

TITLE: Embryology of the Neck and Neck Masses

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A mass in the neck is a common clinical finding that presents in patients of all age groups. The differential diagnosis may be extremely broad, and although most masses are due to benign processes, malignant disease must not be overlooked. The complex embryological development of the neck is crucial to achieving both an accurate diagnosis and successful treatment of neck masses.

Embryology of the Neck

The pharynx occupies the bulk of the foregut during the first few weeks of development. The buccopharyngeal membrane breaks down late in the third week and the mesodermal branchial bars begin to appear. These appear as u-shaped structures in the transverse plane, which fuse ventrally to form 6 pairs of pharyngeal arches. The fifth arch is small and quickly disappears. The arches are separated externally by ectodermal pharyngeal clefts and internally by endodermal pharyngeal pouches. Each arch contains an artery, a nerve, and muscular and cartilaginous structures, which give rise to most of the structures of the neck. The remaining cervical musculature gains contributions from cervical somites.

The first branchial arch contains cartilage with a dorsal portion, known as the maxillary process, and a ventral portion, known as Meckel's cartilage or the mandibular process. Both of these structures eventually regress to leave only the malleus and incus. The ossification of mesoderm around Meckel's cartilage gives rise to the mandible and the sphenomandibular and anterior malleolar ligaments. The muscles of the first arch include the muscles of mastication (temporalis, masseter, and pterygoids), the tensor tympani and tensor veli palatini, the anterior belly of digastric and mylohyoid muscles. The nerve of the first branchial arch is the fifth cranial nerve. Contributions of the first arch artery are thought to persist as the maxillary artery. The first pouch persists as the Eustachian tube, the middle ear and portions of the mastoid bone.

The second branchial arch cartilage is known as Reichert's cartilage and its derivatives include the upper body and lesser cornu of the hyoid bone, the styloid process and stylohyoid ligament, and the stapes superstructure. Muscles of the second arch include the muscles of facial expression, platysma, posterior belly of digastric, stylohyoid, and stapedius. The nerve of the second arch is the seventh cranial nerve. Only very rarely does the artery of the second arch persist, as the stapedia artery, and courses through the crura of the stapes.

The derivatives of the third branchial arch include the greater cornu and inferior body of the hyoid. Muscles of the third arch include the stylopharyngeus and superior and middle pharyngeal constrictors. The artery contributes to the common carotid and proximal portions of the internal and external carotid arteries. The nerve of the third arch is the ninth cranial nerve. The third pouch contributes to the inferior parathyroids and thymus and thymic duct.

The fourth and sixth branchial arches fuse to form the laryngeal cartilages. The muscles of the fourth arch include the cricothyroid and inferior pharyngeal constrictors. The muscles of the sixth arch are the remaining intrinsic musculature of the larynx. The nerve of the fourth arch is the superior laryngeal nerve and the nerve of the sixth arch is the recurrent laryngeal nerve. On the right, the artery of the fourth arch contributes to the subclavian and to the aortic arch on the left. The sixth arch artery becomes the ductus arteriosus and pulmonary artery. The endodermal pouch of the fourth arch becomes the superior parathyroids and possibly the parafollicular thyroid cells.

As the branchial apparatus develops, the first and second arches grow in a cranial to caudal fashion, creating the epipericardial ridge. The epipericardial ridge contains the mesodermal rudiments of the sternocleidomastoid, trapezius, and the infrahyoid and lingual musculature. The nerves of the epipericardial ridge are the hypoglossal and spinal accessory. The proliferation of mesoderm in this area eventually causes overgrowth and narrowing of the third, fourth, and sixth arches into an ectodermal pit, known as the cervical sinus of His. This sinus eventually becomes obliterated. If it fails to be obliterated or is partially obliterated, a branchial sinus, cleft, or cyst of types II, III, or IV may develop.

The thyroid gland originates during the fourth week of gestation as endoderm of the floor of the mouth in between the tuberculum impar and copula of the first and second pouches. It descends as a bilobed diverticulum from the foramen cecum to pass in variable position to the hyoid bone to rest in the lower neck.

Midline Neck Masses

Thyroid Nodules

Thyroid nodules are very common. They occur in 4-7% of the adult population. About 1 in 20 new nodules can be expected to harbor carcinoma. The vast majority of thyroid nodules are colloid nodules, adenomas, or thyroid cysts. The history and physical examination are crucial in providing a clinical setting in which to interpret the fine needle aspiration (FNA), which has established itself in the workup of the thyroid nodule. Thyroid FNA cytopathologic categories include 1) malignant, 2) suspicious, 3) benign, and 4) non diagnostic. When FNA is read as malignant, the chance of malignancy is very high, with a false positive rate of only 1%. The main difficulty with FNA in the identification of malignancy is the differentiation of follicular adenoma versus carcinoma in which the diagnosis hinges on the evidence of extracapsular extension. Lymphoma can be suggested by FNA but open biopsy is often required to confirm the diagnosis. The management of thyroid carcinoma is extensively discussed in other Grand Rounds.

Thyroglossal duct cyst

The second most common midline mass encountered is the thyroglossal duct cyst. As the

bilobed thyroid diverticulum descends from the floor of the pharynx, a thyroglossal duct is created. Failure of involution of any portion of this tract can lead to a thyroglossal duct cyst. Arrest of normal descent of the gland can result in ectopic thyroid tissue. The pyramidal lobe, found in 40% of patients, is actually just the failure of closure of the inferior most portion of the thyroglossal duct. The majority of thyroglossal duct cysts present in children and adolescents as an asymptomatic midline mass at or below the hyoid bone. They commonly elevate with tongue protrusion. External sinuses involving the pharynx may rarely occur, and these may become infected and even form fistulae. The preoperative workup of thyroglossal duct cysts has been a source of controversy. Some recommend checking overall thyroid function with a TSH level prior to excision. An ultrasound is probably the best study to document the presence of normal thyroid tissue. A thyroid scan is of value in patients who are hypothyroid, are unable to tolerate an adequate thyroid ultrasound, or fail to demonstrate a normal thyroid by ultrasound.

The primary management of thyroglossal duct cysts is with surgical excision. However, simple cyst excision results in a high rate of recurrence (50%). This procedure has been largely replaced by the 'Sistrunk procedure.' During this procedure, the central portion of the hyoid is included in the en bloc excision of the cyst, and dissection is carried up into the tongue base. Recurrence rates with this procedure dropped to 4-6%. Patients who are at greatest risk for recurrence are those who have had recurrent infections, externally draining sinuses, or prior incision and drainage. For these patients, a modification of the Sistrunk procedure to include en bloc anterior dissection including portions of the strap muscles is advocated to reduce recurrence.

Thyroglossal duct carcinoma (TGDCa) is uncommon, occurring in approximately 1% of all thyroglossal duct cysts. It is often diagnosed incidentally after surgical excision. 94% of carcinomas are of thyroid origin, with most being papillary, and 6% are of squamous cell origin. Much of the controversy in the management of TGDCa revolves around the best method of management of an otherwise clinically normal thyroid gland. Whether the TGDCa originated within the thyroid follicles of the TGDC or represents metastasis from an occult thyroid primary is an important issue. In a review by Patel et al. they argue that incidentally discovered, well-differentiated thyroid carcinoma of the TGD in a "low risk patient" (under 45 years, tumor less than 4cm, without local tissue invasion or regional metastasis) in the presence of a clinically and radiologically normal thyroid gland can be managed adequately by the Sistrunk procedure alone. Those in a "higher risk group" (greater than 45 years of age, tumor size greater than 4cm, with local tissue invasion or regional metastasis), require more aggressive treatment including the Sistrunk procedure, total thyroidectomy, with or without neck dissection, followed by radioactive Iodine ablation

Thymus gland anomalies

The thymus gland originates from the third branchial pouch and descends into the lower neck and mediastinum. Ectopic thymus tissue can result from failure of descent of one or both lobes of the thymus. Failure of involution of thymopharyngeal ducts may persist as cervical thymic cysts. These are firm, mobile masses usually found in the lower aspect of the neck. The lesions usually present during the first decade of life due to the fact that the thymus tissue is of greatest relative size at birth and reaches greatest absolute size by puberty. Initial workup includes a plain chest radiograph and possibly a CT. Surgical excision is the treatment of choice.

Plunging Ranula

A ranula is either a mucus retention cyst or a mucus extravasation pseudocyst arising from an obstructed sublingual gland. A simple ranula is confined to the oral cavity as a cystic unilateral mass of the floor of the mouth. A plunging ranula may pierce the mylohyoid and present as a paramedian or lateral neck mass with or without an obvious oral cavity ranula. They should be differentiated from dermoid cysts and lymphangiomas. Cyst aspiration consistently reveals fluid with high levels of protein and salivary amylase. CT or MRI will demonstrate a uniloculated cystic mass arising from the sublingual space with extension into the submental, submandibular, or parapharyngeal space. Marsupialization has led to a high rate of recurrence of these lesions. Surgical treatment includes excision in continuity with the sublingual gland of origin.

Lateral Neck Masses

Branchial Anomalies

Developmental aberrations of the intricate branchial system give rise to branchial anomalies. These anomalies may exist either as cysts, sinuses, or fistulae. Generally, branchial clefts with external openings onto the skin are associated with the first and second arches, whereas the third and fourth arches are associated with internal openings.

First Branchial Cleft Cysts are classified as Type I or Type II. Type I is an ectodermal duplication anomaly of the external auditory canal. The cyst is lined by squamous epithelium without skin appendages. These lesions track parallel to the EAC and middle ear and often begin as fistulous tracts at the post auricular or pretragal area. Surgical excision in the noninfected state is the treatment of choice.

In Type II Branchial cleft cysts, the cyst or external opening is localized in the anterior neck, always superior to the hyoid bone. They have been traditionally found in a triangle formed from the EAC curving to meet the mid-hyoid and tip of the chin. The tract courses over the angle of the mandible, through the parotid gland, and terminates near the bony-cartilaginous junction of the EAC. The course of the tract in relation to the facial nerve is variable. 29% may pass medial to the nerve, and even may sometimes split around the nerve. Treatment of these lesions is surgical. Preoperative imaging with MRI to evaluate the lesion in relation to the parotid gland is helpful. The definitive excision requires identification of the facial nerve and a superficial parotidectomy is typically required to avoid inadvertent injury to the small and more superficially located facial nerve. Special care must also be taken at the upper end of the fistula in order to remove not only the portion of the tract between the skin and cartilage of the EAC, but also the flange of cartilage through which the tract passes.

Second Branchial Cleft cysts are the most common (90%) branchial anomalies. They usually present spontaneously as a painless, fluctuant mass of the anterior triangle in infants. These lesions may fluctuate after a URI. The tract courses deep to the second arch derivatives and superficial to the third arch derivatives. If an external opening is present, it is most consistently found at the anterior border of the SCM at the middle and inferior two-thirds junction. It then courses anterior to the SCM, superficial to the IX, XII nerve, to turn medial and pass between the internal and external carotid artery. The tracts typically terminate into the tonsillar fossa. Preoperative CT imaging will help delineate the pathway. The tract is surgically

excised and may require a tonsillectomy.

Third Branchial Cleft Cysts are rare (<2%). They may present in a similar fashion as Second BCC. However, the internal opening is located within the pyriform sinus. The tract pierces the thyrohyoid membrane cephalad to the superior laryngeal nerve, lateral to the hypoglossal nerve, medial to the glossopharyngeal nerve, and posterior to the internal carotid artery. Surgical approach is usually via a standard thyroidectomy approach to fully visualize the recurrent laryngeal nerves and to adequately distinguish between a third and fourth BCC. Often, a partial thyroid lobectomy is required.

Fourth Branchial Cleft Cysts are extremely rare and a true fistula has never been reported. The potential path would lie between the fourth and sixth arch structures. The internal sinus opening would originate near the apex of the pyriform sinus, caudal to the superior laryngeal nerve and travel translaryngeal under the thyroid ala to emerge near the cricothyroid joint, and then descend superficially to the recurrent laryngeal nerve in the paratracheal region. Third and fourth branchial pouch anomalies have been recognized as a potential cause of acute suppurative thyroiditis in children. They present with fever, paratracheal fullness, and tenderness, typically on the left side. In contrast to hematogenous suppurative thyroiditis, the intraoperative cultures show a variety of aerobic and anaerobic organisms of pharyngeal origin. For patients that fail antibiotic therapy, a hemithyroidectomy is recommended only after radiologic or endoscopic proof of a pyriform sinus opening is observed.

Laryngoceles

Laryngoceles are most frequently seen in the adult population, but can present as a lateral neck mass in the pediatric population. They are thought to form congenitally as a result of enlargement of the laryngeal saccule with distension and entrapment of air. Laryngoceles are classified as either internal, external, or combined. The internal laryngocele is confined solely to the larynx and is caused from distension of the saccule, typically to the false vocal cord and aryepiglottic fold. They typically present with hoarseness and respiratory distress and not as neck masses. The external laryngocele will protrude through the thyrohyoid ligament at the entrance of the superior laryngeal nerve. These lesions will present as a soft, compressible, lateral neck mass that may distend with increases in intralaryngeal pressures. If infected they are classified as laryngopyoceles. The combined type has features of both internal and external. CT scan will delineate the lesions. Asymptomatic laryngoceles in children require no surgical treatment. Symptomatic laryngoceles and laryngopyocles should be excised. Internal laryngoceles may be excised or marsupialized endoscopically. For external laryngoceles without a significant internal component, simple excision after identification of the superior laryngeal nerve is appropriate. For a combined type, a lateral thyrotomy may be needed for more complete exposure. In any adult patient, there is a small but significant incident of laryngeal carcinoma that leads to the development of a laryngocele. Therefore, direct laryngoscopy with special attention to the laryngeal ventricle is a crucial part in the management of laryngoceles.

Dermoid and Teratoid Cysts

Teratoid and Dermoid cysts are rare causes of neck masses. These developmental anomalies are composed of different germ cell layers. They are thought to possibly arise from isolation of pluripotent stem cells during migration with resultant disorganized growth or from entrapment of germ cell layers at points of failed embryonic fusion lines. The lesions are

classified according to their composition. Dermoid cysts are composed of mesoderm and ectoderm and may contain hair follicles, sebaceous glands, and sweat glands. They are often midline or paramedian, painless, and do not elevate with tongue protrusion. When presenting as midline masses, they are frequently misdiagnosed as thyroglossal duct cysts even intraoperatively, as some may involve the hyoid bone. The treatment is simple excision in contrast to the Sistrunk procedure for thyroglossal duct cyst. Some have recommended intraoperative cyst aspiration or sectioning as a means of differentiating these two lesions.

Teratoid cysts and Teratomas contain all three germ layers. These lesions commonly present within the first year of life and are usually larger midline or paramedian masses than Dermoid cysts. Teratomas are distinguished by cellular differentiation enough to have recognizable organs or structures. The larger size of these lesions results in secondary aerodigestive compressive symptoms. There is an associated 20% incidence of maternal polyhydramnios which can often lead to the diagnosis with maternal ultrasound. In cases in which the lesion is anticipated to be large enough to cause immediate airway compromise during birth, the appropriate teams can be available to secure the airway. The well encapsulated cyst and poor vascularization found in these lesions enhance the likelihood of successful excision.

Sternomastoid Tumor of Infancy

Sternomastoid tumor of infancy, also known as pseudotumor of infancy, is a fibrotic lesion of the distal sternocleidomastoid. These lesions usually present within the first 7 to 28 days of birth as a firm mass within the SCM. The patient may exhibit a head tuck to the ipsilateral side and chin pointed away from the lesion. An association with breach delivery and forceps delivery has been reported. The etiology is still unknown but it is theorized that hematoma formation in the SCM during traumatic delivery is replaced with subsequent fibrosis. Usually, aggressive physical therapy and range of motion exercises will resolve the lesion, with 80-100% regressing by the first birthday. Only rarely does an untreated case lead to long term torticollis and resultant dysmorphism. Ultrasound will reveal a solid mass that is intrinsic to the SCM. Surgical division of the SCM is only recommended if physical therapy fails.

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