Review Article: Gynecology

The Sentinel Lymph Node Mapping in Gynecological Malignancies

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Abstract

Sentinel lymph node directly receive drainage from a tumor. Sentinel Lymph node detection is an important procedure that minimizes morbidity due to extensive nodal dissection. For evaluation of lymph nodes, sentinel lymph node mappimg is an alternative with lesser side effects .With new technologies, such as the fluorescent dyes indocyanine green (ICG) and near-infrared fluorescence (NIR), and pathologic ultrastaging, SLN detection rate has increased. The aim is to present a clinical aspects of SLN biopsy in gynecological malignancies.

Introduction

Gynecologic malignancies are one of the most common cancers worldwide and one of the most important causes of women death, in particular in low-income countries.[1] The staging of these cancers, is based on the evaluation of the primary tumor, on the lymph node status and in the search of distant metastases.[2]

Sentinel lymph node (SLN) is the first lymph node to receive drainage directly from a tumor. SLN mapping has gained importance in staging of gynecological cancers in the last decade and it has been incorporated into National Comprehensive Cancer Network (NCCN) Guidelines for endometrial, cervical and vulvar carcinomas.[3,4,5] In gynecological tumors preoperative lymphatic mapping and intraoperative SLN detection are parts of Sentinel lymph node procedure.

Sentinel lymph node (SLN) mapping has been proposed as a less invasive technique used for assessment of lymph nodes. Technetium-99m (99mTc), indocyanine green (ICG) and blue dyes can be used alone or combined for identifying SLN. Due to high detection rate, and sensitivity Sentinel lymph node mapping is helpful in early stages of cervical or vulvar cancer.

SLNs are cut at 50-200 μm intervals and two paraffin embedded slides are prepared from each section. One slide is stained with H&E and the other with immunohistochemistry stains (AE1 and AE3 anticytokeratin antibodies) if no metastasis is identified by H&E examination. Tumor deposits from 0.2 mm to <2mm are defined as micrometastasis. And >2mm are defined as macrometastasis and isolated tumor cells (ITCs) are defined as single tumor cells or clusters<0.2mm.

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Endometrial Cancer

Nodal status guides the adjuvant treatment plans. The SLN mapping algorithm is a less invasive technique for evaluation of nodal status. IN Current literature three mods of injection have been described: (i) cervical injection; (ii) endometrial peri-tumoural injection assisted by hysteroscopy; and (iii) myometrial/ subserosal intraoperative injection.[6] 99mTc, blue dyes (1% methylene blue, 1% isosulfan blue or 2.5% patent blue sodium) or ICG, 1 mL deep (1 cm) and 1 mL superficial (3-4 mm) cervical injections are made at 3 o'clock and 9 o'clock positions before hysterectomy. SLNs detection occurs 15-60 minutes after the injection. For intraoperative SLN assessment One step nucleic acid amplification assay (OSNA) is a new method which detects cytokeratin 19 messenger RNA in metastatic lymph nodes. In some retrospective series, it has been shown that removal of SLNs alone does not have a negative effect on oncological outcomes, both in low- and high-risk pathologies as 3-year overall survival and disease-free survival (DFS) were comparable between the SLN algorithm group and lymphadenectomy groups.[7,8]

Cervical Cancer

In cervical cancer as stage IA2 and beyond it, SLN removal is needed, with SLN all enlarged suspicious nodes must be removed. and when SLNs are negative for metastases, the pelvic lymph node dissection can be safely avoided. Side-specific lymphadenectomy is mandatory if SLN is not detected. Cervical injections are done with ICG, blue dye or 99mTC at two or four points.[9] SLN technique can be used in tumors up to 4 cm, the best detection rates, sensitivity and NPV are achieved in tumors smaller than 2 cm.[10] latest version of the NCCN Cervical Cancer Guidelines (version 3.2019) considers SLN biopsy in patients with early-stage cervical cancer <2cm an alternative to complete pelvic lymphadenectomy.[11] In between patient of cervical cancer undergoing only SLN biopsy and complete bilateral pelvic lymphadenectomy after SLN biopsy, recurrence rate is different.

Vulvar Cancer

Vulvar cancer is a rare neoplasm (1% of all cancers in women and until 5% of all gynecologic cancers), and more frequent in older women. Lymphatic metastasis is the most important prognostic features in vulvar cancer. SLN detection is best suited in the patient if they had a simple punch biopsy before surgery.

SLN biopsy is most specific in patients with tumors< 4cm that are located 2cm from the midline and obtained via combined techniques (radiocolloid and patent blue).[12,13] Inguinal bilateral lymphatic drainage could be associated to pelvic spread in lesion close to the clitoris. The primary tumor should be resected with at least 1 cm clear margins and when SLN metastases are >2mm complete ipsilateral lymphadenectomy should be done. Contralateral lymph nodes should also be resected or treated with external beam radiation therapy. Frozen section of SLNs may be used to for deciding to perform complete lymphadenectomy.

Ovarian Cancer

SLN biopsy is investigational in ovarian cancer. In early-stage ovarian cancer incidence of positive LNs is low, ranging from 5% to 15%,[14] while in advanced-stage cancer LNs, dissemination is over 20%,[15] and generally para-aortic SLN are found below or above the inferior mesenteric artery. 99mTC, blue dye or ICG can be used as tracers alone or in combination and injected at the utero-ovarian and infundibulopelvic (IP) ligaments, or only at the IP ligament if hysterectomy had been performed previously, just underneath the peritoneum. ICG is used in early-stage ovarian cancer in diagnosing nodal metastasis. SLN detection failure occurred in patients with: ovarian torsion due to disrupt the lymphatic flow of the ovaries[16] in case of obstruction lymph flow by LN metastases and dermoid cyst with a high number of adhesions preventing access to the ovarian ligaments.

Conclusion

Endometrial cancer: When no metastasis is detected by imaging modalities or intraoperative exploration, SLN mapping is an alternative procedure for lymph node evaluation in staging of apparently early-stage low-risk endometrial cancer patients. Removal of SLNs alone does not have a negative effect on oncological outcomes compared to complete lymphadenectomy.

Cervical cancer: SLN biopsy is completely reliable if bilateral SLNs are detected. SLN mapping may be used in tumors up to 4 cm, but best detection rates are observed in tumors<2cm.

Vulvar cancer: SLN biopsy is a most specific in patient with tumors <4cm that are located 2cm from the midline for inguinofemoral lymph node dissection in selected early-stage patients. For tumors >4 cm, SLN technique is both associated with reduced sensitivity and higher groin recurrences.

Ovarian cancer: The best detection rates were observed with injections at the utero-ovarian and IP ligaments, or only at the IP ligament if hysterectomy had been performed before, just underneath the peritoneum.. Most often high detection rate are found in the para-aortic region.

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