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Sentinel node identification with indocyanine green in early stage breast cancer in a multi-ethnic Latin American population

Abstract

Background/Aim: The purpose of this series of cases was to describe the use and feasibility of indocyanine green (ICG) fluorescence for localization of sentinel lymph node in early-stage breast cancer.

Methods and patients: Sentinel lymph node biopsy using indocyanine green with fluorescence guided surgery using Medtronic's EleVision™ IR platform, was performed on a total of 70 consecutive patients.

Results: ICG successfully identified all 87 lymph nodes excised in 70 surgeries. With a detection rate of 97.14%, the ICG method detected an average of 1.42 SLNs in 68 of 70 patients.

Conclusion: Therefore, ICG fluorescence method is safe and effective addition in early breast cancer clinical staging.

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Introduction

The sentinel lymph node (SLN) is defined as the first lymph node receiving lymphatic drainage from the breast and represents the actual nodal status.[1] Currently, SLN biopsy is a routine procedure for early stage breast cancer. SLN biopsy is based on an ordered dissemination of tumor cells from peritumoral lymphatics to the SLN, and then to more distant lymph nodes.[2] Clinical identification of these nodes is usually performed by injecting a blue dye and a radioisotope into the peritumoral site. Labeled lymph nodes are surgically excised and histologically examined for the presence of disease.[1] Identification and biopsy of the SLN can correctly indicate the status of the draining lymph node basin. Nowdays SNL biopsy is the standard of care for staging the axilla and and decreases the morbidity related to axillary lymphadenectomy (LND).[2]

The most important aspect of SLN biopsy is appropriate selection of patients that will benefit from this minimally invasive procedure.[2] Axillary lymph node status is the most important prognostic factor for early-stage breast cancer. The orderly spread of breast carcinoma theory came into question with publication of the prospective NSABP B-04 Trial in which it was reported that the addition of LND to mastectomy had no effect on disease-free survival or overall survival.[3] Those findings indicate that the disease might already be systemic when it disseminates to regional lymph nodes. Nevertheless, regional lymph node status is critically important for precisely tailoring adjuvant treatment and evaluating prognosis.[1]

The performance of SLN depends significantly on surgeon experience. Currently the gold standard for SLN biopsy is by using a blue dye and lymphoscintigraphy with a radioisotope (RI), usually technetium (Tc-99m). Generally Tc-99m is injected into the ipsilateral subareolar plexus.[1] The RI method requires expensive equipment, authorized radiation protection areas, and access of the nuclear medicine department to RI. These logistic and legislative issues limit SLN biopsy using RI to high-volume centers in developed countries. Since there are some logistical problems as the ones mentioned before, researchers are looking for alternative markers, such as indocyanine green (ICG).[4]

The near-infrared (NIR) fluorescence imaging system uses the characteristic fluorescence spectra of ICG within an optical window. NIR/ICG fluorescence imaging visualizes subcutaneous lymphatic flow and allows the surgeon to directly observe the axillary fluorescent SLN. Although the fluorescence of ICG cannot be directly visualized with the naked eye, it can be confirmed on the monitor in real-time through a platform for near-infrared fluorescence imaging which is less expensive than RI method.[4]

The ICG fluorescence method has valid diagnostic performance for SLN detection. This technique shows a trend toward better axilla staging and may be a useful alternative to RI for SLN biopsy. Several recent meta-analyses demonstrated that ICG-guided SLN biopsy achieved a high detection rate for SLN and was viable for the detection of SLN metastasis.[5]

We present our serie of cases performing the ICG fluorescence method as an alternative way to identify the SNL, using the technology VS3 Iridium in EleVision™ IR platform (Medtronic, Minneapolis MN) that offers high-definition visualization with fluorescence imaging. VS3 Iridium is designed to work with ICG which has excitation at 805 nm and emission band between 825 nm and 850 nm. VS3 Iridium provides excitation light to the surgical field to excite the dye molecules and captures emission from the ICG using an IR sensitive camera, and the Elevision™ platform has the capacity to electronically transform the image to green color.

Methods

Patients

Between June 2019 and August 2022, a total of 70 consecutive patients with proven invasive breast cancer (T1-T2) and clinically node negative breast cancer (N0) were enrolled to undergo SLNB for localization using ICG at Pacífica Salud Hospital. All patients were diagnosed with breast cancer by core needle biopsy. Exclusion criteria included the following: definite lymph node metastasis diagnosed by ultrasonography or biopsy and adverse reaction or allergy to ICG. The study was conducted in a single institution, where all procedures were

performed by a single surgeon after obtaining the patients' consents for photographing and publishing. The ICG was injected periareolarly. The protocol was approved by the Pacifica Salud Hospital Bioethics Review Board.

Materials and surgical technique

In the preoperative holding area 25 mg of indocyanine green (Diagnostic Green LLC, Farmington Hills, MIN, USA) was dissolved in 5 mL sterile distilled water to a concentration of 5 mg/mL for use. After anesthesia induction and draping and sterilization of the operative site, 1 mL of the ICG solution were injected periareolarly.

As the first step of the surgery, the breast-conserving surgery was performed. Then, a transverse skin incision was made in the axilla, and the camera arm of the Elevision™ platform was positioned over the operating field for real-time image-guided biopsy. The lymph nodes that were fluorescence stained were harvested and counted for histopathology analysis (Figure 1).

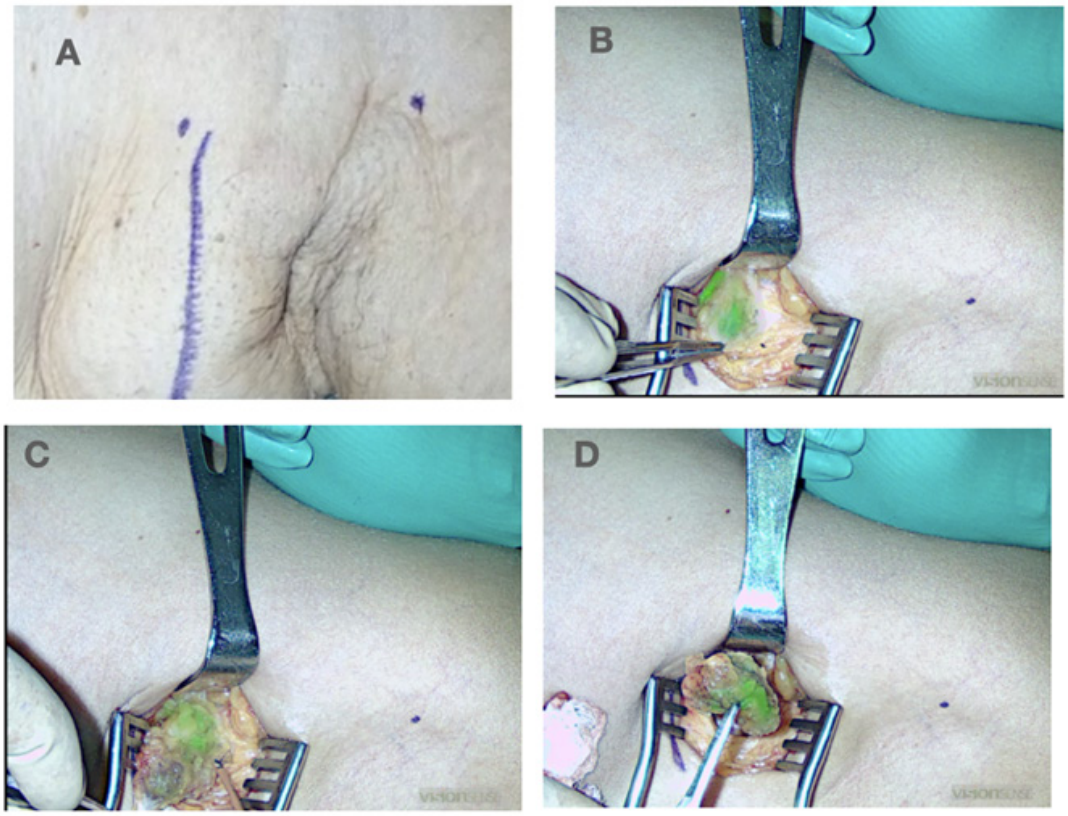

Figure 1 Surgical Technique of SNL identification using fluorescent guided surgery with ICG. (A) Transverse incision in the axilla. (B) Fluorescence SNL real time identification. (C-D) Complete excision of the SNL.

Results

A total of 70 consecutive cases underwent SLNB with ICG for localization. None experienced adverse events or complications related to the intraoperative use of ICG regardless of dose. Thus, the final analysis was based on 70 cases in women with a mean age of 55 years (range 36-82), wherein 42 patients were above 50 years old and 28 were less than or equal to 50 years old. The patients' body mass index (BMI) was between 19.9 kg/m^2 and 38.0 kg/m^2 with a mean of 27.2kg/m^2. The most common primary location of the breast tumor was the upper-outer quadrant (52.85%; n 37), followed by the upper-inner quadrant (22.85%; n 16), then the lower-outer quadrant (15.71%; n 11), and the central area (8.5%; n 6). Furthermore, of the 70 cases, 20 were grade I, 35 grade II, 15 grade III8. Moreover, there were 13 cases with Tis lesions, 35 T1 lesions, 20 T2 lesions, and 2 of T3 lesions.

All lymph nodes that were identified through fluorescence were harvested. A total of 87 lymph nodes were removed in 70 procedures. Eighty four nodes were identified by ICG. Overall, at least one SLN was intraoperatively identified and removed in all but two of the procedures. The ICG method identified an average of 1.42 SLNs (range 1-2) in 68 of 70 cases with a detection rate of 97.14%.

Discussion

The most crucial prognostic factor in the management of breast cancer is the condition of the axillary lymph nodes, which influences the selection of systemic therapy and adjuvant radiotherapy.[6] The radiocolloid method, the blue dye method, and a combination of both are common methods for sentinel node biopsy.[7]

Recent exploratory studies have revealed that fluorescence detection following subareolar injection of ICG may be used to guide SLN biopsy. Fluorescence guiding was demonstrated to be able to transcutaneously visualize the movement of ICG through lymphatic channels and was verified for SLN biopsy in comparison to traditional method.[8]

In this series of cases, a number of breast cancer patients were examined to determine the clinical viability and accuracy of ICG

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fluorescence imaging for sentinel node detection and biopsy. The outcomes show that SLN biopsy can be performed safely with subareolar ICG injection without allergic responses or local toxicity. The detection rate for the SLN in 70 individuals was over 97%, which is equivalent to the rate for the usual method utilizing radioisotope scanning and blue dye staining.[9] The detection rate in this serie of cases (97%) is similar to previous reported in the literature. In a meth-analysis by Sugie and Ikeda with 1736 patients, they reported a detection rate ranged from 88.6 to 100%.[5]

Furthermore, ICG fluorescence imaging was not compared with the more established approach (radiocolloid and blue dye). The reason was that due the pandemic for COVID-19 we experienced logistical problems acquiring the medical supplies because of a shortage of radiocolloids.

Something to consider is that the two patients in which the ICG was not able to detect the SNL had a BMI higher that 35 kg/m^2. The mean BMI of patients in the most notable validation studies, belong to an asian population with a mean BMI of 22 kg/m^2.

Conclusion

Our experience in 70 patients suggests that ICG fluorescence guiding SLN biopsy is safe and effective without need for extended tissue dissection and comparable expenses.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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