Cervical Lymph Nodes

13

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Key Points

- Enlarged cervical lymph nodes are a common finding and the differentiation of benign vs malignant lymphadenopathy is done with a combination of imaging and fine needle biopsy.
- A persistently enlarged lymph node in an adult that does not have reassuringly benign characteristics on ultrasound should be considered suspicious until proven otherwise.
- Benign lymph nodes most often appear ovoid, well-circumscribed, and have a preserved echogenic hilum.
- Malignant lymph nodes most often appear rounded, hypoechoic, and have an absent echogenic hilum. Prominent vascularity may also be present.

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- Cystic necrosis within a lymph node is suggestive of carcinoma; however, this needs to be distinguished from other benign cystic lesions of the cervical region.
- Ultrasound followed by fine needle biopsy should be considered for any persistently enlarged or suspicious-appearing lymph node or neck mass.
- Fine needle aspiration for thyroglobulin washout (or calcitonin, in the case of suspected MTC) should be considered when there is suspicion of metastatic thyroid cancer.

Introduction

Cervical lymphadenopathy may be broadly classified as benign or malignant in nature, with management being determined by the underlying disorder associated with the lymphadenopathy. A careful physical exam is an important component of the initial evaluation of cervical lymphadenopathy and multiple large, firm nodes should raise the level of suspicion for possible malignancy. However, physical examination alone is an unreliable method for assessing lymphadenopathy and ultrasound is considered the preferred imaging modality for the initial evaluation of metastatic lymph nodes. Ultrasound can significantly inform the diagnostic process by assessing the size, morphology, and position of such lymph nodes.

Lymph nodes are described based on their location in the neck (Fig. 13.1).

- Level I extends from the mandible to the hyoid bone in the submental midline region.
- Level II encompasses the region from the skull base to the hyoid bone along the submandibular gland anteriorly to the posterior border of the sternocleidomastoid muscle posteriorly.
- Level III represents lymph nodes between the hyoid bone superiorly and the cricoid cartilage inferiorly, between the

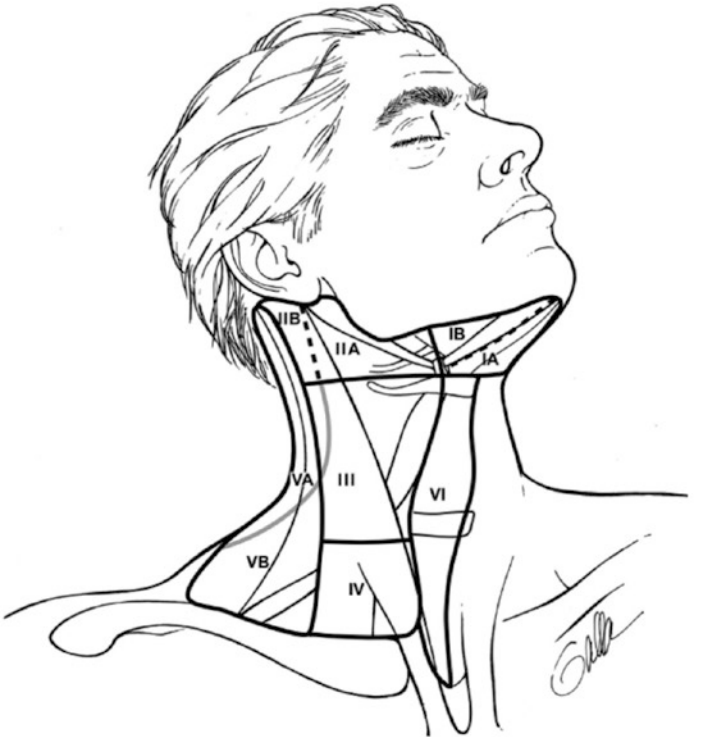

Fig. 13.1 Anatomic boundaries of the levels of the neck used to describe the location of cervical lymphadenopathy

anterior and posterior borders of the sternocleidomastoid muscle.

- Level IV extends from the cricoid cartilage to the clavicle, from the anterior border of the sternocleidomastoid muscle to the lateral edge of the anterior scalene muscle.
- Level V represents the posterior triangle from the posterior border of the sternocleidomastoid muscles to the anterior border of the trapezius muscle.
- Level VI represents the central compartment from the hyoid bone above to the suprasternal notch below, between the medial borders of both common carotid arteries.

Ultrasound characteristics that help to differentiate benign versus malignant lymph nodes include:

Benign
- Normal hypoechoic echotexture
- Elongated shape
- Presence of a central hilar line
- Vascularity limited to the central hila
- Well-defined, smooth border
- High long/short axis ratio

Malignant
- Hyper- or hypo-echogenicity
- Round shape
- Loss of the central hila
- Abnormal or peripheral vascularity on color Doppler
- Irregular borders
- Calcifications (usually micro-calcification)
- Cystic degeneration or focal cysts

Case Presentation

A 64-year-old man presented with a 2-month history of dysphonia. He had no sore throat or dysphagia and no personal or family history of thyroid disease. He was a nonsmoker. On clinical examination, a firm, 3 cm right-sided thyroid mass was noted. Laryngoscopy demonstrated right vocal fold paresis. TSH was normal. Neck ultrasound showed a right thyroid nodule, taller than wide, that was markedly hypoechoic, measuring 2.7 × 2.1 × 3.0 cm with internal vascularity. In the central neck, there was a 0.8 cm round lymph node with indistinct borders and lack of a central hilum (Image 13.1) and in level IV, there was another 2.5 cm enlarged abnormal-appearing lymph node (Image 13.2). A subsequent CT scan confirmed the ultrasound findings.

The patient underwent ultrasound-guided FNA and cytology was consistent with medullary thyroid carcinoma (MTC) (Image 13.3). Preoperative evaluation for MTC was performed including RET oncogene testing and testing for pheochromocytoma, which

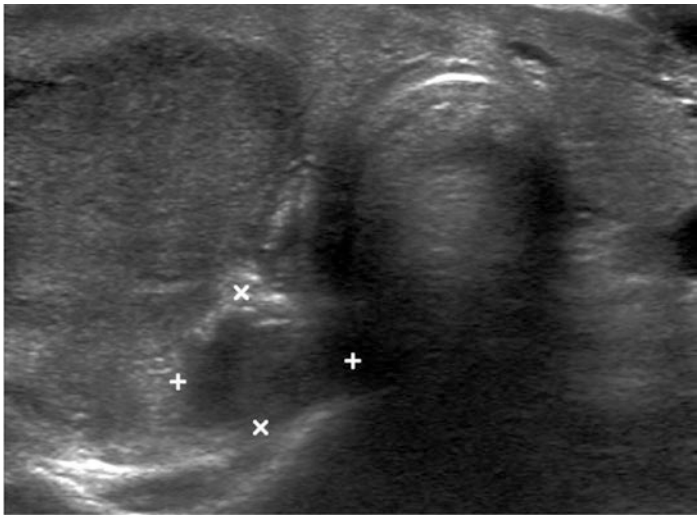

Image 13.1 Level VI abnormal-appearing lymph node. Note the round shape, indistinct borders, and lack of a central hilum

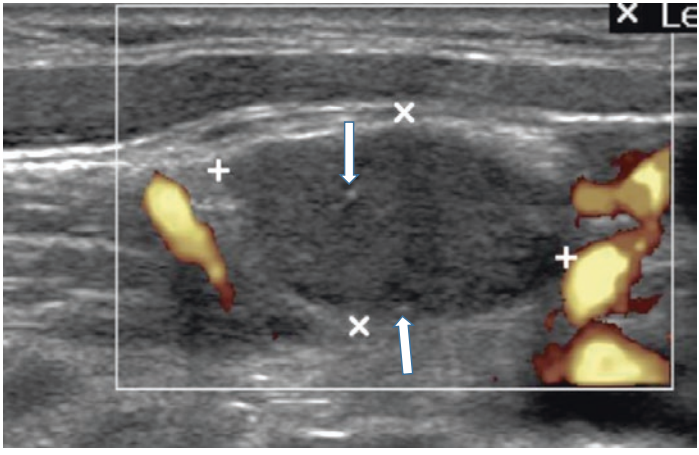

Image 13.2 Level IV abnormal-appearing lymph node. The node appears enlarged, heterogeneous, and demonstrates peripheral vascularity. Again note the lack of a central hilum. There are 2 micro-calcifications (arrows)

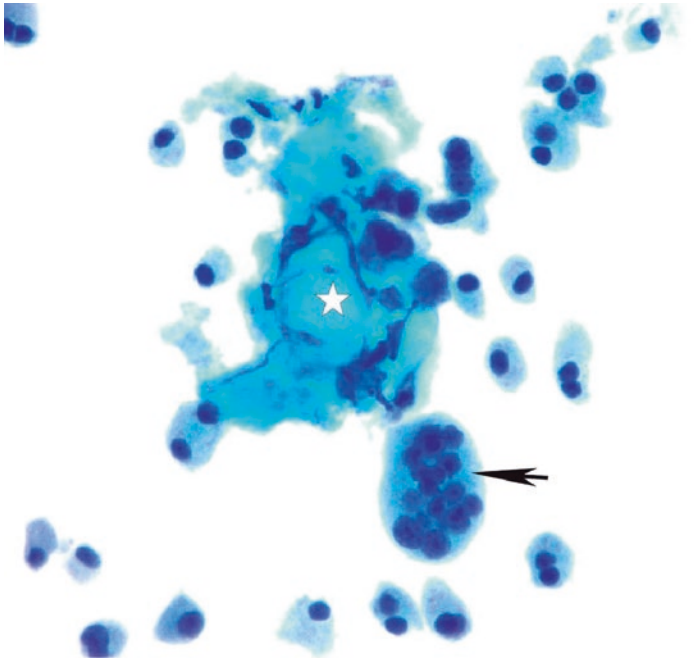

Image 13.3 Round to ovoid, and multinucleated plasmacytoid-shaped cells (arrow) with thick amorphous amyloid deposits (star), consistent with a diagnosis of MTC (Thin-prep cytology, PAP stain, ×60)

was negative. Preoperative calcitonin and CEA values were markedly elevated at 5108 pg/mL (<10 pg/mL) and 163 ng/mL (0–2.5 ng/mL), respectively. The patient underwent total thyroidectomy with bilateral central and lateral neck dissection. Pathology showed a 3.2 cm MTC with extensive bilateral lymph node involvement in 19 of 44 lymph nodes (Image 13.4).

Cervical Lymph Nodes and Lateral Neck Masses: Additional Examples

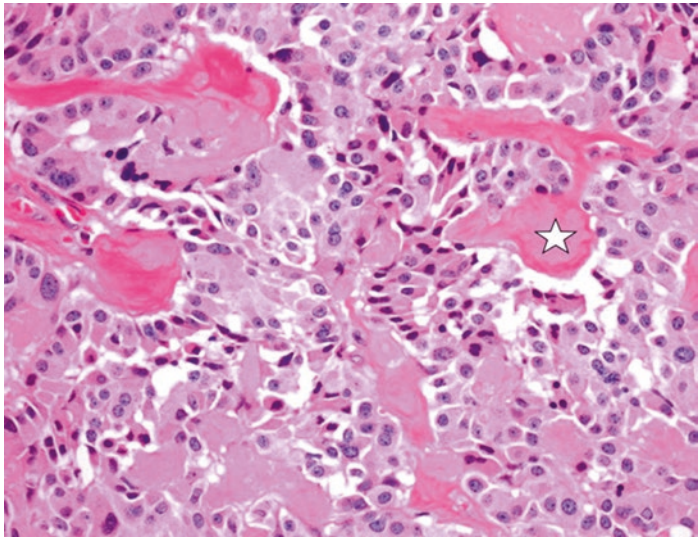

Image 13.4 Nests of irregular spindled and plasmocytoid-shaped cells with amyloid deposits (star) typical of MTC (H&E, ×60)

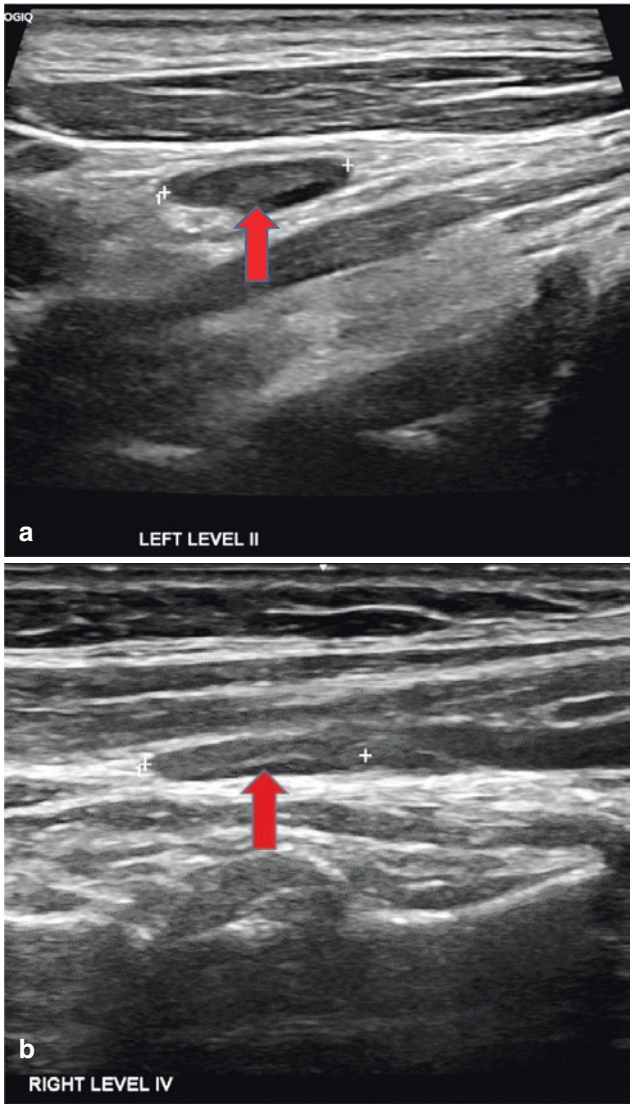

Image 13.5 (**a**–**c**) Benign cervical lymph nodes, each with preservation of the echogenic hilum (red arrows). Benign lymph nodes appear elongated or ovoid and have well-defined borders

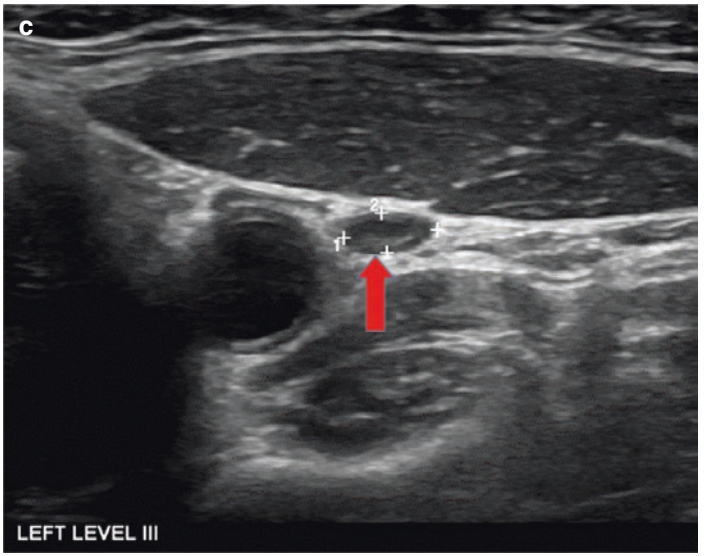

Image 13.5 (continued)

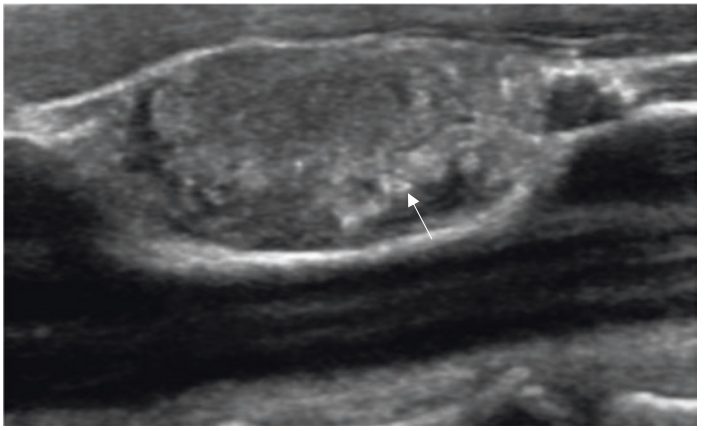

Image 13.6 Solid level IV lymph node metastasis from papillary thyroid carcinoma. Note the rounded nodular contour of the node, irregular border, and scattered micro-calcifications (arrow)

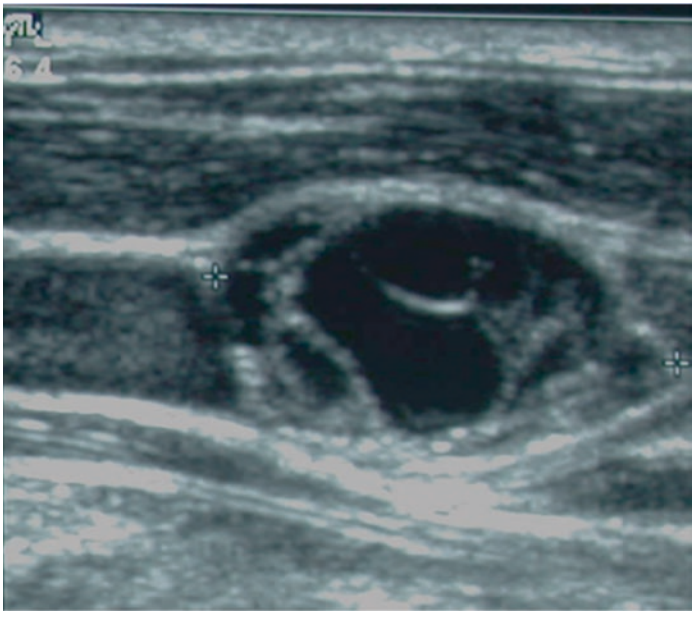

Image 13.7 Cystic lymph node metastasis from papillary thyroid carcinoma

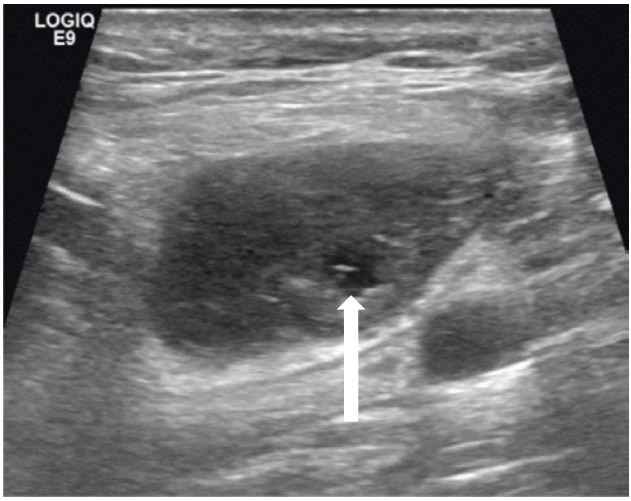

Image 13.8 Metastatic squamous cell carcinoma to a level II lymph node demonstrating irregular shape with an area of cystic necrosis (arrow)

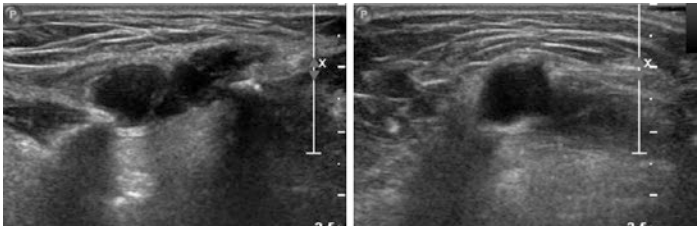

Image 13.9 Ultrasound of a midline thyroglossal duct cyst (left panel sagittal, right panel transverse). These well-circumscribed congenital lesions can be confused with prelaryngeal "Delphian" nodes, which can harbor malignancies from laryngeal and thyroid tumors. Thyroglossal duct cysts usually lie along the thyrohyoid membrane, while prelaryngeal nodes are found along the cricothyroid region

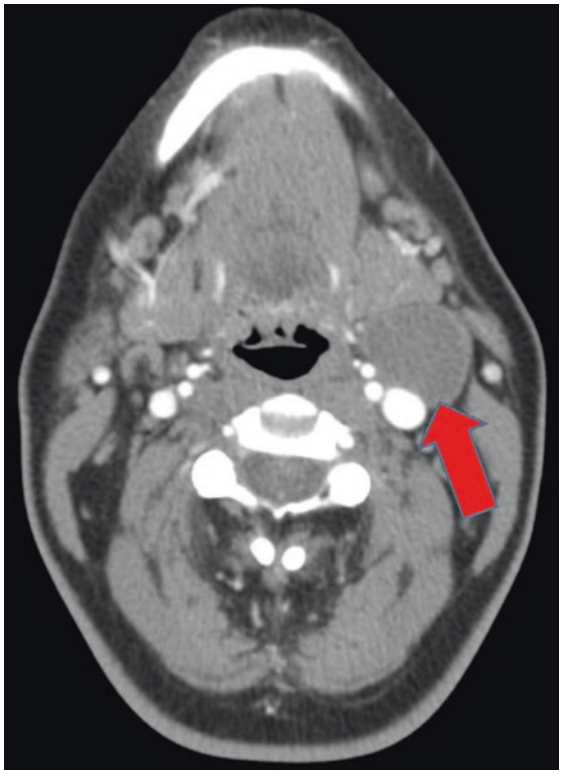

Image 13.10 Axial contrast CT image of a congenital branchial cleft cyst in left level II of the neck. Note the lesion may be confused with a cystic lymph node and has slight mural wall thickening (arrow), likely due to previous infection

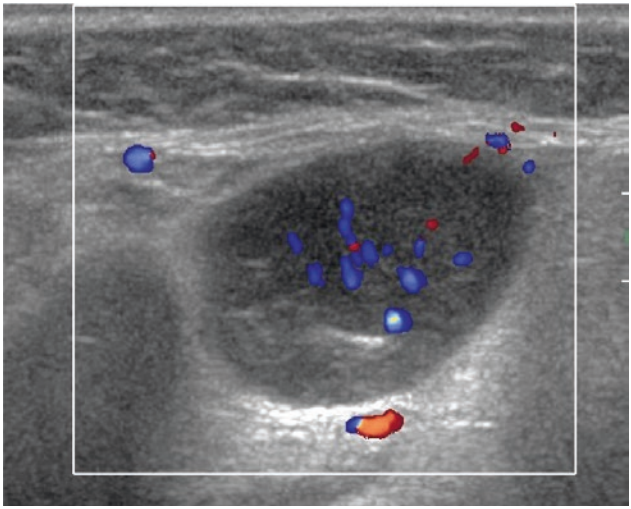

Image 13.11 Lymphoma node that is enlarged, round, and does not have a hilum. These lymph nodes are usually homogeneous, with relatively low level internal echoes. They can be diffusely vascular on color Doppler

Discussion

Cervical lymphadenopathy can be a common finding in the general population and a thorough clinical examination and diagnostic testing are necessary to determine the underlying cause (Table 13.1). Pertinent history includes the patient's age, any symptoms of infection, and other symptoms of localized or generalized malignancy, such as dysphonia, dysphagia, sore throat, and weight loss. A persistently enlarged cervical lymph node in an adult should be carefully evaluated and there should be a high suspicion for malignancy until proven otherwise. Lymph nodes that remain enlarged for more than 4 weeks without any other identifiable cause should have further evaluation.

On physical exam, assessment of nodal distribution is one important factor in the initial evaluation. Lymph nodes up to 3 cm may be followed for a short period of time in level 2, but those that are larger than 2 cm in other regions in the neck are more suspicious for a malignant process. Fixed, firm nodes in multiple regions of the neck are a worrisome finding.

Table 13.1 Differential diagnosis

1. Malignant lymphadenopathy
2. Benign reactive lymphadenopathy (a) Infectious (b) Inflammatory (e.g. Hashimoto's thyroiditis)
3. Benign neck masses (a) Branchial cleft cyst (b) Thyroglossal duct cyst (c) Lipoma (d) Neurogenic tumors (paraganglioma, schwannoma) (e) Vascular lesions (f) Congenital lesions (dermoid cyst, teratoma) (g) Parathyroid adenomas

Ultrasound is the primary initial diagnostic tool in the evaluation of persistent lymphadenopathy. Considering all the characteristics of the lymph node or lesion including size, location, echogenicity, shape, borders, vascularity and taking into consideration patient risk factors for malignancy helps distinguish suspicious from benign lesions.

Benign reactive lymph nodes often appear elongated and ovoid with a well-defined border and with preservation of the echogenic, fat-containing hilum. By comparing the length of the longest and shortest axis of the node, an "L/S ratio" can be calculated, with benign lymph nodes most often having an L/S ratio > 2 (Image 13.5a–c). In contrast, malignant lymph nodes usually display a rounded contour with an L/S ratio < 2, are hypoechoic, and have no visible echogenic hilum. A peripheral halo and prominent vascularity are more commonly seen in malignant processes. Metastatic lymph nodes from papillary thyroid carcinoma may demonstrate punctate calcifications and hyper-echogenicity (Image 13.6). Intra-nodal cystic necrosis is also suggestive of metastases (Images 13.7 and 13.8). However, cystic change can be seen in benign processes, such as in thyroglossal duct cysts, which present high in the midline at the level of the hyoid bone, and in congenital branchial cleft cysts which most often present in the lateral mid-neck (Images 13.9 and 13.10).

Fine needle aspiration is recommended for any suspicious-appearing or persistently enlarged cervical lymph node. In most solid lymph nodes, fine needle aspiration is both highly sensitive and specific for distinguishing benign reactive lymphadenopathy from malignancy. Cystic lymph nodes may be harder to diagnose with needle biopsy because often the biopsy demonstrates only acellular cyst fluid. In some cases, repeat needle biopsy, core biopsy, and even excisional biopsy can be considered if fine needle biopsy is non-diagnostic. Excisional biopsy combined with flow cytometry is especially useful to diagnose lymphoproliferative disorders once fine needle biopsy suggests an abnormal population of lymphocytic cells (Image 13.11). In head and neck squamous cell carcinoma, immunohistochemistry for certain markers such as p16 can help to identify HPV-related cancers and thereby help to guide prognosis and treatment.

To help diagnose differentiated thyroid cancer, thyroglobulin measurement of the fine needle aspiration washout should be employed. Thyroglobulin is only produced by follicular cells, and its presence in non-thyroidal tissue is indicative of metastatic spread of differentiated thyroid cancer. Caution should be taken when sampling thyroglobulin in lymph nodes found in level VI (the central neck), because of a higher risk of inadvertently sampling thyroid tissue in this region, which can lead to false positive results. In contrast, thyroglobulin washout may be less useful in cases of undifferentiated thyroid tumors, such as anaplastic carcinoma, as these thyroid cancers do not reliably produce thyroglobulin. Similarly, MTC will not be detected by thyroglobulin washout and testing will lead to false negative results if this condition is not considered. In some institutions, calcitonin levels can be measured in lymph node aspirates to help diagnose suspected MTC. Ultimately, a high level of suspicion based on patient and ultrasound factors followed by fine needle biopsy are the key components of the evaluation of persistent lymphadenopathy in the cervical region.

Further Reading

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