

A Case of Atypical Lobular Endocervical Glandular Hyperplasia Extending to the Endometrium, with Progression Documented by MRI

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Lobular endocervical glandular hyperplasia (LEGH) is a benign proliferative disorder with gastric-type differentiation and forms cervical multilocular cystic lesions (CMCL). Atypical LEGH is LEGH with apparent nuclear and architectural atypia and is regarded as a precursor of gastric-type adenocarcinoma (GAS) of the uterine cervix. However, the clinical course of atypical LEGH remains unclear. We herein report a case of atypical LEGH in which gradual extension of the lesion area to the adjacent endometrium was documented by regular magnetic resonance imaging (MRI) during the follow-up. A 41-year-old woman was referred to our hospital because of CMCL. CMCL was clinically diagnosed as LEGH based on endocervical cytology, MRI, and gastric-type mucin secretion. MRI showed small cysts in the inner layer and larger cysts in the outer layer of the upper uterine cervix, the so-called "Cosmos pattern". Multiple MRI examinations during the follow-up revealed that CMCL gradually increased in size and extended into the adjacent lower endometrium. Eight years later, the patient underwent total laparoscopic hysterectomy due to an excessive watery vaginal discharge. The pathological diagnosis was atypical LEGH, which was located beside LEGH without atypia and extended to the adjacent endometrium. We have previously reported that an increase in tumor size was important for detecting malignant transformation. This case suggests that progression to the adjacent endometrium may also be a significant sign of malignant transformation. Furthermore, in such cases, a diagnosis may be possible by proactively performing endometrial cytology and histology. *Shinshu Med J 74 : 217—223, 2026*

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I Introduction

Lobular endocervical glandular hyperplasia (LEGH) is a benign proliferative disorder that forms cervical

multilocular cystic lesions (CMCL) in the upper uterine cervix and produces gastric-type mucin¹⁾. LEGH is also known as a potential precursor of gastric-type adenocarcinoma (GAS), a major histological type of human papillomavirus (HPV)-independent adenocarcinoma of the uterine cervix. Recent studies reported that the risk of malignant transformation is higher in atypical LEGH, which is LEGH with apparent nuclear atypia, than in LEGH without nuclear atypia²⁾³⁾. In

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addition, we previously proposed worsening cytological findings and the enlargement of CMCL as important signs for the malignant transformation of LEGH⁴⁾. Since LEGH and GAS generally develop in the upper uterine cervix, GAS is known to frequently extend to the adjacent endometrium⁵⁾. Furthermore, these gastric-type lesions have been reported to occur simultaneously in multiple Müllerian organs, such as the cervix as well as the endometrium and fallopian tubes⁶⁾. However, cases of LEGH directly extending to the adjacent endometrium have rarely been reported, and its frequency remains unknown. We herein report a case of atypical LEGH in which gradual extension of the lesion area to the adjacent endometrium was documented by regular magnetic resonance imaging (MRI) during the follow-up.

II Case Presentation

A 41-year-old woman, gravida 2 para 2, visited a nearby gynecological clinic with a watery vaginal discharge. She was referred to our hospital because CMCL was detected by transvaginal ultrasound sonography. Endocervical cytology with conventional Papanicolaou staining was classified as “atypical glandular cells (AGC)” due to gastric-type differentiation with yellowish gastric-type mucin in contrast to pinkish normal endocervical mucin, despite no cellular atypia⁷⁾. Gastric-type mucin in cervical mucus was also detected by a HIK1083 latex agglutination assay (Cica HIK gastric mucin®, Kanto Chemical, Tokyo, Japan)⁷⁾. In the upper uterine cervix, T2-weighted MRI (T2-WI) showed CMCL with smaller cysts at the inner layer surrounded by larger ones with a clear margin (**Fig. 1A**), the so-called “Cosmos pattern”²⁾. In addition, a low-intensity area in the lower endometrium contiguous from CMCL was noted, which suggested direct extension to the endometrium. The lesion size including CMCL and the low-intensity area in the endometrium was 33×15 mm (**Fig. 1A**). There were no findings indicative of malignancy. According to our diagnostic protocol⁸⁾, the initial clinical diagnosis of this CMCL was LEGH. We informed the patient of the possibility of co-existing small GAS lesions and the risk of future progression to GAS, and proposed management

options, including hysterectomy, cone biopsy, or follow-up. The patient selected follow-up examinations every 3–6 months without any surgery.

During the follow-up period, conventional endocervical cytology was repeatedly performed, and the diagnosis was consistently AGC due to differentiation into gastric-type cells, with no glandular cellular atypia being detected. Therefore, we did not perform endocervical or endometrial biopsies.

Pelvic MRI was repeatedly performed at the ages of 46, 48, and 49 years. Images obtained at the age of 46 years showed that the lesion size together with the cervix and endometrium had slightly increased to 44×22 mm, with a growth rate of 33 % calculated based on the longest diameter from the values at the age of 41 years (**Fig. 1B**). However, there were no image findings indicative of malignancy as well as no cytological atypia. MRI at the age of 48 years showed that the lesion size remained unchanged at 45×18 mm, with a growth rate of 36 % being calculated in the same manner (**Fig. 1C**). Small cysts also appeared in the low-intensity area in the endometrium on T2-WI resembling endocervical cysts, again strongly suggesting the direct extension of LEGH to the endometrium. Since repeated endocervical cytology showed no cellular atypia, we did not perform endocervical or endometrial biopsy, and the follow-up was continued.

At the age of 49 years, the patient requested hysterectomy because of a large volume of a watery vaginal discharge. Preoperative MRI showed that the lesion had increased to 50×20 mm, with a growth rate of 52 %, and small cysts in the low-intensity area in the endometrium on T2-WI had increased from MRI findings obtained at the ages of 41, 46, and 48 years (**Fig. 1D**). According to our previous study, malignant transformation is suspected when CMCL increases by more than 38 %⁹⁾. Therefore, we considered surgery to be necessary to confirm the definitive diagnosis of CMCL even though several Papanicolaou smears performed from the age of 41 years had not detected AGC. After obtaining written consent from the patient and her family, total laparoscopic hysterectomy and bilateral salpingectomy were performed at the

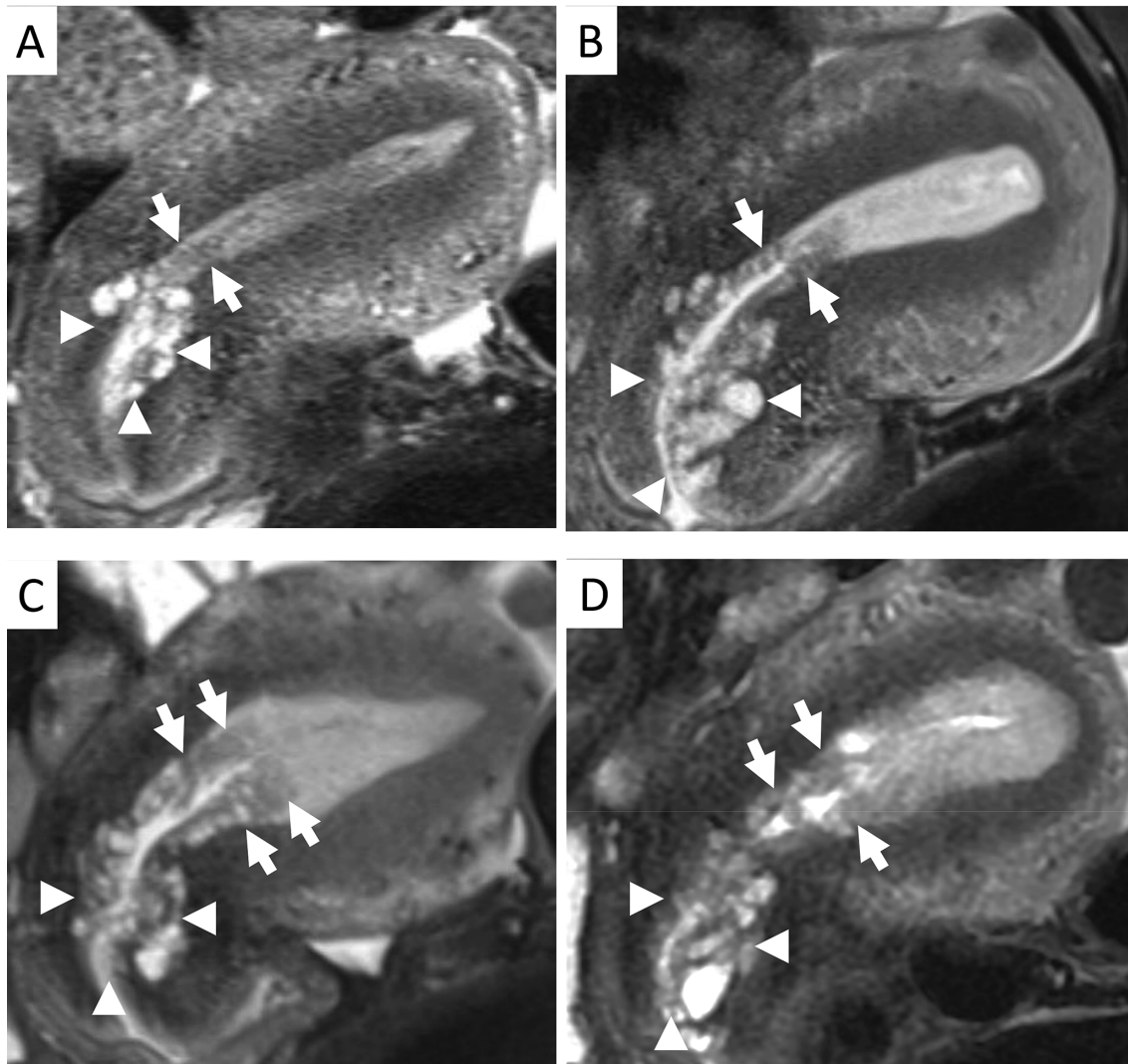


Fig. 1 Sagittal fat-suppressed T2-weighted MR images (T2-WI) at the ages of 41 (A), 46 (B), 48 (C), and 49 years (D). Clustered small cystic lesions were observed at the inner endocervix and were surrounded by larger cysts with a clear margin in the uterine cervix (arrowheads). The low-intensity area with small cysts and continuous to CMCL on T2-WI gradually extended to the uterine endometrium and the cyst inside was also enlarged (arrows).

age of 49 years. During surgery, there was no dissemination in the pelvic cavity and peritoneal washing cytology was negative.

Macroscopically, there were multiple small cysts in the uterine cervix and the lower uterine segment (**Fig. 2**). Microscopically, the lesions in the cervix showed that endocervical glands with a lobular structure has proliferated and contains a large amount of PAS-positive mucin. In this lesion, immunostaining for HIK1083 and Claudin 18 was positive and the Ki-67 index was 1 %, findings that were consistent with LEGH (**Fig. 3A-E**). In addition, complex papillary struc-

tures along with focal cellular atypia were detected without stromal invasion, and the Ki-67 index was 30 % ; therefore, the final diagnosis was atypical LEGH (**Fig. 3A, F-I**). In the uterine endometrium, atypical glands resembling atypical LEGH were detected, continuing with the cervical lesion. Although the normal endometrial stroma was edematous because of the secretory phase, the stroma surrounding atypical LEGH of the endometrium was fibromatous. No abnormalities were found in the uterine endometrium. In contrast, atypical glands were not recognized in the uterine myometrium or fallopian tubes. These findings

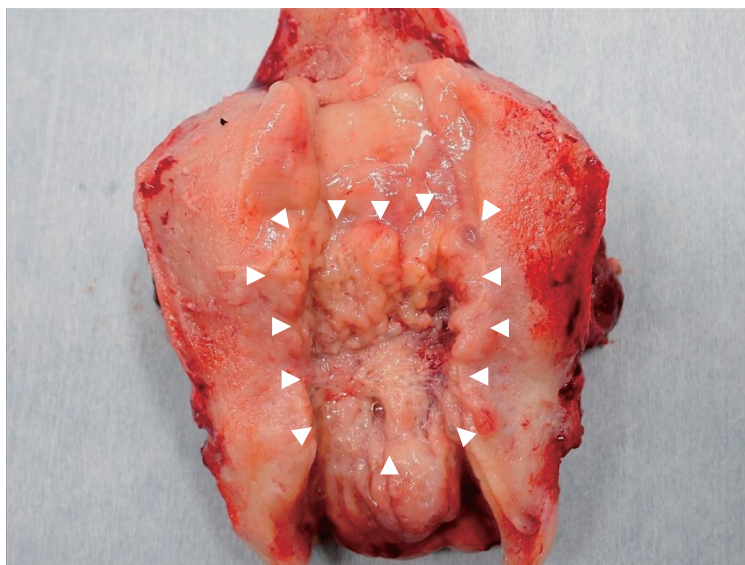


Fig. 2 Macroscopic findings of the uterus. Multiple small cysts were observed in the uterine cervix and lower uterine segment (arrowheads).

suggested that atypical LEGH extended from the uterine cervix to the endometrium.

III Discussion

To the best of our knowledge, there have been no case reports of atypical LEGH in which MRI captured the gradual spread of cervical lesions toward the endometrium. Furthermore, gastric-type AIS may occasionally extend into the endometrium; however, there have been only two reports of atypical LEGH progressing to the endometrium, with only one case reported^{10,11)}. In the present case, during the eight years of follow-up observations for LEGH, MRI showed almost no change in the size of cervical CMCL; however, the endometrial lesion connected to the cervical lesion had grown.

Most cases of uterine cervical adenocarcinoma are associated with persistent HPV infection¹²⁾, whereas GAS, which accounts for 20–25 % of all uterine adenocarcinoma cases, is a representative non-HPV-related adenocarcinoma with a more aggressive clinical behavior than HPV-related adenocarcinoma¹³⁾. GAS is characterized by resistance to conventional radiotherapy and platinum-based chemotherapy and is associated with a less favorable prognosis than squamous cell carcinoma and usual-type endocervical adenocarcinoma, posing significant therapeutic chal-

lenges in advanced or recurrent settings¹³⁾. However, the clinical symptoms and morphological findings of these carcinomas were similar to those of LEGH⁹⁾. Therefore, a proper preoperative diagnosis of CMCL is very important and it is crucial to detect the malignant transformation of LEGH at the earliest stage possible during follow-ups. We previously provided a protocol for the diagnosis and management of CMCL, including Nabothian cysts, LEGH, or GAS, using the combination of MRI, endocervical cytology, and gastric-type mucin⁸⁾. Furthermore, a case report of LEGH that progressed to malignancy during the follow-up showed that worsening endocervical cytology and an increase in tumor size were important for detecting malignant transformation⁴⁾. Another case report clarified that the cut-off value for the proliferation rate suggesting malignant transformation is 38.1 %⁹⁾. In the present case, AGC was not detected in endocervical cytology of the uterine cervix. However, the size of CMCL increased by more than 38 % and lesions characteristically extended to the uterine endometrium on MRI.

Only one case of atypical LEGH involving the endometrium has been reported¹⁰⁾. LEGH and atypical LEGH were detected in the uterine cervix, and LEGH and mucinous adenocarcinoma *in situ* had extended to the uterine endometrium. Although the preopera-

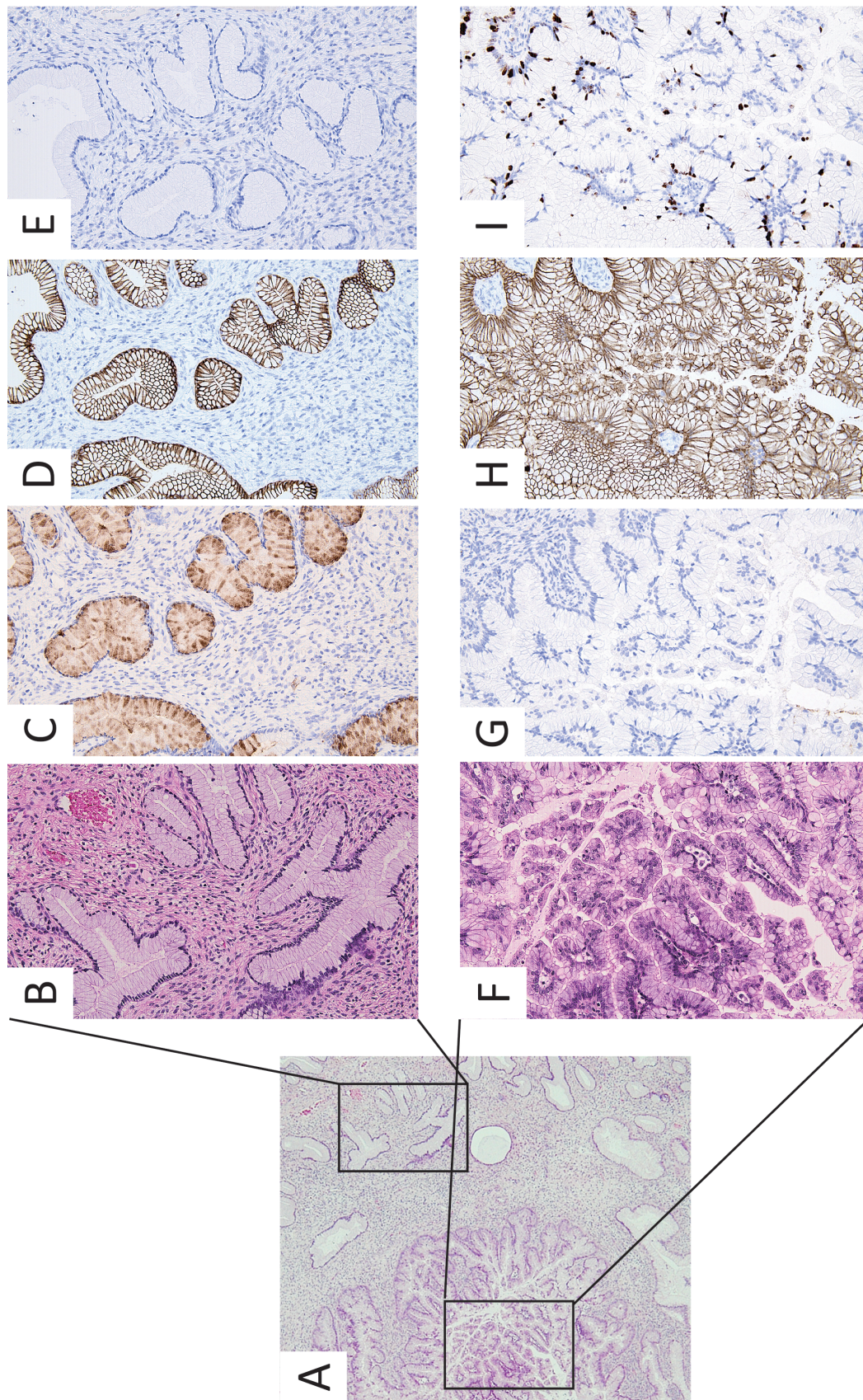


Fig. 3 Microscopic findings of LEGH (A-E) and atypical LEGH in the uterine cervix (A, F-I). A : Hematoxylin and Eosin staining (H & E) ($\times 40$). Endocervical glands with a lobular structure had proliferated and contained a large amount of cytoplasmic mucin. B : H & E ($\times 200$). No significant architectural and cytological atypia was observed. C : Immunohistochemistry for HIK1083 was positive ($\times 200$). D : Immunohistochemistry for Claudin 18 was positive ($\times 200$). E : Immunohistochemistry for Ki-67 ($\times 200$). The Ki-67 index of the lesion was 1 %. F : H & E ($\times 200$). Complex papillary structure along with cellular atypia was confirmed without stromal invasion. G : Immunohistochemistry for HIK1083 was negative ($\times 200$). H : Immunohistochemistry for Claudin 18 was positive ($\times 200$). I : Immunohistochemistry for Ki-67 ($\times 200$). The Ki-67 index of the lesion was 30 %.

tive diagnosis was unknown, histopathological findings of the removed uterus showed that cervical LEGH was continuous with the endometrial lesion and, thus, the cervical lesion was considered to have progressed to the endometrium. In the present case, LEGH and atypical LEGH were detected in the uterine cervix, and atypical LEGH had extended to the uterine endometrium. This finding suggests the potential of progression to the endometrium in particular as a sign of malignant transformation. Therefore, when monitoring the clinical course of CMCL, attention must be paid to progression to the endometrium. To date, MRI has not been used to capture the progression of LEGH lesions in the cervix into the endometrium. The low-intensity area of T2-WI with small cysts and continuous CMCL gradually extended to the endometrium (**Fig. 1**). A pathological examination revealed that low-signal intensity areas on T2-weighted endometrial images were atypical LEGH, which possibly reflecting the fibromatous stroma surrounding atypical LEGH in the endometrium.

We previously reported that worsening endocervical cytology during the follow-up of LEGH is important for detecting malignant transformation⁴⁾. However, in the present case, AGC was not detected. This may have been because the brush did not reach the lesion during cervical cytology and, thus, atypical cells

were not collected. In our experience, AGC has been detected by endometrial cytology in cases of CMCL undergoing follow-ups. Although it was not performed in the present case, endometrial cytology may have detected AGC. Furthermore, the pathological findings of the removed uterus in this case revealed atypical glands on the surface of the endometrium; therefore, a preoperative diagnosis may have been made by endometrial biopsy.

In summary, we have previously reported that an increase in tumor size was important for detecting malignant transformation. The findings in the present case suggest that progression to the adjacent endometrium may also be a significant sign of malignant transformation. Furthermore, in such cases, a diagnosis may be possible by proactively performing endometrial cytology and histology.

A review by Ohya et al.¹⁴⁾ includes preoperative MRI images for this case but lacks detailed descriptions beyond the MRI images. This report is the first to provide a detailed account of the patient's course from initial consultation to treatment and pathological diagnosis.

Conflict of Interest Statement

The authors have no conflicts of interest relevant to this article.

References

- 1) Nucci MR, Clement PB, Young RH: Lobular endocervical glandular hyperplasia, not otherwise specified: a clinicopathologic analysis of thirteen cases of a distinctive pseudoneoplastic lesion and comparison with fourteen cases of adenoma malignum. *Am J Surg Pathol* 23: 886-891, 1999
- 2) Takatsu A, Miyamoto T, Fuseya C, et al: Clonality analysis suggests that STK11 gene mutations are involved in progression of lobular endocervical glandular hyperplasia (LEGH) to minimal deviation adenocarcinoma (MDA). *Virchows Arch* 462: 645-651, 2013
- 3) Mikami Y, Kiyokawa T, Hata S, et al: Gastrointestinal immunophenotype in adenocarcinomas of the uterine cervix and related glandular lesions: a possible link between lobular endocervical glandular hyperplasia/pyloric gland metaplasia and 'adenoma malignum'. *Mod Pathol* 17: 962-972, 2004
- 4) Kobara H, Miyamoto T, Otsuki T, Ohya A, Shiozawa T: Worsening cytology and lesion enlargement are useful indicators for malignant transformation of lobular endocervical glandular hyperplasia during follow-up: A case report. *Gynecol Oncol Rep* 32: 100571, 2020
- 5) Kido A, Mikami Y, Koyama T, et al: Magnetic resonance appearance of gastric-type adenocarcinoma of the uterine cervix in comparison with that of usual-type endocervical adenocarcinoma: a pitfall of newly described unusual subtype of endocervical adenocarcinoma. *Int J Gynecol Cancer* 24: 1474-1479, 2014

- 6) Mikami Y, Kiyokawa T, Sasajima Y, et al: Reappraisal of synchronous and multifocal mucinous lesions of the female genital tract: a close association with gastric metaplasia. *Histopathology* 54: 184–191, 2009
- 7) Miyamoto T, Kobara H, Shiozawa T: Biology and management of lobular endocervical glandular hyperplasia. *J Obstet Gynaecol Res* 48: 3056–3067, 2022
- 8) Ando H, Miyamoto T, Kashima H, et al: Usefulness of a management protocol for patients with cervical multicystic lesions: A retrospective analysis of 94 cases and the significance of GNAS mutation. *J Obstet Gynaecol Res* 42: 1588–1598, 2016
- 9) Kobara H, Miyamoto T, Ando H, et al: Limited frequency of malignant change in lobular endocervical glandular hyperplasia. *Int J Gynecol Cancer* 10: 1480–1487, 2020
- 10) Dinges MM, Jaggesarsingh D, Petersen TH, Behbakht K, Singh M: Lobular endocervical glandular hyperplasia with extensive mucinous differentiation of endometrium and endometrial mucinous adenocarcinoma in situ: a case report and review of literature. *Gynecol Oncol* 122: 686–688, 2011
- 11) Busca A, Mirkovic J, Parra-Herran C: Gastric-type endocervical adenocarcinoma involving the endometrium and clinically mimicking endometrial neoplasia: A diagnostic challenge. *Am J Surg Pathol* 42: 983–985, 2018
- 12) An HJ, Kim KR, Kim IS, et al: Prevalence of human papillomavirus DNA in various histological subtypes of cervical adenocarcinoma: a population-based study. *Mod Pathol* 18: 528–534, 2005
- 13) Nishio S, Mikami Y, Tokunaga H, et al: Analysis of gastric-type mucinous carcinoma of the uterine cervix—An aggressive tumor with a poor prognosis: A multi-institutional study. *Gynecol Oncol* 153: 13–19, 2019
- 14) Ohya A, Fujinaga Y: Magnetic resonance imaging findings of cystic ovarian tumors: major differential diagnoses in five types frequently encountered in daily clinical practice. *Jpn J Radiol* 40: 1213–1234, 2022

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