZE evaluation.⁶ Compared to ultrasonography, MRI is more useful for identifying the JZE, which is distinguished by low signal intensity on T2-weighted

MRI.⁷ Although the thickness of the JZE naturally changes with age and with the stages of the menstrual cycle, the mean JZE thickness among reproductive-age women is approximately 5–8 mm.⁴ Embryologically, the JZE is said to be derived from the Müllerian duct, unlike the outer muscularis. Although their exact physiological significance remains unclear, Noe et al.⁸ suggested that the outer myometrium (neometra) is responsible for the forces of labor, while the endometrial–subendometrial unit (archimetra) plays a role in sperm transportation and implantation. The three cases presented here further suggest that the JZE may regulate menstrual flow and duration.

Adenomyosis is considered the most typical pathological condition of the uterus with thickening of the JZE.⁶ The presence of bright foci on T2- or T1-weighted MRI supports the diagnosis of adenomyosis. In general, a maximal junctional zone thickness of >12 mm is highly predictive of adenomyosis.⁵ Since typical adenomyosis has a limited area of thickening, the JZE does not thicken uniformly. In addition, scattered high-intensity foci indicating uterine glands are often observed on the T2-weighted MRI scan, and since the uterine wall is thickened, the uterine volume naturally increases. However, the uterine volume was not increased in these three cases, and the JZE was thickened uniformly. Furthermore, there was no high-intensity region in the thickened JZE. Since the JZE thickening exceeded 8 mm in all three cases, the possibility of adenomyosis cannot be ruled out; however, these are clearly not cases of typical adenomyosis.

Color Doppler examinations were performed on all cases, and no abnormal blood flow was found in any of them. However, the resistance index and pulsatility index of uterine arteries by pulsed Doppler imaging were not measured. Ideally, this should have been performed for the evaluation of HMB possibly associated with malignant disease.⁹

The patients' symptoms in these cases were relieved by hormone therapy; therefore, no surgical treatment was performed. Whether hormone therapy will be effective in similar cases in the future requires accumulation of similar cases. In addition, histopathological analysis was not conducted as neither the uterus nor the lesions were

removed. Therefore, microscopic examination of JZE thickening, which is theorized to be the cause of HMB, was not done. In the future, histopathological examination must be conducted in similar cases where hysterectomy is necessary. Changes in JZE thickening over time should have been investigated as well. In case 2, MRI performed before hysteroscopic submucosal myomectomy 4 years previously confirmed no JZE thickening. Therefore, after treatment, it is necessary to examine whether JZE thickening was also reduced along with the symptoms or remained unchanged.

Conclusion

We found that some cases of AUB-N are caused by JZE thickening. Hence, even if there are no abnormalities in the uterus on pelvic examination and ultrasonography, it is important to consider that uniform (circumferential) thickening of the JZE (≥ 8 mm) may lead to HMB. Therefore, gynecologists may consider performing MRI when an AUB-N case is encountered. If MRI can reveal the cause of the HMB, thereby eliminating the patient's fear of malignancy, then it would be well worthwhile to perform an MRI scan.

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Data availability

Owing to the nature of this report, participants of this case report did not agree for their data to be shared publicly; hence, supporting data are not available.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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