

**TITLE: Branchial Anomalies**

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The study of branchial anomalies covers a wide variety of pathological conditions. Each condition is the result of abnormalities in embryologic development. For this reason, the treating clinician should be familiar with the normal developmental process.

Between the 2<sup>nd</sup> and 6<sup>th</sup> week of gestation, the branchial apparatus undergoes development. At that time, the neck is shaped like a hollow tube with circumferential ridges (arches). Between the arches are other ridges termed clefts and pouches. The clefts are on the outside (ectoderm) and the pouches are on the inside (endoderm). Each arch leads to the development of a specific cartilage, artery, muscle component, and cranial nerve, all of which are neural crest in origin. Although there are six arches, only five form structures (I-IV and VI); the 5<sup>th</sup> arch fails to develop in humans.

The first arch is referred to as the "mandibular arch" as it lays the framework for the development of the mandible through Meckel's cartilage. It also gives rise to the malleus head and neck as well as the incus body and short process. The muscles that are associated with the 1<sup>st</sup> arch are the muscles of mastication, anterior belly of the digastric, mylohyoid, tensor tympani, and tensor veli palatini. The cranial nerve is the trigeminal nerve (CN V), and the arteries are the maxillary and internal carotid arteries.

The second arch is the "hyoid arch." Its cartilage is Reichert's cartilage which gives rise to the stapes, malleus manubrium, incus long process, styloid process, and part of the hyoid bone (lesser horn and upper body). The muscles that this arch gives rise to are the muscles of facial expression, buccinator, platysma, stapedius, stylohyoid, and posterior belly of the digastric. The cranial nerve is the facial nerve (CN VII), and the artery is the stapedia artery.

The third arch gives rise to the remainder of the hyoid bone (greater horn and lower body), stylopharyngeus, glossopharyngeal nerve (CN IX), and the common carotid artery. The fourth arch gives rise to the thyroid, epiglottic, and cuneiform cartilages as well as the cricothyroid and inferior constrictor muscles. In addition, the fourth arch leads to the development of the superior laryngeal nerve and the subclavian artery and aortic arch. The sixth arch gives rise to the cricoid, arytenoid, and corniculate cartilages. The muscles are all the

intrinsic muscles of the larynx except the cricothyroid. The nerve associated with the sixth arch is the recurrent laryngeal nerve while the artery is the pulmonary artery.

The branchial pouches also give rise to various structures with the clefts usually providing the covering for those structures. There are four clefts and four pouches in human development. The first pouch gives rise to the eustachian tube, middle ear, mastoid, and the inner layer of the tympanic membrane. The second pouch gives rise to the tonsils, root of the tongue, foramen cecum, and part of the pharynx. The third pouch is divided into two wings; ventral and dorsal. The ventral wing gives rise to the thymus while the dorsal wing gives rise to the inferior parathyroid glands. The fourth pouch gives rise to the superior parathyroid glands and the parafollicular C-cells of the thyroid gland.

One can see that when abnormalities in the development of the branchial apparatus occur, numerous pathologic conditions can arise. When the first branchial arch is involved in abnormal development, the resulting abnormalities are termed “First Arch Syndrome.” These abnormalities involve the eyes, ears, palate, and mandible. Two main syndromes associated with “First Arch Syndrome” are Treacher Collins and Pierre Robin.

Treacher Collins Syndrome, also termed mandibulofacial dysostosis, is a syndrome typically inherited in an autosomal dominant fashion. Features include midface and mandibular hypoplasia, cleft palate, and multiple ear and eye anomalies. The ear anomalies can include microtia, anotia, stenotic or atretic external auditory canals, and a malformed malleus and incus. The eye anomalies include coloboma of the lower eyelids and down-sloping palpebral fissures. Pierre Robin syndrome is characterized by three main features; a u-shaped cleft palate, micrognathia, and glossoptosis (posterior displacement or retraction of the tongue).

When abnormalities occur in the development of the second branchial arch, a malformed auricle (microtia) and ossicles (stapes, malleus, and incus) may be the result. In addition, hyoid malformation and muscular asymmetry of the face may also be seen. Third arch anomalies typically involve hyoid malformations and carotid artery aneurysms. Fourth branchial arch anomalies mainly involve the larynx and include laryngeal stenosis, laryngoptosis (low position of the larynx), chondromalacia, double aortic arch, and pulmonary artery sling.

Abnormalities involving the first branchial pouch include atresia and diverticuli of the eustachian tube, both of which can lead to recurrent bouts of otitis media. In addition, one may see a bifid tongue, perforated tympanic membrane and branchiogenic nasopharyngeal cysts. The mastoid antrum and tympanic cavities may also be absent.

When there are errors in the development of the second branchial pouch, a thyroglossal duct cyst may occur. Thyroglossal duct cysts result from the failed involution of the thyroglossal duct and thus a cyst may be seen anywhere from the base of the tongue to the upper mediastinum. They occur in roughly 7% of the population, and are best noted as midline neck masses that are closely associated with the hyoid bone. They will typically move with tongue protrusion and swallowing. The treatment of a thyroglossal duct cyst is surgical resection through a Sistrunk procedure.

Another anomaly that may be noted with errors in the development of the second branchial pouch is a lingual thyroid. This anomaly results from the failed descent of the thyroid gland during development. In 90% of cases, the atopic thyroid remains at the base of the tongue. In most cases, the lingual thyroid is not noted until early adulthood given the fact that most are asymptomatic. In other cases, the lingual thyroid may cause dysphagia or even airway compromise. The lingual thyroid usually appears as a reddish mass at the base of the tongue due to the fact that it is very vascular. In 2/3<sup>rd</sup> of cases, this is the only functional thyroid tissue, thus thyroid function studies should be performed in order to determine if there is other functioning thyroid tissue prior to treatment. If the patient is asymptomatic, close observation may be all that is required. If symptoms are present, treatment options include surgical resection or radioablative therapy. In 70% of cases, the patient will be hypothyroid and thus will require lifelong thyroid replacement therapy.

DiGeorge Syndrome is the most notable syndrome involved with developmental anomalies of the third and fourth branchial pouches. This syndrome involves a partial deletion of chromosome 22, and is most notable for the congenital absence of the thymus and parathyroid glands. This leads to hypocalcemia and tetany as well as impaired cellular immunity. Other features of this syndrome as well as the chromosome involved can be remembered by the acronym CATCH-22: **C**ardiac anomalies, **A**bnormal facies, **T**hymic aplasia, **C**left palate, and **H**ypocalcemia. Other anomalies associated with the third and fourth branchial pouches include accessory parathyroid glands and thymic cysts.

When errors occur in branchial cleft development, the most notable outcome is a branchial cleft cyst. However, other anomalies may result as well. For instance, when errors occur with the development of the first branchial cleft, external auditory canal stenosis or atresia as well as preauricular skin tags and pits may result. When the second branchial cleft is involved, cervical sinuses may result. Errors in the development of third branchial cleft could yield a thymic cyst.

As stated previously, the most notable anomaly involved with improper development of the branchial cleft is the branchial cleft cyst. There are four recognized types, and most are unilateral in presentation. However, 2-3% of cases may present with bilateral cysts.

The first branchial cleft cyst can be broken down into two types by the Work classification. A type I cyst is of ectoderm origin and usually involves the preauricular area. The sinus tract associated with this type of cyst starts in the preauricular area, parallels the external auditory canal while typically staying lateral to the facial nerve, and ends either in the external auditory canal or the middle ear. A type II cyst is more common than the type I cyst, and is made up of ectoderm and mesoderm. This cyst will typically appear around the angle of the mandible or in the submandibular region. The tract its sinus takes is from the angle of the mandible or submandibular region into the substance of the parotid gland going medial or lateral to the facial nerve, and ending in the conchal bowl or at the bony-cartilaginous junction of the external auditory canal.

A second branchial cleft cyst is the most common type of branchial cleft cyst, representing roughly 95% of all cases. This cyst typically appears as a mass just anterior and

medial to the Sternocleidomastoid muscle in the neck. The tract that the sinus takes goes from this region of the neck, along the carotid sheath and between the external and internal carotid arteries. It then passes superficial to the 9<sup>th</sup> and 12<sup>th</sup> cranial nerves before piercing the tonsillar fossa.

The third branchial cleft cyst is rarer than a first or second branchial cleft cyst, and typically only occurs on the left side of the neck. These cysts appear in a similar location as the second branchial cleft cyst, but their sinus tract differs. Instead of passing through the internal and external carotid arteries, the sinus tract will go behind the two. It will also run deep to the 9<sup>th</sup> nerve while staying superficial to the hypoglossal, superior and recurrent laryngeal nerves. It will then open into the apex of the pyriform sinus.

The fourth branchial cleft cyst is the rarest of all, with roughly 200 cases reported in the literature. This cyst is usually lower in the neck than the second and third cyst, with its tract taking a much different course than the other cysts. The sinus tract will go deep to the common carotid before looping around the aorta on the left or subclavian on the right. At this point, the tract will go deep to the superior laryngeal nerve while staying superficial to the recurrent laryngeal nerve. At this point, it pierces the thyrohyoid membrane and enters the pyriform sinus at its apex. Of note, both third and fourth branchial cleft cysts may be closely associated with the thyroid gland. For this reason, if a patient is suffering from recurrent thyroid infections/abscesses, a third or fourth branchial cleft anomaly must be considered.

When working up a branchial cleft cyst, one must of course start with a detailed history and physical examination. Following this, imaging studies are usually obtained. There are multiple modalities, but typically a CT scan is ordered. On CT, a branchial cleft cyst appears as a homogeneous mass with a central area of low attenuation and a smooth enhancing rim. Although CT does provide for a good radiographic evaluation of the cyst, it does have some drawbacks. It is more expensive than an ultrasound, and results in more radiation exposure. In addition, children may require sedation in order to obtain the exam. On ultrasonography, branchial cleft cysts will appear as a lesion with an area of low echogenicity and lack of internal septations. This is the easiest and most cost effective imaging modality. However, it is not as helpful with surgical planning and thus is typically not ordered alone. MRI is another option available for imaging, although is not commonly obtained due to its high cost and need for sedation in children. On MRI, a branchial cleft cyst will appear hypointense on T1 and hyperintense on T2. Other imaging modalities include fluoroscopic fistulography and barium esophagoscopy. Both of these can help with delineating the path of the sinus tract, which will aid in surgical planning.

Treatment of the branchial cleft cyst is dependent on whether an infection is present or not. If the cyst is infected, antibiotics should be given for 2-4 weeks in an attempt at clearing the infection prior to surgical resection of the cyst. If an abscess has formed, it will usually require drainage. If possible, the least invasive procedure should be attempted to drain these abscesses because the more dissection that is performed, the harder it will be to completely remove the cyst at a future operation secondary to scar formation. For this reason, needle aspiration should be considered first. If the abscess persists, then an incision and drainage should be performed.

The definitive treatment of a branchial cleft cyst is complete surgical excision of the tract and cyst. For first branchial cleft cysts, the facial nerve must be identified as the tracts are usually closely associated with the nerve. It has been recommended by some surgeons to wait until the patient is two years of age to allow for a more favorable anatomic location of the facial nerve. However, this is controversial as this could lead to more infections and more scarring, making it more difficult to remove the cyst and tract in the future.

When a third or fourth branchial cleft cyst is suspected, one should start by examining the pyriform sinus with a direct laryngoscopy, looking for a sinus opening. If there is one, a Fogarty vascular catheter could potentially be threaded through the sinus and into the tract, greatly aiding in the identification of the tract when the neck is entered. For both of these cysts, the surgeon should also identify the recurrent laryngeal nerve in order to avoid injuring it during dissection because both of these cysts' tracts are usually closely associated with it.

Another treatment option available for fourth branchial cleft cysts comes in the form of endoscopic cauterization of the sinus opening through the pyriform sinus during a direct laryngoscopy. This has been described in multiple studies and case reports with good results. For instance, Verret et al performed endoscopic cauterization on 10 patients without surgical excision of the cyst and tract. Seven patients showed no recurrence of the disease after 3 years of follow-up. The other three patients in their study were lost to follow-up.

Branchial anomalies are numerous and can involve multiple areas of the head and neck. An understanding of the embryology and pathology associated with these anomalies will greatly aid the clinician in the treatment of these patients.

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