Gastric-type Endocervical Adenocarcinoma Associated with Peutz-Jeghers Syndrome: A Case Report with Imaging Findings

Qingwen Xiao[1,3], Kuiming Jiang[2,3]*

[1] Department of Radiology, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

[2] School of the First Clinical Medical Sciences, Jinan University, Guangzhou, Guangdong, China

[3] Department of Radiology, Guangdong Women and Children Hospital, Guangzhou, Guangdong, China

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Abstract: Gastric-type endocervical adenocarcinoma (GAS) is the most common disease of cervical cancer that is not caused by HPV but is not taken seriously. We describe a woman diagnosed with GAS and Peutz-Jeghers syndrome (PJS) in this report. A 44-year-old woman experienced sporadic vaginal bleeding for one month. In addition, ten years ago, the patient was diagnosed with PJS. In place of the usual cervical structures, computed tomography and magnetic resonance imaging revealed an irregular cystic-solid mass, mostly composed by cystic tissue. Due to the development characteristics of gastric-type endocervical adenocarcinoma, preoperative imaging is of tremendous assistance in diagnosing patients. There is no previous case of predominantly cystic GAS with such a complete history and characteristic imaging findings. This discovery may aid future diagnoses of similar cases.

***Keywords*:** gastric-type endocervical adenocarcinoma, human papillomavirus, peutz-jeghers syndrome, magnetic resonance imaging, computed tomography

1. Introduction

China's most prevalent malignant reproductive system tumor is cervical cancer. The International Endocervical Cancer Criteria and Classification (IECC) categorizes cervical adenocarcinoma into human papillomavirus (HPV)-associated and non-HPV-associated subtypes.[1]The majority of cervical malignancies are attributable to HPV infection. With the increasing popularity of HPV vaccination and cervical cancer screening in recent years, the incidence of HPV-associated cervical cancer is likely to decline dramatically, while the proportion of non-HPV-associated cervical cancer will increase proportionally. [2] Non-HPV-associated cervical cancer presents benign imaging features, but it has a high degree of aggressiveness, which results in bad outcomes.

Gastric-type endocervical adenocarcinoma(GAS) is the most common disease of cervical cancer not caused by HPV, it is a mucinous adenocarcinoma with gastric differentiation that shares similar pathological characteristics with pyloric gland epithelium. [3]Asian women are more susceptible to suffering the illness than others.[4,5] Historically, the prevalence of non-HPV-associated cervical cancer was significantly lower than that of HPV-associated cervical cancer. It lacks typical clinical features such as contact vaginal bleeding and has poor prognosis, requiring early diagnosis and clinical treatment. However, imaging information (US, CT, MRI) was rarely reported, and it is difficult to get a complete picture of GAS, which was unfavorable for early diagnosis.

The present case report describes the case of a 44-year-old woman with cervical gastric adenocarcinoma. The diagnosis was made by combining her clinical data, laboratory examination, and imaging examination, and confirmed by pathology. This patient was exceptional in that she also had Peutz-Jeghers syndrome (PJS). The study was reviewed and approved by the Institutional Review Board of Guangdong Women and Children Hospital.

2. Case presentation

A 44-year-old woman presented intermittent vaginal bleeding for one month before admitted to the gynecological department. The patient's menstrual cycle was regular, but being abnormal in last menstruation. This patient had no other obvious discomfort symptoms, such as lower abdomen pain or indications, such as dizziness and heart palpitations. Additional details regarding the past sickness of the patient, the patient reported having thalassemia herself. She underwent a gastroscopic polypectomy in August 2011 for "gastric polyposis." In September 2011, the patient with PJS had partial jejunostomy and descending colectomy.

She examined a suite of testing, including laboratory tests, US, CT, MR, and the thinprep cytologic test (TCT). Positive

tumor markers included CA199 levels greater than 700 KU/L, and negative tumor markers were CA125, CA153, AFP, CEA, etc. Both her HPV and TCT test findings were negative.

An ultrasound (US) examination of the gynecology revealed intrauterine fluid and cervical hypertrophy with multiple cystic masses (Figure 1A). The largest cystic region within the mass, measuring 4.0×3.5 cm. In the bilateral adnexal regions of the uterus, no anomalies of significance were observed. The CT scan indicated an irregular cystic-solid mass that displaced the normal cervical structures on the plain scan. The whole area of the mass is approximately 7.5×7.1×7.2 cm. There was no obvious enhancement in the cystic part of the mass, but a slight enhancement in the solid part on the enhanced scan. No calcification was founded in the internal or adjacent area (Figure 1B). MRI revealed the cervical myometrium was full and filled with variable cysts. And patchy equal intensity presented on T1-weighted sequence and mixed intensity on T2-weighted sequence, respectively (Figure 1C, E). Enlarged lymph nodes could be seen in the pelvis, the larger ones next to the left iliac vessels, measuring approximately 1.6×1.0 cm. Contrast-enhanced MRI findings were approximately consistent with CT findings, but the solid portion showed uneven enhancement (Figure 1F). Diffusion-weighted images (DWI) revealed the presence of high intensity of the solid components (Figure 1D). Additionally, a cervical biopsy showed low-grade cervical intraepithelial neoplasia (CIN I).

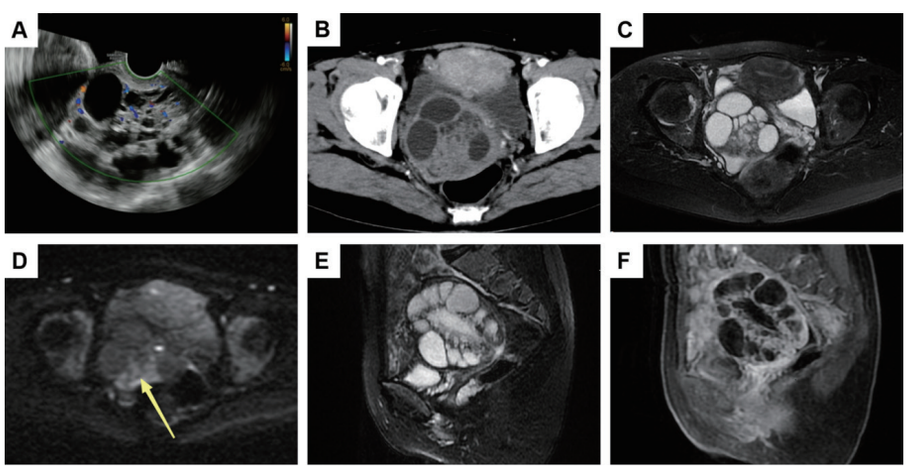

Figure 1. A. Ultrasound image. B. Contrast-enhanced CT (axial image). C. MRI; T2-weighted image (axial image). D. MRI; Diffusion-weighted images (axial image) (b=800mm2/s). E. MRI; T2-weighted image (sagittal image). F. MRI; T1-weighted contrast-enhanced (sagittal image).A.ultrasound image showed intrauterine fluid and cervical hypertrophy with multiple cystic masses. B. Contrast-enhanced CT showed a cystic-solid mass at the uterine cervix with slight enhancement of the solid part. C, E. T2-weighted image showed the myometrium of the cervix is filled with high-signal cysts. D. Solid components showed high intensity on DWI (arrows). F. T1-weighted contrast-enhanced showed solid portion heterogeneous enhancement.

This patient underwent surgery, Enlargement of the cervix can be seen during surgery. Multiple cysts and necrotic tissue can be seen after an incision of the excised cervix. Some cysts contain pus. And the final surgical approach was radical hysterectomy + ovariectomy + pelvic lymphadenectomy due to intraoperative frozen section: (cervical) compatible with adenocarcinoma (possibly stomach). After surgery, the pathology reveals the cervical gastric adenocarcinoma (Figure 2A) and that it has infiltrated practically the whole layer of cervical stroma, involved the cervical canal and lower part of the uterine body, and produced vascular tumor thrombus. Lymph nodes were discovered to be positive in both the left and right pelvic, respectively. (Figure 2B). There were no malignant pathological signs observed in the remaining tissues.

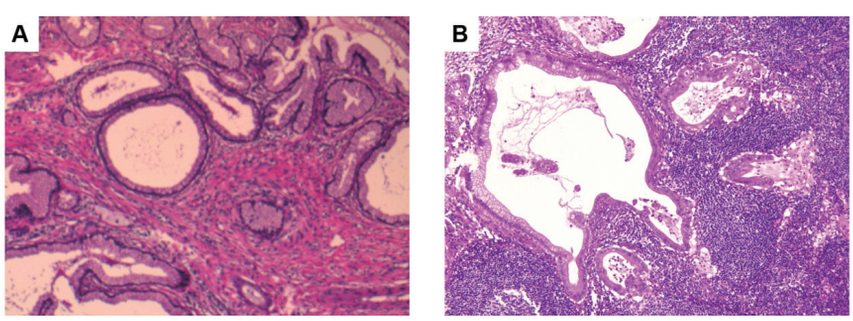

Figure 2. Pathological diagnosis result for the patient with gastric-type endocervical adenocarcinoma and pelvic lymph node metastasis. A. Photomicrograph of resected uterine specimens at low magnification(original magnification ×10). B. Photomicrograph of lymph node metastasis at low magnification(original magnification ×10)

3. Discussion

We described a case of GAS with PJS. According to a study, the age of patients with PJS-GAS was smaller than those without PJS, the average age of onset was 33 years and 55 years, respectively. In imaging findings, the majority of GAS lesions were localized in the middle and upper portions of the cervical canal, and there were no apparent exophytic lesions. Early tumors are often small and difficult to diagnose, but they are often accompanied by metastases to surrounding tissues in the middle and late stages. [3,6] On MRI, in our case shows that the cervical muscularis are filled with multiple cysts. On MRI, GAS tends to appear as an infiltrating tumor. It is mostly located inside the cervix or all of the cervix. Both cystic and solid manifestations can occur in GAS, but the probability of cystic manifestations in GAS is higher than that in UEA, which often presents as a small cyst or solid portion centrally located and surrounded by larger cysts in a radial pattern. [7] Specifically, a disruption of the low-signal-intensity ring in GAS could be a good preoperative diagnostic criterion for parametrial invasion. [8]

PJS is an autosomal dominant genetic disease. It is distinguished by melanin pigmentation on the lips, face, fingers, and toes, as well as many gastrointestinal polyps. The deletion of the liver kinase B1 (LKB1) gene situated in the 13.3 areas of the short arm of chromosome 19 would impact the control of DNA damage response, cell proliferation, senescence, apoptosis, and cell differentiation, and aerobic glycolysis in patients with PSJ. The incidence of LKB1 mutation among PJS patients is as high as 94%. [9] Approximately 85% of patients acquire malignant tumors before the age of 70 if LKB1-encoded proteins are rendered inactive. Studies have demonstrated that GAS and PJS are tightly connected, with around fifty percent of GAS attributable to PJS. When GAS is combined with PJS, assays for tumor markers, mainly MUC6 and HIK1083, are needed. [5] In addition, GAS is typically negative on HPV testing, and cervical cytological abnormalities are rare, resulting in a low rate of preoperative diagnosis. In our patient's laboratory results, her CA199 was greater than 700 KU/L. Studies indicate that around one-half of GAS patients have increased serum Ca199 levels. Lili Chen et al. discovered that the CA199 level of GAS is frequently greater than that of endocervical adenocarcinoma patients without GAS. They believe that CA 199 may be a useful tumor marker for the clinical diagnosis of GAS, particularly MDA.[10]

GAS is extremely invasive, susceptible to distant metastases, challenging to treat, and has a poor prognosis. In addition to the cervix, odd places such as the omentum, peritoneum, etc. are also invaded by GAS. Karamurzin. discovered that GAS is a distinct and physiologically aggressive form of endometrial adenocarcinoma of the cervix.[11] Most patients are identified at an advanced stage, and pelvic, abdominal, and distant metastases are not uncommon. Nearly 35% of patients had ovarian involvement, 20% had abdominal disease, and 13% had high-risk features such as extraperitoneal recurrence. [12]Due to the high malignancy of GAS, which is prone to distant metastases, the indications for postoperative chemoradiotherapy should be relaxed. In our case, each pelvic lymph node contained one lymph node metastasis, which was discovered by postoperative pathology. Postoperative additional radiotherapy and chemotherapy are advised if any of the high-risk characteristics are present, which includes a positive lymph node, positive margin, and periuterine invasion. [13]GAS had a considerably lower disease-specific survival rate than usual-type endocervical carcinoma (UEA). [5,14]Shin Nishio et al. found in a retrospective study of 95 GAS patients and 233 UEA patients who underwent radical hysterectomy with pelvic lymphadenectomy or para-aortic lymph node biopsy, or both. 72 of the 328 patients experienced recurrence: 38 (40 %) of 95 patients with GAS and 34 (14.6 percent) of 233 individuals with UEA. Recurrence was much more prevalent in patients with GAS (P=0.0023). The five-year survival rate for GAS patients is just about 32%. (UEA about 70 percent).(12)

It is noted that GAS should be distinguished from benign lesions of the cervix, such as Nabothian cyst, a multicystic structure of varying size with a clear margin of the septum without solid component. Unlike GAS, Nabothian cysts are benign and limited in the lower cervix, with smaller size. Both are characterized by multiple cystic lesions of the cervix, but GAS has a poorer outcome than Nabothian cyst. [15] With such a poor prognosis for GAS, it becomes even more important that we diagnose it correctly. Some scholars believe that lobular endocervical glandular hyperplasia (LEGH) is a preexisting lesion of GAS. Compared with LEGH, GAS often demonstrates predominantly solid parts, associated with various-size cystic structures, and GAS shows higher intensity than LEGH on DWI.

In conclusion, we must increase our knowledge of GAS. For non-HPV infections, particularly in patients with PJS, imaging must be paired with vaginal discharge and other symptoms. To rule out the likelihood of GAS, lesions in the cervical region should be recognized, according to imaging results. Preoperative pelvic MR imaging can offer a more accurate estimate of tumor size and para-uterine invasion in patients with GAS.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

QiX collected, sorted, and analyzed the data and drafted the manuscript. JiX collected and sorted the data. LZ interpretation of data for the work, KuJ reviewed and revised the manuscript. All authors contributed to the article and approved the submitted version.

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Data Availability Statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.