Annexure-XVI

correspondence

Isolated Tumor Cells in Sentinel Lymph Nodes: A Management Dilemma

TO THE EDITOR:

In a randomized, multicenter, noninferiority trial, Hasegawa et al[1] demonstrated that sentinel lymph node (SLN)–navigated neck dissection can replace elective neck dissection in the management of node (N)–negative (N0) neck in patients with early oral cavity cancer (OCC), given similar survival rates and better postoperative functional outcomes. In the trial protocol, the authors reported that the presence of isolated tumor cells (ITCs) in the SLNs would be treated as metastatic and would lead to completion of neck dissection, given the patient safety because of the paucity of literature regarding the implication of ITCs on the prognosis of head and neck cancers.[2] The incidence of occult metastasis in the SLNs was 40.9% (54 of 132): macrometastasis in 18.9% (25 of 132), micrometastasis (mi) in 15.2% (20 of 132), and ITCs in 6.8% (9 of 132). However, as per the final analysis, completion neck dissection (one- or two-stage) was performed in 34.1% (45 of 132) patients having macro- or micrometastasis in SLNs; patients with ITCs were observed. The authors have not reported the survival data and recurrence rates in this subset of patients having ITCs.

The role of ITCs in the management of solid tumors continues to evolve. The incidence of ITCs in early-stage OCCs has been reported ranging from 2% to 16% in various studies.[2-6] The American Joint Committee on Cancer Staging Manual (8th edition) defines ITCs as "single tumor cells or small clusters of cells ≤ 0.2 mm in greatest diameter, generally without stromal response in the lymph node." [7(p16)] ITCs represent the tumor cells in transit that are not proliferating and hence categorized as N0 except for melanoma and Merkel cell carcinoma where they are designated as N1 and as N0(i+) (N0 with ITCs) for breast and gynecologic cancers. Similarly, micrometastases represent tumor deposits > 0.2 mm but ≤ 2.0 mm in size and are denoted using *mi* designator as N1mi. However, the concepts regarding the staging rules continue to evolve and further studies are warranted in this context.[8]

Presence of micro- or macrometastasis in the SLNs warrants a completion neck dissection. Whether the same holds relevant for ITCs is still not well-defined. Surgical consensus guidelines published in 2019 following Eighth International Symposium on Sentinel Node Biopsy in Head and Neck Cancer recommended that any SLN harboring ITCs should be considered metastatic for completion neck dissection. In the Sentinel European Node Trial to assess the oncologic safety of SLN biopsy in OCCs, 16% (12 of 75) of the patients were found to have ITCs and subsequently had a completion neck dissection.[6] However, the evidence to support that these ITCs would result in high disease recurrence if not treated is limited. In a recently published trial (Senti-MERORL), 99 of the 132 patients who had SLN dissection were diagnosed as pSN0 (absence of metastasis in SLNs following pathologic examination) following serial step sectioning and immunohistochemistry; of these 99 patients, eight developed regional recurrence. Eleven of these 99 patients were detected to have ITCs and none of them developed neck node recurrence.

Garrel et al[9] observed that eight of the 99 patients who were diagnosed as pSN0 following serial step sectioning and immunohistochemistry developed neck recurrence; however, in this cohort of 99 patients, 11 were detected to have ITCs but none of them developed neck node recurrence. Variable techniques of identification of ITCs in different studies—routine hematoxylin and eosin examination using 1-2 sections, ultrasectioning at 100- to 200-μm intervals, scrape cytology, and/or immunohistochemistry with anticytokeratin antibodies—further blur their predictive and prognostic role.

With the publication of two recent trials[1,9] that have provided the evidence to support the role of SLN biopsy in the N0 neck in early-stage OCCs without affecting the oncologic safety, there is likely to be a wide acceptance of this procedure worldwide. Presently, the data are sparse to elucidate whether the presence of ITCs in an SLN mandates a completion neck dissection or mere follow-up can suffice; however, it is a potential area that needs to be explored in larger prospective trials.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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