Sentinel Node Biopsy by Transvaginal Natural Orifice Transluminal Endoscopic Surgery in a Patient with Early-Stage Cervical Cancer: A Case Report

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Abstract
Sentinel lymph node biopsy (SLNB) has emerged as an accurate tool to identify lymph node metastases in patients with cervical cancers. This procedure is generally performed by conventional or robotic-assisted laparoscopy, but SLNB by transvaginal natural orifice transluminal endoscopic surgery (vNOTES) has been described for the surgical staging of endometrial cancer. This transvaginal approach seems to be associated with reduced surgical morbidities and could be of particular interest in managing cancer patients. In this article, we report the use of a retroperitoneal vNOTES approach to perform SLNB in a patient with cervical cancer, and we provide a step-by-step description of the surgical technique. This surgical approach seems to be the least invasive way to perform pelvic SLNB and could represent a valuable approach to properly managing patients with early-stage cervical cancers after a free-margin conization. However, more studies are needed before expanding the use of this surgical approach outside study settings.
Introduction

Sentinel lymph node (SLN) biopsy (SLNB) has emerged as an accurate tool for identifying lymph node metastases in some gynecological malignancies such as endometrial and cervical cancers [1–3]. This procedure is generally performed by conventional or robotic-assisted laparoscopy, but SLNB through transvaginal natural orifice transluminal endoscopic surgery (vNOTES) has been described for the surgical staging of endometrial cancer [4]. This transvaginal approach may be associated with reduced surgical morbidities and could be of particular interest in managing cancer patients [5]. Although never reported before, this innovative approach could be implemented to perform SLNBs in cases of cervical cancer with similar benefits [6]. However, the transperitoneal approach generally used to perform vNOTES SLN mapping of endometrial cancer requires the realization of a hysterectomy to access the pelvic retroperitoneal space [4, 7]. This approach appears unsuitable for cervical cancer, for which hysterectomies should be performed by laparotomic radical surgeries after a proven absence of lymph node metastases [2, 8]. Alternatively, a total retroperitoneal vNOTES approach has been described, allowing direct access to the pelvic retroperitoneal space without the obligation to excise the uterus [9]. This retroperitoneal approach appears adaptable for cases of cervical malignancies. In this study, we report its use to perform an SLNB in a patient with early-stage cervical cancer after a free margins conization.

Case Report

A 35-year-old woman, gravida 3 para 3, was referred for early-stage cervical cancer. The patient underwent conization for persistent cervical high-grade squamous intraepithelial lesions for 2 years, resulting in a 1.8-cm squamous cervical cancer with a stromal invasion of 3 mm, no lymph-vascular space involvement, and negative surgical margins (stage pT1b1). Abdominopelvic magnetic resonance imaging (MRI) showed no cervical, vaginal, or parametrial signal abnormalities and no infrarenal, pelvic, or inguinal retroperitoneal adenopathy. We performed a bilateral SLNB, performed through a retroperitoneal vNOTES approach to complete the lymph nodes assessment as described below and demonstrated in online supplementary Video 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000524828).

The patient was placed in a dorsal lithotomy position under general anesthesia, and prophylactic intravenous antibiotics with cefuroxime 1.5 g and metronidazole 500 mg were administrated. The operating table was maintained horizontal without Trendelenburg tilt. A total of 2 mL of indocyanine green (ICG) solution at a 1.25 mg/mL concentration was injected into the cervix at the 3 and 9 o’clock positions. Access to the pelvic retroperitoneal space was achieved through a 2-cm incision in the left lateral vaginal fornix using a cold scalpel. Gentle dissection was performed using the tip of the index finger, providing access to the left obturator fossa. A 7-cm GelPoint® V-Path Transvaginal Access Platform (Applied Medical, Rancho Santa Margarita, CA, USA) was used as a vNOTES port, and CO2 was insufflated to a pressure of 12 mm Hg to expand the left pelvic retroperitoneal space. Three trocars were used to insert a 10-mm rigid 30° endoscope and 5-mm instruments such as Johan graspers, a bipolar grasper, and a Caiman® articulating sealing device. Careful dissection was performed from the caudal part of the obturator fossa to develop the left pelvic retroperitoneal space with exposure to critical anatomical structures such as the obturator nerve and vessels, internal and external iliac vessels, the ureter, the umbilical artery, and the uterine artery. The lymph nodes were inspected for ICG uptake under visual guidance using a near-infrared fluorescent...
optic device (ENDOCAM Logic 4k®, Richard Wolf GmbH, Knittlingen, Germany). SLNs were identified and separated from the surrounding tissues through careful dissection using the Caiman® sealing device. Once the left pelvic SLNB was completed, the same procedure was performed on the contralateral side. At the end of the procedure, colpotomies were closed with 2 separate running sutures using a Vicryl 2-0 thread. Clindamycin vaginal cream was administered once a day for the first 7 postoperative days.

The intervention lasted 96 minutes, and we observed no complications. Two pelvic SLNs were biopsied on the left (in contact with the umbilical artery and medial to the external iliac vein) and one on the right side (below the external iliac vein). Definitive histopathological analyses with ultrastaging showed no SLN metastases. The patient subsequently underwent a laparotomic radical hysterectomy type C1 (Querleu-Morrow classification) with bilateral salpingectomy and pelvic/para-aortic lymph node dissection up to the inferior mesenteric artery. We observed no metastasis on 48 analyzed lymph nodes, and the definitive staging was FIGO IB1. According to the discussion in the multidisciplinary tumor board, adjuvant chemo- and radiotherapy were not indicated due to an estimated low risk of relapses. Oncological follow-up visits with clinical examinations and pelvic MRIs have initially been planned for every 4 months.

**Discussion**

The SLNB represents an essential tool for guiding the proper management of patients with early-stage cervical cancer [2, 10]. If negative, radical surgery with extended lymphadenectomy is needed, whereas only chemoradiotherapy and brachytherapy are indicated in the case of lymph node involvement [2]. In an era of increasing use of laparotomy for radical surgeries, preoperative SLNB with a minimally invasive approach could reduce the number of unnecessary invasive interventions eventually responsible for adhesion formation and severe side effects associated with postoperative radiotherapy in the case of lymph node involvement. vNOTES could represent a valuable and potentially advantageous alternative to conventional laparoscopy, in performing SLNB for selected patients with early-stage cervical cancers after conization.

vNOTES appears as a minimally invasive technique that limits surgical trauma, and this approach could be of particular interest in managing vulnerable oncological patients [4, 6]. SLNB through vNOTES for endometrial cancer appeared comparable to conventional laparoscopy in terms of safety and efficacy while avoiding visible scars and being associated with shorter hospital stays and fewer perioperative morbidities [4]. To implement vNOTES for the management of cervical cancer, we proposed an ICG-based SLN mapping with a total retroperitoneal approach adapted to the technique first described by Baekelandt for early-stage endometrial cancers [9]. Unlike the transperitoneal method [4, 7], the retroperitoneal vNOTES approach allows direct exposure of the pelvic retroperitoneal space without entering the peritoneal cavity and without the need to perform a hysterectomy. These features expand its utility to patients with no indications of concomitant hysterectomy as for cervical cancer and potentially improve the SLNs’ detectability due to easier and earlier retroperitoneal space inspection and reduced manipulations (e.g., during the hysterectomy) eventually responsible for fluorescent ICG tracer leakage from lymph vessels. Compared to conventional laparoscopy, retroperitoneal SLN mapping by vNOTES allows inspection of the pelvic retroperitoneal space in a more logical sequence, starting from the cervix and following the lymphatic path, with a potential improvement in the identification of SLNs. In addition, the proximity to the parametrium and its inspection with a look coming from the caudal part of the obturator fossa could improve the detection of parametrial SLNs.
According to current guidelines, in the case of early-stage cervical cancer with negative SLNs, radical surgery and lymphadenectomy should be performed [2]. In contrast, this extensive intervention should be avoided in the case of lymphonodal involvement [2]. Lymphonodal staging is therefore of critical relevance and should be performed through radiological examinations (computed tomography scan, MRI, and/or positron emission tomography/computed tomography scan) and when negative, by more sensitive SLNBs to assess for possible subclinical metastases [2, 11]. At present, 2 main surgical strategies comprising SLNBs exist: (1) SLN mapping by laparotomy with intraoperative pathological assessment and radical hysterectomy with lymphadenectomy in the case of negative SLNs or (2) a two-step approach with SLN mapping by conventional laparoscopy and definitive pathological analyses with ultrastaging and an eventual second intervention with a laparotomic radical surgery if SLNs are negative. Because the intraoperative evaluation of SLNs appears unreliable to detect micro- and macrometastases [12], strategies based on definitive analyses should be preferred. Due to the new rise of open surgery for radical hysterectomies [8], the unreliability of intraoperative assessment of SLNs, the complications associated with extensive lymphadenectomies [13], and the severe morbidity related with combined treatment (surgery and adjuvant chemoradiation), two-step strategies appear more and more indicated to reduce the number of unnecessary, highly morbid interventions. From this perspective, SLNB by retroperitoneal vNOTES could represent a valuable tool in the future management of early-stage cervical cancer, where SLN metastases are found in around 20% of cases [14]. This retroperitoneal approach, which does not involve entering the peritoneal cavity, appears to be the least invasive way to achieve SLN mapping. This approach allows definitive pathological assessment of SLNs with the subsequent indication for laparotomic radical surgery in the case of negative lymph nodes. In the case of lymphonodal involvement, radical surgery is avoided, and secondary effects associated with radiotherapy could be reduced by this retroperitoneal approach, which presents minimal surgical traumas and no adhesion formations. However, as a precaution for oncological safety, we suggest limiting this procedure to patients with free conization margins and low-risk factors for parametrial invasion (tumor size <2 cm, no lymph-vascular space involvement, superficial stromal invasion) [11], to minimize the risk of tumor cells spread, potentially associated with cervical and parametrial mobilization associated with this surgical approach.

SLN mapping by retroperitoneal vNOTES could be a valuable tool to be integrated into future two-step strategies aimed at reducing the morbidity associated with surgical treatment of cervical cancer. Although we should wait for the results of clinical trials such as PHENIX, SENTIX, and SENTICOL III, systematic pelvic lymphadenectomy will probably be replaced by SLN mapping [11], and vNOTES could represent an interesting option in selected patients. In addition, recently described predictive models based on conization specimens and SLN histopathological analyses could determine low-risk patients, for whom less invasive surgeries such as simple hysterectomy or trachelectomy could be indicated [15, 16]. Although we should wait for the publication of clinical trials such as SHAPE (NCT03705650) and GOG (NCT01649089), conservative surgeries could be indicated for the future treatment of low-risk patients, and SLNB through vNOTES associated with conization could represent a valuable strategy for the identification of this subgroup of women.

**Conclusion**

To the best of our knowledge, this is the first report of SLNB with a vNOTES approach for cervical cancer. This surgical approach seems to be the least invasive way to perform pelvic SLNB and could represent a valuable approach to properly managing selected patients with
early-stage cervical cancers. However, strong evidence of its feasibility, practical advantages, and long-term oncological outcomes are needed before expanding the use of this surgical approach outside study settings.

**Statement of Ethics**

This study protocol was reviewed and approved by the institutional review board CER-VD (Lausanne, Switzerland) with approval number 2021-02346. A written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

**Conflict of Interest Statement**

The authors declare that they have no conflict of interest regarding the publication of this case report.

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**Author Contributions**

Yannick Hurni: collected data, edited the video, and drafted the initial manuscript. Daniela Huber: guarantor, performed the operation, conceptualized and designed the study, and reviewed.

**Data Availability Statement**

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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