

Case report

Isolated tumour cells in a sentinel lymph node of apparent early-stage ovarian cancer: Ultrastaging of all other 27 lymph nodes

Stefano Uccella^{a,b,*}, Mariachiara Bosco^a, Anna Fagotti^c, Simone Garzon^a, Pier Carlo Zorzato^a, Raffaele Tinelli^d, Elena Biletta^e, Irene Porcari^a, Daniele Liscia^e, Giovanni Scambia^c, Massimo Franchi^a

^a Department of Obstetrics and Gynaecology, AOUI Verona, University of Verona, Verona, Italy

^b Division of Obstetrics and Gynaecology, Department of Maternal, Neonatal and Infant Health, ASL Biella, Italy

^c Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, UOC di Ginecologia Oncologica, Roma, Italy, Università Cattolica Del Sacro Cuore, Roma, Italy

^d Department of Obstetrics and Gynecology, Brindisi, Italy

^e Division of Pathology, Department of Surgery, ASL Biella, Italy

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ABSTRACT

Sentinel lymph node (SLN) biopsy in apparent early-stage ovarian cancer may spare the surgical staging with extensive retroperitoneal dissection and its associated morbidity. However, SLN biopsy in ovarian cancer is still experimental and under investigation. A 46-year-old post-menopausal woman with bilateral apparent stage IC1 endometrioid ovarian cancer underwent surgical staging by SLN biopsy and subsequent comprehensive laparoscopic pelvic and *para*-aortic lymphadenectomy. Out of 4 SLNs submitted to ultrastaging, one was positive for isolated tumour cells (ITCs). We submitted to ultra-staging all the other 24 pelvic and *para*-aortic non-SLNs, which were reported negative for disease. This is the first reported case of comprehensive lymphadenectomy after SLN biopsy with universal ultrastaging of all non-SLNs in ovarian cancer. The presence of ITCs in only one SLN, with all other 27 lymph nodes negative at ultrastaging, is consistent with the SLN concept and the assumption of a reliable lymphatic pathway in ovarian cancer.

1. Introduction

Ovarian cancer is the most lethal gynaecologic malignancy (Siegel et al., 2020). Only 20–25 % of cases are diagnosed at an apparent early stage, and 30 % of them are upstaged due to the intraoperative or pathologic identification of lymphatic and peritoneal spread (Park et al., 2013).

Because lymphatic metastases determine the upstaging from stage I to stage III, impacting prognosis and treatment planning, lymph nodes assessment is mandatory for the appropriate staging of apparent early-stage ovarian cancer. The standard lymph nodes assessment consists of pelvic and *para*-aortic lymphadenectomy up to the renal vessels (NCCN). However, the procedure is potentially associated with severe surgical morbidity, which may delay the adjuvant treatment, and the therapeutic effects are still debated (Bogani et al., 2017; Colombo and Pecorelli, 2003).

Sentinel lymph node (SLN) biopsy has emerged in gynaecologic

malignancies as an alternative to a pelvic and *para*-aortic lymphadenectomy (Rossi et al., 2017; Uccella et al., 2018). This technique has the advantage to reduce surgical complexity and morbidity, maintaining staging accuracy. However, SLN biopsy in ovarian cancer is still experimental. A recent review of the first 43 published cases of SLNs in apparently early-stage ovarian cancer has shown very high detection rates (Uccella et al., 2019). Preliminary findings of a large prospective trial conducted to evaluate the diagnostic accuracy of this technique in early-stage ovarian cancer are promising (Scambia et al., 2019; Uccella et al., 2019). However, only the final results of current trials will validate the SLN technique in ovarian cancer (Uccella et al., 2019).

Regardless of validation, one assumption of the SLN mapping is that the SLN is the first lymph node involved by tumour cells that metastasize following a reliable lymphatic pathway (de Boer et al., 2009). Based on this assumption, we used the enhanced pathological assessment by ultrastaging, which allows the detection of micrometastasis (MM) and isolated tumour cells (ITCs) (de Boer et al., 2009), to test the SLN

* Corresponding author: Department of Obstetrics and Gynaecology, AOUI, University of Verona Italy, Piazzale Aristide, Stefani 1, 37124 Verona, Italy.
E-mail address: stefano.uccella@univr.it (S. Uccella).

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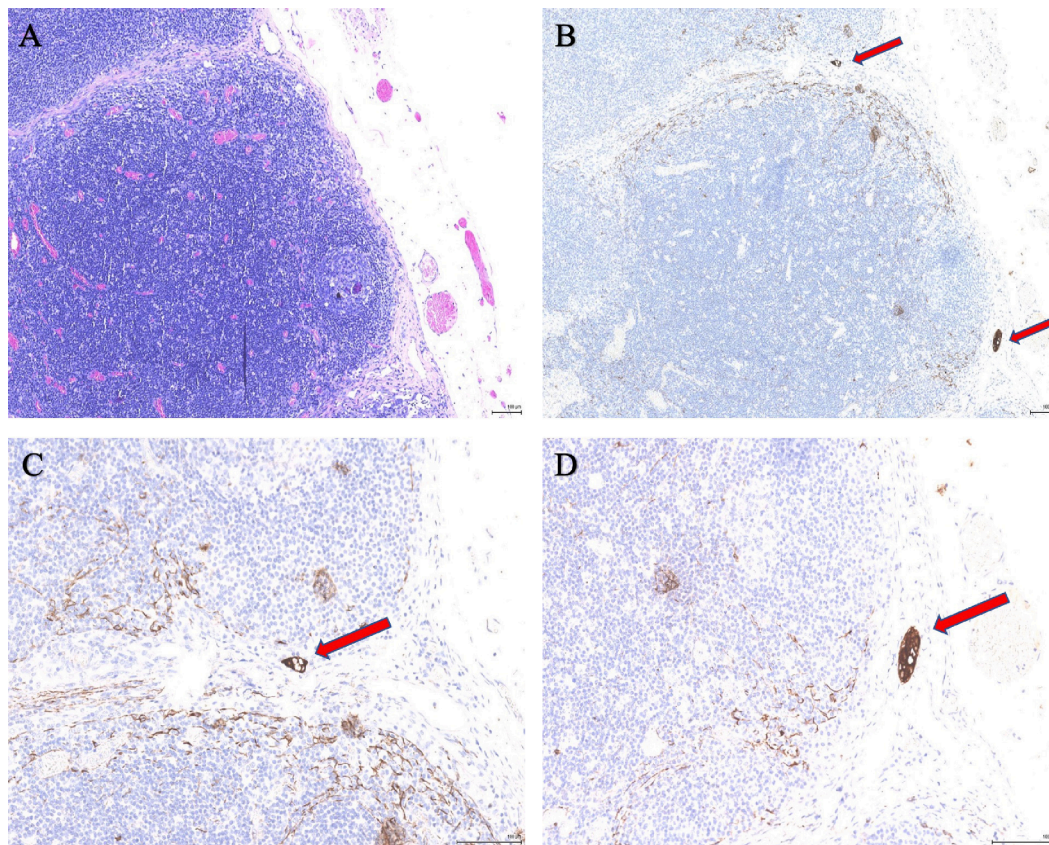


Fig. 1. Histological appearance of Isolated Tumor Cells (ITCs) in the same sentinel lymph node.

assumptions in ovarian cancer by performing the pathologic ultrastaging of all harvested pelvic and *para*-aortic lymph nodes from a patient with apparent early-stage ovarian cancer who had only one SLN with ITCs. We expected to detect all non-SLNs negative or lymphatic metastasis only in the non-SLNs associated with the positive SLN.

2. Case presentation

A 46-year-old post-menopausal woman was referred to our institution with the incidental diagnosis of suspicious bilateral ovarian masses and a disease apparently confined to the ovaries.

She underwent laparoscopic exploration and bilateral adnexectomy. The frozen section showed a bilateral grade 2 endometrioid ovarian cancer with a surgical spill. The patient had previously consented to participate in the SELLY trial (Scambia et al., 2019; Uccella et al., 2019); therefore, indocyanine green was injected bilaterally into the proper ovarian and infundibulopelvic ligaments to obtain the sentinel node mapping before routine completion of staging for apparent early-stage ovarian cancer with systematic pelvic and *para*-aortic lymphadenectomy up to the renal vessels.

Final pathology confirmed a grade 2 bilateral stage IC1 endometrioid carcinoma of the ovaries. On routine staining with hematoxylin and eosin, all the 28 collected nodes showed no macroscopic disease (2 left + 1 right pelvic + 1 *para*aortic SLNs, and 24 non-SLNs). The 4 SLNs were submitted to ultrastaging according to the Memorial Sloan-Kettering Cancer Center (MSKCC) protocol (Kim et al., 2013), and only one turned out to be positive for ITCs (one left pelvic SLN) (Fig. 1). Subsequently, all the other 24 non-SLNs were evaluated for low-volume disease, and no sign of the low-volume disease was found. The final TNM staging was T1c, N0 (i +), and M0.

3. Discussion

The present case of apparent early-stage ovarian cancer is consistent with the general assumption underlining the SLN concept of a reliable lymphatic pathway. To date, only one study reported the presence of ITCs in two *para*-aortic SLNs in a patient with apparently early-stage ovarian cancer (Uccella et al., 2019). However, ultrastaging was not performed, and possible low-volume disease may have been missed. The present case is the first where all lymph nodes collected during the surgical staging by systematic pelvic and *para*-aortic lymphadenectomy have been submitted to ultrastaging. The observation that one of the four SLNs had low-volume metastatic disease (ITCs) and all the other 27 lymph nodes (the other 3 SLNs and the 24 non-SLNs) were negative at ultrastaging is consistent with a lymphatic spread of ovarian cancer following the same general concept of other malignancies. This observation supports the concept that the SLN technique identifies the first nodal station of lymphatic dissemination even in ovarian cancer (Dogan et al., 2019).

Nevertheless, although observed results are those expected, one case report cannot make solid conclusions on the validity of the SLN technique in ovarian cancer. Although this report is the first proof of concept for SLN in patients with epithelial ovarian cancer, we cannot conclude regarding its diagnostic accuracy, which requires the final results of current trials (Uccella et al., 2019). In addition to the presence of a reliable lymphatic pathway, high detection rate, low false-negative rate, and absent therapeutic effect of lymphadenectomy must be demonstrated before systematically implementing the SLN technique (Scambia et al., 2019; Uccella et al., 2019).

The identification of ITCs only in the SLN is additionally consistent with a low-volume disease representing the early phases of the lymphatic spread (de Boer et al., 2009). However, ITCs in the SLN associated with ITCs, MM, or macrometastases in other non-SLNs have

been reported (Kennard et al., 2019). Therefore, the main observation supporting a reliable lymphatic pathway in ovarian cancer may be considered the negative non-SLNs at ultrastaging associated with the three negative SLNs.

In conclusion, this report contributes to the literature on SLN in ovarian cancer providing results that support the SLN investigation in ovarian cancer. The finding of micrometastasis only in the SLN with all the other non-SLNs negative at ultrastaging is consistent with the assumption of a reliable lymphatic pathway and the concept that identified SLN represents the “true” sentinel lymph node.

Ethical statement

The patient provided written informed consent to participate in the SELLY trial and additional consent for case report presentation.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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