Recent Progress in Sentinel Node Navigation Surgery

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The sentinel node (SN), also called the sentinel lymph node, is the first node to receive lymphatic drainage from primary tumors. Sentinel node navigation is a method to identify the SNs and determine operative procedures according to the status and distribution of SNs. If the concept that lymph node metastasis first appears in SN is valid, lymph node dissection can be avoided with no evidence of metastasis in SNs even in cases of significant metastatic risk. Although the SN concept has been investigated since the early 20th century, clinical applications have been realized only after a tracer method and appropriate assistive equipment have been developed. The method, along with gamma probing, utilizes dye-guided and radioisotope injections near the tumors to identify the SNs on the direct drainage pathway. The SN concept attracted attention in clinical settings after Dr. Donald Morton and his colleagues of John Wayne Cancer Institute (JWCI) in the United States reported its significance in the treatment of melanoma in 1992.1 Multi-center prospective trials incorporating several thousand cases in the United States and Europe on the application of the SN concept to breast cancer have been completed, registered, and are now in the follow-up stage. In the surgical treatment of breast cancer, breast-conserving surgery has recently become widely used. The prevalence of sentinel node navigation biopsy has lead to avoiding unnecessary axillary lymph node dissection.2 The United States, Europe, and Japan have applied this method to breast cancer treatment in clinical settings without waiting for the results of large-scale clinical trials. However, since sentinel node navigation surgery is not currently covered under the national health insurance system, each facility is treating the cases as clinical studies so that research budgets may cover the expenses. Since this method has already been widely used in clinical practice, it is necessary that appropriate medical treatment fees be immediately brought under the health insurance umbrella. In order to accomplish this goal, the Japan Society of Sentinel Node Navigation Surgery has established a multi-center cooperative database of sentinel node navigation surgery for breast cancer cases in Japan, with more than 1,400 cases currently registered. This society is also planning to revise the original Japanese evidence-based guidelines on sentinel node biopsy in breast cancer.

Recent single-institutional studies have reported on the application of the sentinel node concept to other solid tumors such as gastrointestinal carcinoma. U.S. and European studies on colon cancer and Japanese studies on gastric cancer are assessing the method in multi-center cooperative studies, raising the expectation for the clinical application of individualized treatment and minimally invasive surgery in gastrointestinal carcinoma treatment.

Research in the United States and Europe has advanced the idea of the sentinel node as an...
index in the accurate diagnosis of lymph node metastasis of colon cancer, and has used the results to advocate the application of adjuvant chemotherapy. In general, since there are many patients in the U.S. and in Europe with abdominal subcutaneous fat and fewer lymph nodes for pathological examination, diagnosis of metastasis using the sentinel node as an index is also useful from a medical economic perspective.

Among gastrointestinal carcinoma, the application of the method for individualized and minimally invasive surgery for gastric cancer holds the greatest promise. The past 5 years has seen an increase in presentations at various academic conferences on SN navigation in gastric cancer and has attracted vast attention. For patients with negative SN metastasis, laparoscopic surgery is feasible as a curative treatment. This trend is unique to Japan, which has a high frequency of early gastric cancer detection. Currently, this method is attracting attention in Asian countries such as Korea, which has a high frequency of gastric cancer. Limited laparoscopic surgery for node negative cases is the most practical treatment for gastric cancer due to anatomical characteristics. Theoretically, patients with gastric cancer with negative SN, to which local excision can be applied, can be cured by laparoscopic local excision of the gastric tumor. With additional research and technological improvement, the clinical significance of SN navigation in individualized early gastric cancer treatment will increase.

Research indicates that the sentinel node concept is valid for esophageal cancer cases diagnosed as cT1 and T2N0. However, since SNs are multiple and are distributed widely in the esophagus, treatment requires gathering a sample of the nodes through excision. Thus, even for cases with negative SN metastasis, it is currently difficult to implement non-invasive surgery. However, identifying the SN basin as the primary region for dissection may contribute to consider the additional dissection of the cervical lymph node, according to SN status. Sentinel node navigation is also useful for selecting a surgical approach (transthoracic or transhiatal) in carcinoma of esophagogastric junction including Barrett’s adenocarcinoma, which is increasing in the U.S. and in Europe. Current research has shown the treatment effect of chemoradiotherapy for cT1N0 esophageal cancer with risk of lymph node micrometastases. Even when micrometastases for cT1N0 esophageal cancer are present, there is a high probability that the metastasis is confined to the sentinel node. It is possible to use scintigraphy as another method in determining the radiation field, including the sentinel node.

Therefore, clinical studies investigating the SN concept for diagnosis and treatment of a variety of cancers such as head and neck cancer, thyroid cancer, cervical cancer, prostate cancer, and lung cancer are progressing. Although the technical details and clinical applications vary depending on the characteristics of each organ, common efficacy is observed in individualized treatment based on accurate diagnosis of lymph node status.

Recent observations of the importance of the SN in lymph node cancer metastasis have been made. For example, a factor produced by cancer cells inhibits the functions of macrophage or dendritic cells, which are immunocompetent cells in the SNs, thus promoting metastasis. Furthermore, a lymphangiogenetic factor, produced by cancer-specific cells, reaches the SNs by lymph drainage and there promotes lymphangiogenesis and metastasis. These observations not only clarify the mechanism of metastasis, but also are useful in developing new treatment methods targeting the SNs.

The keywords in cancer treatments in the 21st century are minimally invasive surgery and individualized treatment. There is great hope that SN navigation could become one of the effective methods to accomplish these goals. High quality clinical trials are necessary to demonstrate the legitimacy of this theory in various organs.

References
