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Review

Management of the lateral neck in well differentiated thyroid cancer

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Abstract

Lateral neck lymph node metastases in well differentiated thyroid cancer are common, ranging from 30% to 60%, with the majority of these foci identifiable only as microscopic deposits. A skilled ultrasound evaluation of the lymph nodes in the lateral neck is recommended for all patients presenting with newly diagnosed thyroid cancer undergoing surgical management. Ultrasound guided fine needle aspiration biopsy may be used to cytologically confirm suspected lateral neck nodal metastases prior to surgery. For patients with large volume nodal disease, extranodal extension, or multiple nodal metastases, computed tomography (CT) scan of the neck with contrast is an important additional imaging modality to accurately localize disease prior to surgery. Primary surgical management for lateral neck disease typically includes lateral neck dissection in conjunction with total thyroidectomy. Postoperative adjuvant radioactive iodine is typically recommended for patients with clinically evident nodal metastases, or for those with over 5 micrometastatic nodes. In the recurrent or persisting disease setting, complete surgical resection of local and regional disease remains the main treatment approach. However, sub-centimeter nodal disease may take an indolent course, and active surveillance may be a reasonable approach in selected clinical circumstances. Conversely, external beam radiation therapy (EBRT) may be considered for scenarios with unresectable disease, or microscopic residual disease following surgery in a clinically unfavorable setting. Two multi-kinase inhibitors (sorafenib and lenvatinib) are now FDA approved for treatment of RAI refractory thyroid cancer and now play an important role in the management of progressive, metastatic and surgically incurable disease.

Keywords: Papillary thyroid cancer; Lymph node; Papillary; Metastasis

Introduction

The incidence of well differentiated thyroid cancer (WDTC) is rising, in part related to an increased diagnosis of small volume disease, with overall excellent outcomes.[1,2] Lateral neck nodal metastases from WDTC is a relatively common finding, particularly with an increasing use of ultrasound and fine needle aspiration biopsy which now enables the detection of nodal disease at a subclinical state. Other patients presenting with high volume nodal metastases and extranodal spread are at clearly elevated risk for future recurrence and may require more extensive workup and treatment. The divergence between the high incidence of detectable metastatic disease and the low incidence of clinically meaningful neck metastasis represents the foundation of adopting a conservative approach towards managing the lateral neck. Increased use of imaging will inevitably lead to an increase in discovery of subclinical disease. Such a trend has the potential to cause stage migration and overtreatment. This review covers the incidence of metastatic nodal disease, patterns of spread, evaluation of the neck, clinical significance of lateral neck disease, therapeutic approaches, management of recurrent or persisting lateral nodal metastases, and provides the background

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necessary to adopt a balanced approach to the treatment of WDTC metastatic to the lateral neck.

Incidence and patterns of metastatic lymph node spread in the lateral neck

Involvement of the lateral neck lymph nodes (LNs) by foci of metastatic WDTC is common, with occult disease identified in 30–60% of cases.[3–6] Up to 80% of these nodes harbor microscopic foci that are being detected with increasing frequency due to the widespread use of ultrasound, fine needle aspiration biopsy, and improved experience of ultrasonographers. Importantly, micrometastases carry less clinical significance as compared with macrometastases.[7] By the 2015 American Thyroid Association (ATA) guidelines, patients harboring up to 5 micrometastatic nodes limited to up to 2 mm tumor foci remain at low risk for recurrence and do not necessarily require radioactive iodine administration.[13] In contrast, large metastatic nodes or nodes with extrathyroidal extension carry a significantly higher risk of recurrence.[13]

The location of LN metastases follows patterns based on the location of the primary thyroid cancer. Nodal metastasis of WDTC typically first involves the central compartment (level VI) before spreading to the lateral compartments of neck (Fig. 1).[6,8] A meta-analysis to investigate the value of central neck involvement as a predictor of lateral compartment metastasis showed central neck metastasis resulted in a 7.64 increase risk of lateral LN involvement.[9] Early work from Japan and Germany reported on LN distribution in WDTC,[6,10] and Sivanandan and Soo characterized LN distribution by neck levels.[11] In neck dissection specimens performed for therapeutic indications, the majority of patients had multiple levels of LN metastasis present (82%), with levels III and IV most commonly involved. Levels I and V were rarely involved and metastases here were observed only in the context of multi-level disease. Upper pole carcinomas have a higher propensity to metastasize directly to levels II and III.[12]

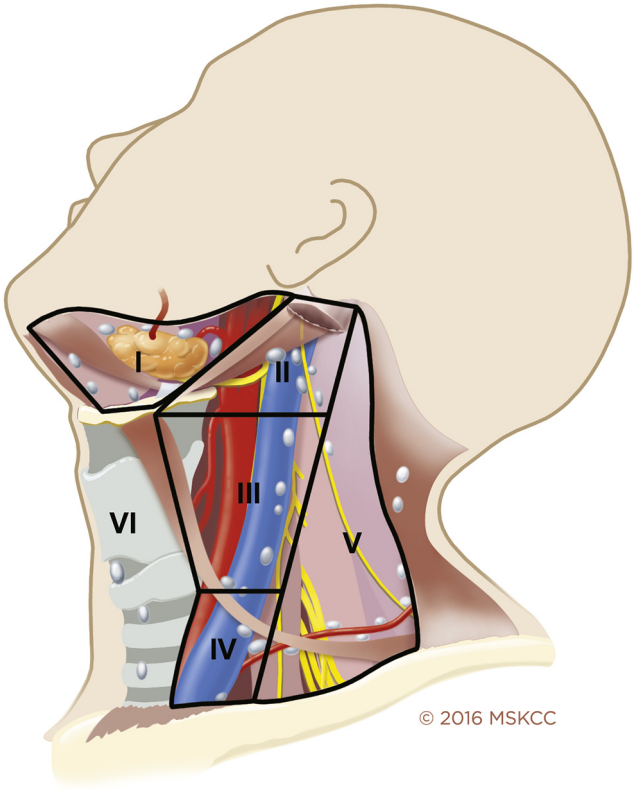

Figure 1. Levels of the neck.

Evaluation of the lateral neck compartment

Before surgical treatment, preoperative imaging and sometimes laboratory tests are used to stage patients with WDTC. Preoperative evaluation for lymph node metastasis may alter surgical planning. Ultrasound (US) evaluation of the lateral neck of all patients undergoing thyroid cancer surgery is strongly recommended by the ATA.[13] Utilizing US preoperatively detect non-palpable LN metastases in about one third of patients.[14] Ultrasound findings suggestive of metastatic LNs include: enlarged size, loss of a fatty hilum, a round shape, taller than wide shape, hyperechogenicity, cystic change, calcifications, and peripheral vascularity. When suspicious LNs are identified, the ATA recommends US-guided FNA of suspicious lymph nodes >8–10 mm. Lymph nodes 8–10 mm in size that can be localized on anatomic imaging may be considered targets for surgical removal. Although metastatic foci as small as 2–3 mm in size can sometimes be identified on imaging, the clinical benefit of treating such foci has not been clearly demonstrated. Thyroglobulin washout of the FNA sample can also be useful in some cases to establish a diagnosis of metastatic thyroid cancer, particularly for cystic LNs when cytologic evaluation of the FNA is equivocal, or when cytologic and sonographic evaluations are conflicting.

In patients with clinical suspicion for advanced disease including an invasive primary tumor, bulky lymph node involvement, extranodal extension of disease, or multiple nodal metastases, cross sectional imaging with a neck CT or MRI scan with contrast is recommended and may convey critical information that is not demonstrated on the US. The use of intravenous contrast helps to delineate the anatomic relationship between metastatic disease and other structures. Nodal disease in the retropharynx, superior mediastinum, and deep tracheo-esophageal groove is often not detectable by US. In addition, the identification and assessment of extranodal disease, and its relationship with the great vessels, trachea, larynx, esophagus, and neural structures, is more accurately conveyed with cross sectional imaging than US. It is now accepted that the added information gained from the use of iodinated contrast with a neck CT scan far outweighs historical concerns

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