Chapter

Thyroid Anatomy

Sinan Binboga, Eyup Gemici and Elif Binboga

Abstract

In ancient times, the Celsius first identified the masses in the neck and reported that their surgical removal was fatal. The sources related to thyroid surgery show that the success of the neck masses with the surgical intervention was limited until the second half of the nineteenth century. Among the names leading the development of thyroid surgery in contemporary times are Emil Theodor Kocher, Theodor Billroth, William James Mayo, and William Stewart Halsted. In this chapter, we will be investigating thyroid gland embryology, histology, and anatomy that is essential to the practicing thyroid surgeon.

Keywords: thyroid gland, anatomy, embryology, histology, vascularization

1. Introduction

This chapter will discuss the thyroid anatomy including macroscopic/microscopic structure, thyroid embryology, and also vascular composition and innervation. The nuclear medicine imaging, ultrasound, and biopsy of the thyroid in the evaluation of nodules and differentiation of benign from malignant disease have a very precious place. Generally, the neck is the part of the body that separates the head from the torso. The midline in front of the neck has a prominence of the thyroid cartilage termed the laryngeal prominence. Between the laryngeal prominence and the chin, the hyoid bone can be felt; below the thyroid cartilage, a further ring that can be felt in the midline is the cricoid cartilage. Between the cricoid cartilage and the suprasternal notch, the trachea and isthmus of the thyroid gland can be felt. The quadrangular area is on the side of the neck and is bounded superiorly by the lower border of the body of the mandible and the mastoid process, inferiorly by the clavicle, anteriorly by a midline in front of the neck, and posteriorly by the trapezius muscle. The main arteries in the neck are the common carotids, and the main veins of the neck that return the blood from the head and face are the external and internal jugular veins. The thyroid is located in front of the neck between the levels of the C5 and T1, joined by the isthmus, bridging to the trachea. The basic anatomy is best appreciated in **Figure 1**. The size and shape of the thyroid lobes vary widely in normal patients. The shape of lateral lobes is longitudinally elongated in tall subjects, whereas in shorter subjects, the gland is more oval. In the newborn the thyroid gland is approximately 19 mm, with an anteroposterior (AP) diameter of 8–9 mm. By 1 year of age, the mean length is 25 mm with 12–15 mm AP, whereas the mean length is approximately 40–60 mm, with mean 13–18 mm AP in adults. The thyroid gland is slightly larger and heavier in women. It shows a little more growth in pregnancy and menstruation [1–4]. The thyroid gland is an organ of the endocrine system that maintains body metabolism, growth, and development through the synthesis, storage, and secretion of thyroid hormones. These hormones include

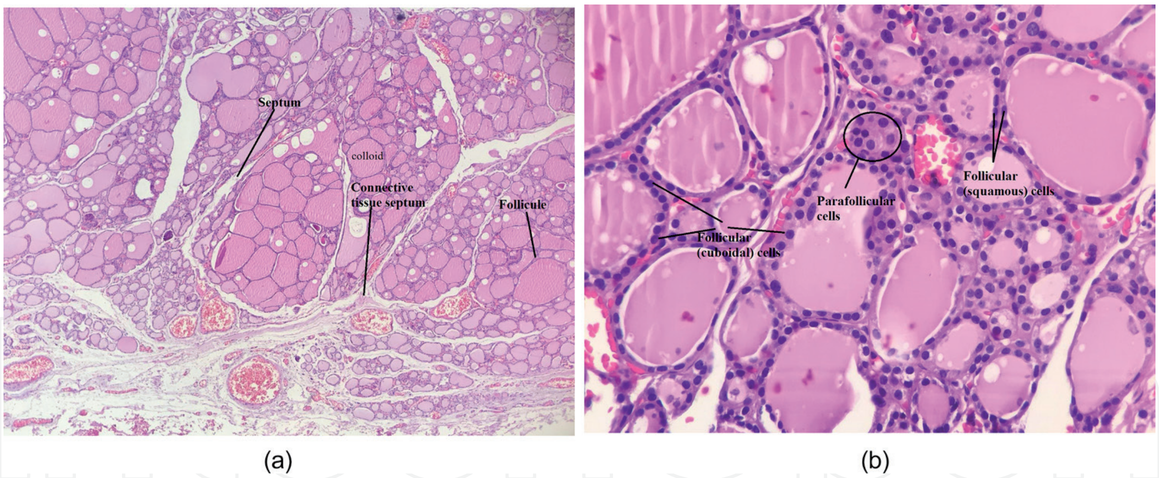

Figure 1.
a) General thyroid gland histology including fibrous capsule,septum, follicules and reticular fiber meshwork
b) Thyroid gland cell types; parafollicular and follicular cells

triiodothyronine (T3), thyroxine (T4), and calcitonin. Food-energy metabolism of cells is stimulated by T3 and T4. Calcitonin has a minor role in regulation of calcium levels. Disorders of the thyroid may result from thyroid gland dysfunction, which is regulated by the pituitary and hypothalamus glands. An appreciation of the embryological development of the thyroid and parathyroid glands facilitates comprehension of some of the various anatomical and pathological processes. The worldwide guides of various associations such as the American Thyroid Association (ATA), American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), and Associazione Medici Endocrinologi (AME) are used in the evaluation of the pathological processes [5].

2. Embryology of the thyroid gland

The primordial thyroid gland is one the earliest endocrine organs. It is detectable during the starting day 24 in the embryo. Throughout the 4th to 7th weeks of gestation, it slowly migrates to the final location. It is developed from pharyngeal endoderm cells and derived from the foramen caecum in the tongue base and also connected to the tongue base via thyroglossal duct until week 10. It consists of two lobes, and both lobes (lobus dexter and lobus sinister) are connected together with isthmus. There is a small lobe known as “the pyramidal lobe” mostly derived from the left lobe of the thyroid and attached to the hyoid bone. Calcitonin-secreting parafollicular thyroid (“C”) cells are derived from a combination of cells migrating from the neural crest and a fifth pharyngeal pouch structure [5, 6].

There are clinically relevant various pathologic consequences of this embryogenesis, for example, hypothyroidism, thyroglossal duct cyst, medullary carcinoma, and fistulas.

3. Histology of the thyroid gland

The thyroid gland is a unique endocrine gland with follicles and extracellular components storing large amounts of hormone in an inactive form [7]. The gland is enveloped by a fibrous capsule, and a fine collagenous septum divides the thyroid gland into lobules consisting of numerous thyroid follicles which are closely packed ring-shaped structures with an average diameter of about 200 μm [8]. The follicles are embedded within the meshwork of reticular fibers (**Figure 1a**) [9].

The thyroid follicles are the main functional and structural components of the gland which synthesize and release T3 and T4 in the center of follicles. Each follicle is filled with colloid, which is a gelatinous substance containing the stored form of T3 and T4. In active glands, the colloid is predominantly basophilic, whereas in inactive glands, it is acidophilic. In highly activated glands, this colloid is not only reduced in amount but also shows vacuoles [9].

There are types of thyroid cells, i.e., follicular cells and parafollicular cells. The follicular or principal cells are responsible for T3 and T4 production. These cells are usually simple cuboidal cells but may change to simple squamous (inactive) or columnar cells (active) depending on their states of secretion (**Figure 1b**). H&E staining of thyroid gland shows that the follicular cells have basophilic cytoplasm and a round nucleus with one or more distinct nucleoli. Golgi apparatus is located in the supranuclear position. Ultrastructurally, the cells contain the organelles showing both secretory and absorptive characteristics and short microvilli on the apical surface of cells. In basal location, cells contain a large number of rough endoplasmic reticulum. In apical location, cells contain small vesicles morphologically related to Golgi apparatus and a large number of endocytotic vesicles lysosomes defined as colloidal resorption droplets [10].

Parafollicular or clear cells (C cells) are the second type of thyroid cells, located within the follicular epithelium or as small clumps adjacent to the follicles. These cells are relatively large oval or ellipsoid cells with round nuclei and pale cytoplasm and are found lying on the basal follicular membrane. These cells have an extensive unstained cytoplasm often difficult to distinguish in H&E sections and therefore called "C" cells [7]. These cells produce calcitonin hormone released in response to high blood calcium and inhibits the activity of the osteoclasts [11].

4. Macroscopic anatomy of the thyroid gland

The thyroid gland is enveloped by the fascia consisting of the anterior and posterior parts of the deep cervical fascia. The gland weighs approximately 10–20 g, and each lobe measures an average of 5 cm in length, 2.5 cm in width, and 1.5 cm in depth [12]. The gland is slightly heavier and bigger in size during menstruation and pregnancy [13]. Thyroid lobes are located lateral to the trachea and esophagus, anteromedial to the carotid sheath, and posteromedial to the strap muscles (sternohyoid, sternothyroid, and superior belly of the omohyoid) and are innervated by the ansa cervicalis (ansa hypoglossi), overlying from the level of the fifth cervical vertebra down to the first thoracic vertebra (**Figure 2a**) [13, 14]. The shape of the gland varies from an H to a U form, consisted of two elongated lateral lobes with superior and inferior poles that are joined at the midline by an isthmus. The length of the isthmus is in between 12 and 15 high, connecting the two lobes. Occasionally, the isthmus may be absent, and the gland exists as two separate lobes (**Figure 2b**).

A pyramidal lobe presents in approximately 50% of patients extending toward the hyoid bone, to which it may be attached by a fibrous or fibromuscular band [14]. The most lateral extension of the thyroid lobes is the Zuckerkandl tubercles (ZTs). These tubercles are condensed thyroid parenchyma located in the cricothyroid junction, at the junction point of the medial thyroid with the ultimobranchial bodies, and have an important vicinity with the recurrent laryngeal nerve (RLN). ZTs develop from the embryologic fusion of the ultimobranchial body with the median anlage and the lateral thyroid anlages of the fourth pharyngeal pouch. The dissection of this tissue is important because the RLN is located below the ZTs located in the posterolateral of the thyroid gland [15, 16].

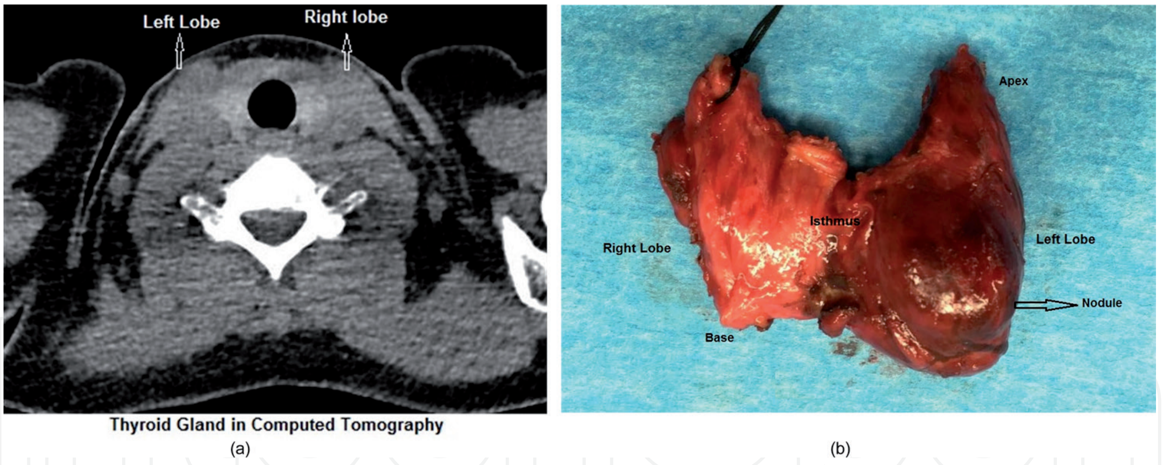

Figure 2.
a) Thyroid gland in computed tomography b) Macroscopic anatomy of the thyroid gland

Thyroglossal duct extends along the path of thyroid descending from the foramen cecum at the base of the tongue to the lower neck. The cysts of this duct are the most commonly encountered congenital cervical anomalies in humans. They are usually asymptomatic but occasionally become infected by oral bacteria. The carcinomas of the duct are extremely rare, and approximately 1–2% of are found to be cancer, which are usually papillary carcinomas (85%) [12, 17, 18].

A thin layer of the front and back of the deep cervical fascia wraps the thyroid lobes. This fascia joins the capsule by two suspensory ligaments, namely, the anterior and posterior suspensory ligaments. The anterior suspensory ligament extends from the superior medial aspect of each thyroid lobe to the cricoid and thyroid cartilage. The posterior ligament, known as the Berry ligament, connects the thyroid to the cricoid cartilage and upper rings of the trachea. The ligament of Berry is closely attached to the cricoid cartilage and has important surgical implications due to its connection to the RLN. The RLN usually enters deep into the posterior suspensory ligament [14]. During the retracting of the thyroid gland on the medial side, it should not be compelling, because it may cause RLN to be stretched and injured. In addition, rupture of the vena thyroidea media may occur bleeding. Care should be taken not to cause nerve damage during the dissection and hemostasis to control bleeding. There are two superior and two inferior parathyroid glands. The parathyroid glands are small structures adjacent to or occasionally embedded in the thyroid gland. Usually, two pairs of parathyroid glands lie in proximity to the thyroid gland. The inferior glands migrate further and have more chance of being in ectopic sites [19, 20].

5. Microscopic anatomy of the thyroid gland

The thyroid gland is a highly vascular organ, among other endocrine organs, in a sense that there is a rich blood flow with large amounts of anastomosis in the gland. Arterial supply is bilateral from both the external carotid system and superior thyroid artery and subclavian system with the lower thyroid branch of the thyrocervical trunk. It may be a single thyroid ima artery arising from the brachiocephalic artery [21].

The superior thyroid arteries originate from the ipsilateral external carotid arteries and are divided into anterior and posterior branches in the apex of the thyroid lobes. Inferior thyroid arteries originate from the thyrocervical shortly after the origin of the subclavian arteries. The inferior thyroid arteries extend from the

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neck to the back of the carotid sheath and enter the thyroid lobes at the midpoints. Thyroidea ima, the arteries born directly from the aorta or innominate, enters the isthmus or replaces a missing lower thyroid artery in 1–4% of individuals. The inferior thyroid artery passes through the recurrent laryngeal nerve (RLN) and requires the identification of RLN before the arterial branches are ligated. The inferior thyroid artery provides an arterial supply of the cervical esophagus with subclavian artery and branches directly from the aorta, intercostal arteries, and tracheobronchial arteries [22].

There are three main venous pathways of the thyroid: superior, middle, and inferior thyroid veins. The superior thyroid vein accompanies the superior thyroid artery and drains to the internal jugular vein but not accompanied by the middle thyroid vein. There are several inferior thyroid vessels that frequently flow into the internal jugular or brachycephalic veins [12].

5.1 Innervation of the thyroid

RLN is a branch of the vagus nerve, responsible from the laryngeal motor function and feeling. The left RLN is looped from the vagus nerve to the back of the aorta, and the right RLN revolves around the right subclavian artery. During thyroidectomy, since these nerves rise along the trachea near the thyroid gland, the surgeon should pay attention to protect them. The inferior thyroid artery and its terminal branches are closely related to the RLN at the entrance point of the thyroid gland. Sometimes, the nerve can be confused with a branch of the artery. Compared to the artery, it is less regular, rounded, and elastic [23]. A small, red, curved vein called vasa nervorum is usually seen in the wall of the nerve. The left RLN rises straight along the tracheoesophageal groove, while the right RLN is more inclined and lateral than the left one. However, numerous variations have been defined, so care should be taken in every case. In the two upper tracheal rings, the RLN is embedded at the back of the suspensory ligament, called the Berry ligament. This ligament extends to backward of the recurrent nerve and tightly connects the thyroid to the trachea and esophagus. At this point, there is a posterior artery near the recurrent nerve, which gives a small branch to the thyroid gland and is not easy to be attached to this artery (**Figure 3**) [23, 24].

The superior laryngeal nerve is also a branch of the vagus nerve. On the pharynx side, the internal carotid descends from the back of the artery and is divided into

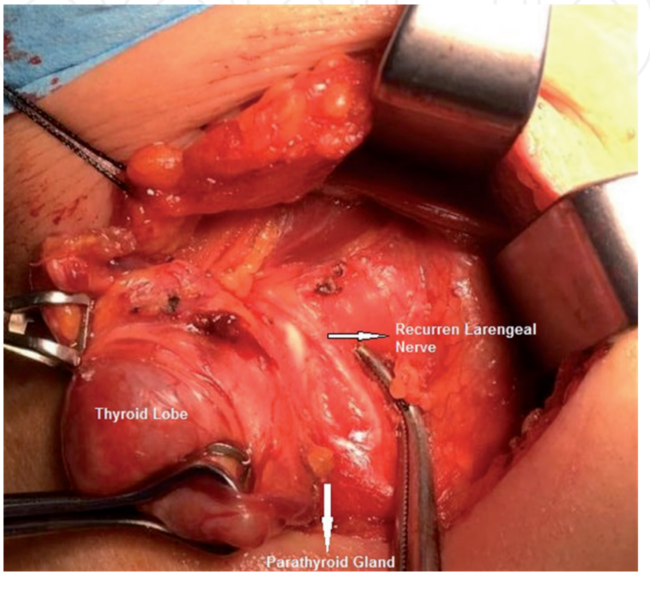

Figure 3.
Thyrid gland location with nerve and parathyroid gland

two arms: the external laryngeal nerve as the motor nerve and the internal laryngeal nerve as the sensory nerve. The superior laryngeal nerve contributes to the pitch of voice, and its paralysis can lead to significant contraction of pitch range, vocal fold vibratory phase asymmetry, and acoustic aperiodicity, thus leading to an overall poor vocal quality [24]. There is a close relationship between the superior thyroid artery and the external branch of the superior laryngeal nerve. This nerve injury may cause high-pitched noises. In order to prevent damage to the external branch of the superior laryngeal nerve, it is recommended to ligate the superior thyroid arteries as low as possible during thyroidectomy. The cricothyroid artery, a branch of the superior thyroid artery, is located in the cephalic portion of the upper pole and moves toward the midline on the cricothyroid ligament. This vessel may be damaged during cricothyroidotomy and may cause bleeding. Care should be taken in large area hemostasis to control bleeding. Ligating the veins one by one prevents nerve damage. Classification of the external branch of the superior laryngeal nerve according to the risk of potential damage [12] is given below.

Type 1: The nerve crosses the superior thyroid vessels more than 1 cm above the border of the thyroid upper pole.

Type 2a: The nerve crosses the vessels less than 1 cm above the border of the thyroid upper pole.

Type 2b: The nerve crosses the vessel below the border of the thyroid upper pole.

The recurrent laryngeal nerve (on the right, after exiting the superior thoracic cavity) may be located in the neck root, in the lateral carotid artery, in the medial trachea, and in the triangle formed by the superior thyroid lobe.

The right recurrent laryngeal nerve usually enters the larynx at an angle of 0–30° in the tracheoesophageal groove. In the left recurrent laryngeal nerve, this angle is about 15–45°. Recurrent laryngeal nerve passes through the posterior of the inferior thyroid artery in 61% of cases, anterior in 32%, and the branches of the artery in 7% of cases. The lower parathyroid glands are located proximal to the inferior laryngeal nerve, and the upper parathyroid glands are located distal to the nerve. Recurrent laryngeal nerve is found in 60–70% of cases in the tracheoesophageal groove, 20–25% in the lateral of the trachea, and 5% in the posterior of the trachea.

In 35–80% of cases, RLS is divided into branches before entering the larynx. Typically, extralaryngeal branching is in two forms as motor and sensory branch. However, two to eight extralaryngeal branches have been described in the literature. Its linear extension and its light yellow color make it known macroscopically.

The right inferior laryngeal nerve is 32 cm long, and the left is approximately 43 cm long. Since the left inferior laryngeal nerve has a longer course in the tracheoesophageal groove, the majority of nerve injuries occur in this side.

Nonrecurrent laryngeal nerve was reported in 0.3–0.8% of cases. Nonrecurrent laryngeal nerve exits the cervical section of the vagus at the level of the larynx or thyroid gland and directly enters the larynx at the level of the cricothyroid joint without forming a loop [25].

The intraoperative methylene blue spraying technique could be used in thyroid surgery. Methylene blue will be sprayed over the thyroid lobe and perilober area. Tissues, especially parathyroides, the recurrent laryngeal nerve, and the inferior thyroid artery could be evaluated [26].

Recurrent nerve damage after thyroid surgery varies between 0 and 11%. Complications are more frequently seen in subtotal thyroidectomies and secondary surgeries than total thyroidectomies and primary surgeries, whereas they are inversely correlated with surgeon experience. Posterior cricoarytenoid muscle palpation without electromyography provided that follow-up of glottic pressure applications and peroperative observation of vocal folds. However, the fact that the practice is both difficult and does not give very healthy results is an important limitation of this method. Postoperative complications were reduced, and surgical duration was significantly reduced by the use of peroperative recurrent nerve monitoring. Measurements are made with surface electrodes integrated in endotracheal intubation tubes. The device alerts the surgeon with sound. In addition, the current changes in the device screen can be recorded and provide legal basis for the surgeon [27].

In patients undergoing peroperative recurrent nerve monitoring, selection of anesthesia is important.

The continued effect of the muscle relaxant agent will affect the results completely. Intubation can be done without using any muscle relaxant. And also, it can be done with using agents which effect in a short time and break down in a short time. For this purpose, succinylcholine is often preferred as a short-acting depolarizing neuromuscular blocking agent [28].

If there is a nerve injury, different methods of recurrent nerve repair, such as microsuturing gluing and grafting, have been proposed [29]. Direct microsuture is preferable when the defect is no longer than 5 mm and the primary repair can be completed without tension [30]. After transection of RLN, immediate reconstruction could be performed by a direct, "end-to-end" anastomosis of neural stamps, by three to four perineural stitches of 7-0 nylon thread, using microsurgical instruments [31]. Cyanoacrylate glue has also been proposed for nerve repair but has been criticized for its toxicity, excessively slow resorption, and risk of inflammatory reaction in the perineural tissues [32].

When the proximal stump of the RLN cannot be used, grafting should be done using the transverse cervical nerve, supraclavicular nerve, or ansa cervicalis [33]. First, start to identify ansa cervicalis on the surface of the internal jugular vein, and branches to the sternothyroid muscles could be dissected. The proximal end of the major branch could anastomosed to the distal RLN stump [34].

5.2 Lymphatics of the thyroid

The lymphatic drainage of the thyroid gland is wide and flows in a versatile pattern. The Hollinshead pattern of drainage is divided into four different ways as the median superior drainage, median inferior drainage, right/left lateral drainage, and posterior drainage [35].

The median superior drainage passes through three to six lymphatic vessels originating from the upper edge of the isthmus and the upper middle edge of the lateral lobes. These lymphatic veins move upward in the direction of the larynx and end in the digastric nodes. Some of the lymphatics can flow into one or two (Delphian) nodes in the throat immediately above the isthmus [23]. Secondarily, the anterior tracheal nodes under the thyroid through the lymphatic channels move downward from the upper jugular nodes on either side of the neck or from the Delphian nodes to the frontal side of the thyroid gland [12, 36].

The median inferior drainage consists of several lymphatic vessels draining to the inferior portion of the isthmus and the lower medial parts of the lateral lobes [36, 37]. These lymphatic channels follow the inferior thyroid veins to terminate before the tracheal and brachycephalic nodes [12, 13]. Right and left lateral drainage patterns originate from the lymphatic bodies at the lateral border of each lobe [12, 25]. The superior thyroid artery and vein are ascended, followed by the lower thyroid artery at the bottom [13, 36]. Between these two groups, the lymphatic ducts move lateral, anterior, or posterior to the carotid sheath to reach the lymph nodes of the internal jugular vein [12–14, 36]. In rare cases, these lymphatic vessels drain directly into the subclavian vein, jugular vein, or thoracic duct without flowing to the lymph node [38].

The posterior drainage pattern begins in the lymphatic vessels draining to the inferomedial parts of the lateral lobes to discharge into the lymph nodes along the RLN track [12, 36]. Rarely, a lymphatic body that rises posteriorly to the upper part of the lobe reaches to the retropharyngeal nodes [36].

Several models of lymphatic drainage of the thyroid gland have been proposed, and all of them are true and comprehended from the same basis. Another simplified drainage model is that emergency lymphatic drainage enters the periglandular nodes, followed by the preterminal and paratracheal nodes along with the RLN and then to the mediastinal lymph nodes [14, 36].

Although lymph node metastasis is known to increase recurrence, its effect on prognosis and survival is still being discussed [39, 40]. All patients with lateral LN recurrence could be therapeutic neck dissection and RAI ablation therapy as adjuvant treatment [41].

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