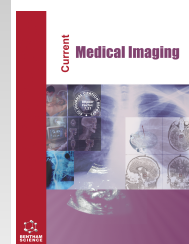




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CASE REPORT

Recurred Uterine Cervical Cancer Initially Manifesting as Hemorrhagic Cyst: A Case Report

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Abstract:

Background:

Recurrence of uterine cervical cancer is common and often shows a dismal prognosis. Local recurrence usually manifests as solid soft tissue lesions and has rarely been reported to have cystic lesions.

Case Presentation:

Herein, we report a case of recurrent uterine cervical cancer with initial manifestation as a hemorrhagic cyst, assessed using strain sonoelastography, CT, and MRI.

Conclusion:

Although cystic recurrence is uncommon, newly detected simple or complex cystic lesions should be closely monitored.

Keywords: Recurrent cervical cancer, Hemorrhagic cyst, Sonoelastography, Magnetic resonance imaging, Ultrasonography, Uterine cervical cancer.

Article History

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1. INTRODUCTION

Uterine cervical cancer continues to be a major public health issue and a growing global burden despite great improvements in screening, detection, and treatment of cervical abnormalities [1]. Uterine cervical cancer is the fourth most widespread cancer, representing approximately 520,000 new cases yearly, and is one of the leading causes of female deaths worldwide [2]. Recurrent cervical cancer is defined as local tumor regrowth or the development of lymph nodes or distant metastases at least 6 months after the primary lesion has regressed [1]. Since cervical cancer spreads *via* the lymphatic system, the most common sites for recurrence are the pelvic floor or lymph nodes, and hematogenous diffusion rarely occurs [1, 3].

Uterine cervical tumors are evaluated using several imaging tools, including ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI).

The preferred modality to evaluate cervical malignancies is MRI. Recently, several reports have shown that the US has a diagnostic accuracy similar to MRI and is gaining interest owing to its accessibility and economic efficiency [4 - 6]. Sonoelastography is a novel method that has advanced quickly in recent years with a focus on detecting normal and pathologic cervical tissue and diagnosing benign and malignant cervical lesions [7, 8].

Herein, we report a case of recurrent uterine cervical cancer with initial manifestation as a hemorrhagic cyst, assessed using strain sonoelastography, CT, and MRI.

2. CASE PRESENTATION

In November 2015, a 70-year-old woman with no significant past medical history was referred to Chung-Ang University Hospital for abnormal cytology, which suggested carcinoma *in situ*. She denied any vaginal bleeding or discharge. The family history was negative for cancer disease. Laboratory findings are as follows: leukocyte: 7,140 /mm³ (reference value: 3,000–9,500 /mm³), hemoglobin: 12.0 g/dl (reference value: 11–15 g/dl), platelet: 463,000 /mm³

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(reference value: 140,000–400,000 /mm³). There were no significant findings on liver function tests, urinalysis, coagulation tests, electrocardiogram, and chest x-ray. The tumor marker, cancer antigen (CA) 125, showed normal (10.5 U/mL, reference value: 0–35 U/mL). The human papillomavirus (HPV) DNA chip revealed HPV 16 positive. Since cervical biopsy revealed cervical intraepithelial neoplasia (CIN) III, she underwent a total abdominal hysterectomy. During follow-up, recurrent high-grade squamous CIN was detected using a Pap smear. The patient was treated with brachytherapy. Owing to her history of CIN III, the patient was advised to visit a gynecologist every 3 months. The results of cytology and human papillomavirus (HPV) tests were cytology-negative and HPV 16 positive until July 2018. Squamous cells suspected of invasion were detected using a Pap smear test on the vaginal vault as she had undergone upper vaginectomy. During surgery, the pathological finding was squamous cell carcinoma (SCC) in situ, with a clear resection margin. Unfortunately, 9 months after the operation, a high-grade squamous CIN was found on a Pap smear, and vulvar recurrence was diagnosed by biopsy. No focal lesions were detected on follow-up images (Fig. 1; upper left panel). We decided to perform a vulvectomy, urethrectomy, and

suprapubic cystostomy.

The follow-up MRI on 26 March 2020 showed a 1.8 cm cystic lesion with an enhanced thin wall in the right vaginal vault (Fig. 1; upper middle panel). It contained a fluid-filled level that showed debris or hemorrhage. There were no solid internal portions. Subsequent US revealed an approximately 1.8 cm cystic lesion with echogenic material (Fig. 2; upper left panel). Due to the benign characteristics observed in the lesion, we opted for a conservative treatment plan accompanied by scheduled 6-month follow-up evaluations.

After 6 months, a follow-up CT and MRI were performed in October 2020, which demonstrated enhanced wall thickening with a stable size (Fig. 1; lower and Fig. 3; left panel). Subtle perilesional fat infiltration was observed. Two weeks later, positron emission tomography (PET)/CT using 18F-fluorodeoxyglucose (FDG) was performed for further evaluation, and it revealed moderate hypermetabolism (maximum standardized uptake value 5.0), which preferred inflammatory lesions over tumor recurrence (Fig. 1; right panel). At the same time, the patient's white blood cell count increased to 11,150 /mm³ (reference value: 3,000–9,500), implying inflammatory changes.

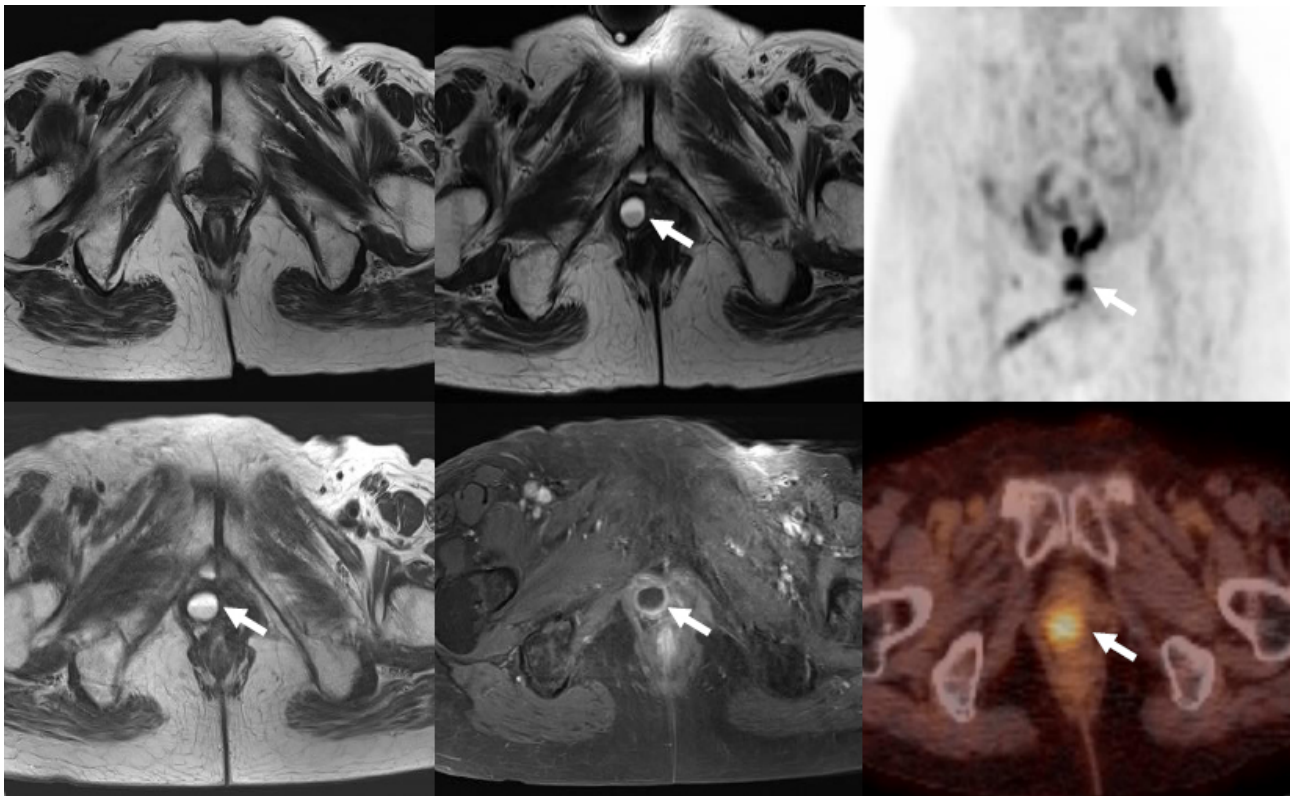


Fig. (1). Magnetic resonance imaging (A) and ¹⁸F-FDG Positron emission tomography-CT.

An axial T2-weighted image (upper left) shows no focal lesions in the vaginal vault. Axial T2-weighted images at the 6-month follow-up (upper middle) shows a 1.8 cm well-margined, unilocular cystic lesion with a thin wall and heterogeneous debris-like signal intensity with fluid-fluid level (arrow) arising from the right wall of the vaginal vault. The fluid content was hyperintense on T2-weighted images and had high signal intensity on T1-weighted image (not shown), suggesting hemorrhagic fluid. The 6-month follow-up T2-weighted (lower left) and enhanced fat-suppressed T1-weighted images (lower middle) showing the increased size and thick-walled enhancement of the cystic structure (arrow). Two weeks after, ¹⁸F-FDG PET-CT was done. Whole BODY (MIP- Maximum Intensity Projection) image (upper right) and fused axial image (lower right) show the cystic lesion with moderate hypermetabolism (maximum standardized uptake value (SUVmax): 5.0).

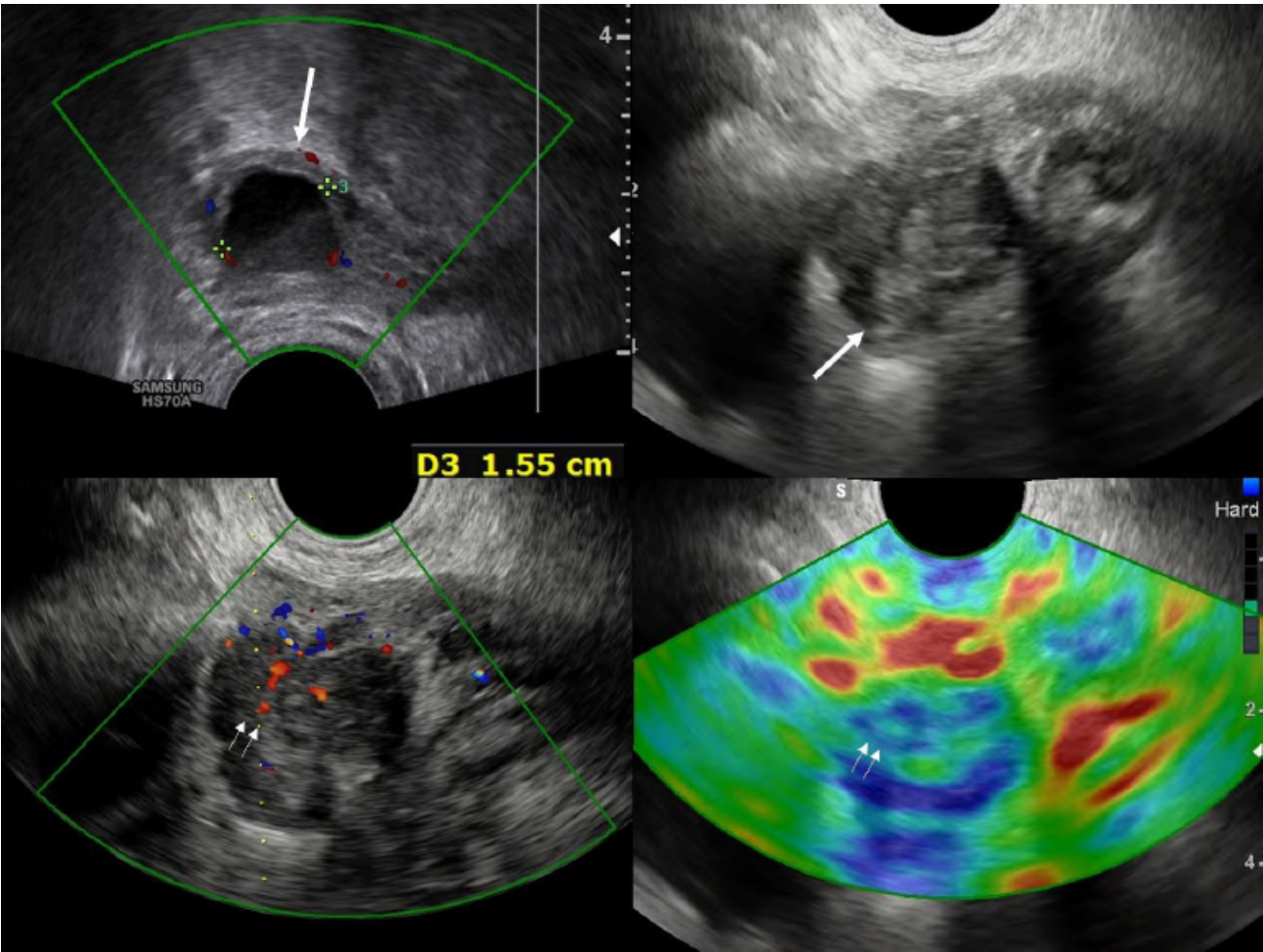


Fig. (2). Ultrasound findings (B). Initially, a transvaginal US image (upper left) showed 1.8 cm cystic lesion with heterogeneous echogenic content (arrow). Colour Doppler US showed no demonstrable blood flow, suggesting a benign lesion rather than a recurrence (not shown). The follow-up transvaginal US image (upper right) shows a completely solid mass with irregular margins and heterogeneous echogenicity (arrow). Color Doppler US (lower left) shows increased internal vascularity (small arrows). On strain sonoelastography (lower right), large, stiff blue areas with central green areas within the mass (small arrows) are noted, suggesting malignancy. A transvaginal US–guided biopsy was performed, and squamous cell carcinoma was pathologically confirmed.

However, the size of the cystic lesion gradually increased at 6- and 9-month follow-ups (2.6 → 3.2 → 3.7 cm) (Fig. 3; middle and left). Simultaneously, an increase in the tumor marker SCC antigen was reported (2.70 ng/mL, reference value: 0–1.5 ng/mL). Subsequently, transvaginal US was performed. Doppler US and sonoelastography revealed surrounding vascularity and increased stiffness (Fig. 2; upper right and lower). US-guided core needle biopsy showed

squamous cell carcinoma with keratin pearl, suggesting the presence of recurrent SCC.

The patient was referred to a multidisciplinary team and was treated with weekly cisplatin and concurrent radiotherapy. The lesion responded and decreased in size on the follow-up CT. At the time of writing this report (2 years after confirmation of tumor recurrence), the patient is still alive. The timeline of disease progression is shown in Table 1.

Table 1. Timeline of patient’s events.

Time (Year/Month)	Event and Management
0 (2015-12)	CIN III, total hysterectomy and BSO
0/8 (2016-08)	VAIN or recurrent HSIL of cervix, brachytherapy
3/4 (2018-04)	SCC in situ, HPV 16+, S/P vaginectomy
3/9 (2019-09)	Vulvar CIS, S/P vulvectomy, urethrectomy, suprapubic cystostomy
4/3 (2020-03)	Newly noted 1.8 cm cystic lesion at vaginal vault, antibiotics therapy

(Table 1) contd.....

Time (Year/Month)	Event and Management
4/10 (2020-10)	Enhanced wall thickening with stable size (2.3 cm), antibiotics
5/6 (2021-06)	Increased size (3.0 cm → 3.7 cm), Biopsy: squamous cell carcinoma
5/8 (2021-07)	Concurrent chemoradiation therapy and response: decreased size
7/6 (2023-06)	Follow-up and survival

Abbreviation: CIN, cervical intraepithelial neoplasia
BSO, bilateral salpingo-oophorectomy
VAIN, vaginal intraepithelial neoplasia
HSIL, high grade squamous intraepithelial lesion
SCC, squamous cell carcinoma
HPV, human papilloma virus
CIS, carcinoma *in situ*

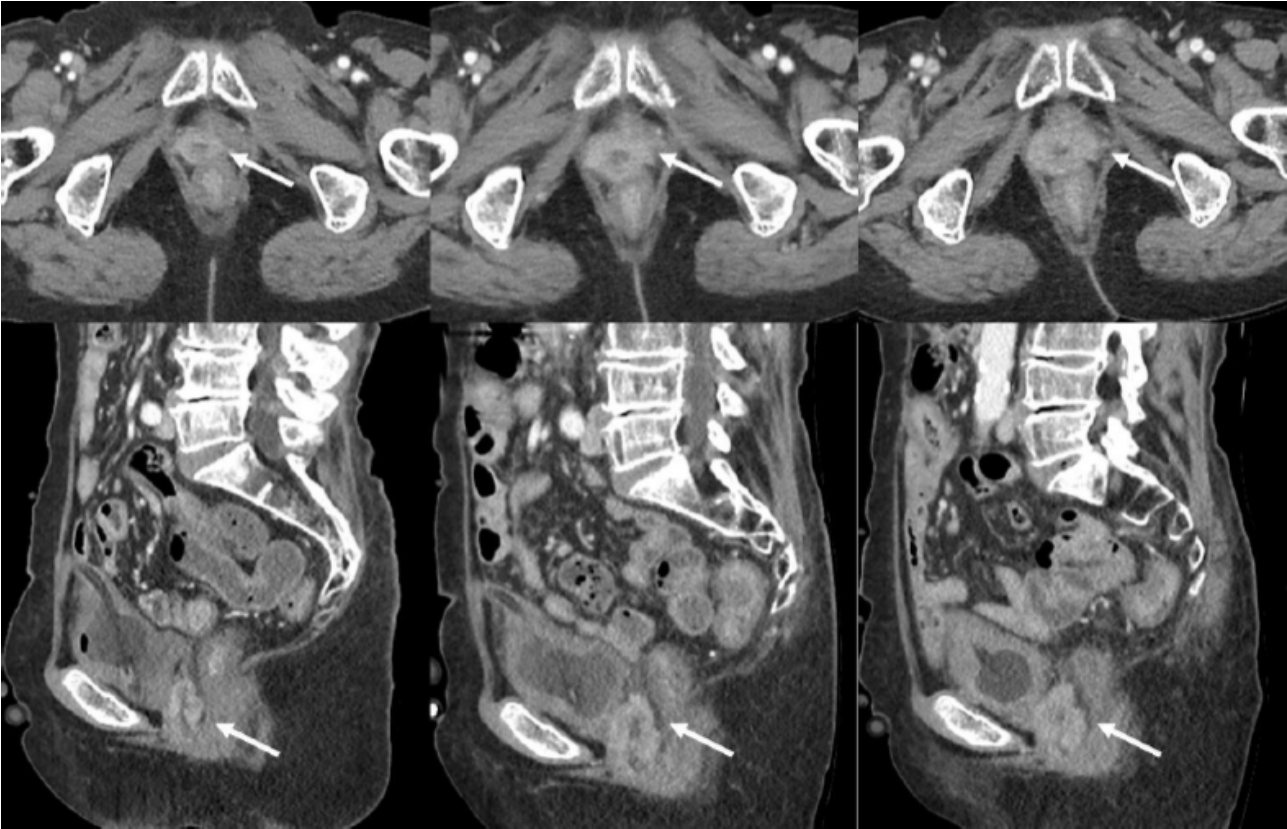


Fig. (3). Abdomen-pelvis computed tomography (C).
On serial axial and sagittal reformatted images, the cystic lesion (arrows) gradually increased in size (2.3 cm → 3 cm → 3.7 cm) and wall thickness (left: 3-month, middle: 6-month, right: 9-month follow-up CT).

3. DISCUSSION

Half of patients diagnosed with uterine cervical cancer have an early-stage I disease, and the 5-year survival rate exceeds 50% [9]. However, the recurrence rates are also high, ranging from 4 – 32% [1]. Typically, most recurrences occur within the first 2 – 3 years after initial treatment; thus, the National Comprehensive Cancer Network guidelines recommend every 3 – 6 month follow-up evaluations for the first 2 years, followed by every 6 months for the next 3 years [10]. The symptoms of recurrence are common and include vaginal bleeding, pain, fatigue, and weight loss. Imaging modalities, including CT, MRI, and pelvic US, are suggested for the surveillance of asymptomatic patients with a history of

cervical cancer. However, their detection rates are low (Table 1) [9].

About 30 – 45% of cervical cancer recurrences occur in the central pelvic area, including the vaginal vault, cervix, uterus or parametria [1]. Currently, MRI is the best imaging technique for detecting local tumor recurrence after treatment. The sensitivity and specificity of MRI have been reported to be 82 – 100% and 78 – 100%, respectively. On MRI, tumor recurrence may appear as a nodular, hyperintense, and solid lesion with early enhancement and diffusion restriction. However, MRI has limitations in differentiating recurrent tumors from post-treatment or post-operative changes [1].

PET, which provides functional or metabolic assessment,

has been recognized as a valuable tool in various aspects of cervical cancer management [11, 12]. Several studies have demonstrated that FDG-PET is superior to conventional imaging techniques in the detection of metastatic disease, especially concerning lymph node metastasis [13, 14]. However, false-positive or false-negative results in gynecological cancers are common [14].

Sonoelastography is a novel technique that provides quantitative and qualitative tissue elasticity information. Tissues are deformed when pressure is created by US waves or light mechanical compression. This deformation was analyzed using computer software, showing different elasticities with different colors. Several studies have shown that elastography of cervical pathologies can significantly improve diagnostic quality [15, 16]. US with elastography should always be considered as a complementary imaging modality to differentiate malignancies. The combined use of B-mode US and elastography can significantly improve diagnostic accuracy [7].

In our reported case, there have been multiple recurrences of CIN, even after a total hysterectomy. As several treatments have been performed, determining tumor recurrence is problematic. In this case report, we present a recurrent cystic mass in a patient diagnosed with SCC of the cervix that developed in the vaginal vault and significantly increased in size and solid portion during the follow-up period. To the best of our knowledge, a recurrent cervical cancer that initially manifests as a hemorrhagic cyst has not yet been reported.

Local recurrent lesions are generally solid soft tissue masses. Vaginal or periurethral cystic lesions without solid components can be overlooked as benign. Especially, differential diagnoses of vaginal cystic lesions include cysts of embryonic origin, epidermal cysts, and endometriosis [17]. Possible alternative diagnoses for a periurethral cystic lesion encompass urethral diverticula, Skene's gland cyst or abscess, Gartner's duct cyst, and Bartholin's gland cysts [18]. Several imaging modalities, including CT, MRI, and sonoelastography, demonstrated malignant features during follow-up. In addition to local cystic recurrence, cystic metastases are extremely rare in patients with cervical cancer, especially SCC [19]. However, cystic changes are not rare in the metastatic lymph nodes of head and neck SCC, including the tongue, tonsils, and nasopharynx [20, 21]. The possible pathogeneses are as follows: The most common type of cystic metastasis is spontaneous or treatment-related keratin breakage, giving the node a pseudocystic appearance. The other type is a true cystic lesion lined with a neoplastic epithelium.

CONCLUSION

In conclusion, we reported a rare case of local recurrence of cervical cancer initially manifesting as a hemorrhagic benign-looking cyst in the vaginal vault. Although cystic recurrence is uncommon, newly detected simple or complex cystic lesions should be closely monitored.

LIST OF ABBREVIATIONS

US = Ultrasound

CT = Computed tomography
MRI = Magnetic resonance imaging
CIN = Cervical intraepithelial neoplasia
HPV = Human papilloma virus
SCC = Squamous cell carcinoma
PET = Positron emission tomography

AUTHORS' CONTRIBUTION

Conceptualization: PSB; investigation: JYK and PSB; writing - original draft preparation: JYK and PSB; Writing - review and editing: PHJ and LES. Approval of the final manuscript: All authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Informed consent was obtained from the patient.

STANDARDS OF REPORTING

CARE guidelines were followed for this study.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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