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Pharyngeal Arches, Cleft and Pouches

The head and neck develop during the 4-5th intrauterine week. The connective tissue growth of mesenchymal tissue in the cranial region of the fetus results in the formation of arches separated by cleft. At the same time out pocketing on the lateral wall of the pharynx known as the pharyngeal pouches develops. They separate the arches on the endodermal (internal) surface while cleft separate the arches on the ectodermal (external) surface. The term branchial arches are also known as pharyngeal arches since it more accurately describes human anatomy. Each branchial arch is lined externally by an ectoderm-lined recess, referred as a pharyngeal/branchial cleft and internally by a layer of endoderm, referred to as pharyngeal/branchial pouch. Initially there are four pharyngeal clefts, but only the 1st cleft gives rise to a permanent structure, the external auditory meatus, the space created by the 2nd, 3rd and 4th pharyngeal cleft give rise to the cervical sinus. The fetus develops six pharyngeal arches. The 5th regress immediately. Each arch has own innervation, a muscular component, cartilaginous or skeletal support and a vascular component. The branchial (or pharyngeal) arches represent the embryological precursor of the face, neck, and pharynx. Refer to Table 1 regarding the component's distribution of the arches.

Table 1. Pharyngeal Arches

ARCH	Musculo-skeletal	Nerves	Vascular
First	Dorsal: Maxilla (bone and cartilage), zygomatic bone, part temporal bone Ventral: mandible, Meckel's cartilage, malleus, sphenomandibular ligament muscles of mastication, mylohyoid, anterior digastric belly, tensor veli palatini and tympani	Motor: Trigeminal nerve (5th cranial nerve) Sensory: Trigeminal nerve, skin of the face, mouth and nose, 2/3 anterior tongue sensation	Maxillary Artery (branch of external carotid)

Second	Reichert's cartilage - develops into stapes, styloid process, stylohyoid ligament and upper/lower horn of hyoid bone	Motor: Facial nerve (7th cranial nerve) Sensory: Facial nerve, taste sensation and anterior 2/3 of the tongue	Stapedial artery regress before birth Hyoid artery - give rise to corticotympanic artery
Third	Lower body and greater horn hyoid	Motor: Glossopharyngeal nerve (IX cranial nerve) Sensory: taste and general sensation posterior 1/3 tongue	Common carotid artery Proximal portion Internal Carotid
Fourth	Laryngeal cartilages	Motor: Superior laryngeal branch vagus nerve (10th cn) - constrictor, levator palatini and cricothyroid Sensory: Superior laryngeal branch - root of the tongue	Right: proximal portion subclavian artery Left: aortic arch
Fifth	regress		
Sixth	Cricothyroid SCM muscle trapezius muscle	Motor: recurrent laryngeal branch vagus nerve (10th cn) - intrinsic muscle of the pharynx Sensory: taste sensation from epiglottis and pharynx, general pharynx sensation, esophagus,	Right: proximal portion pulmonary arteries Left: ductus arteriosus

		tympanic membrane, external auditory meatus and external ear, gag reflex, parasympathetic innervation viscera	

Pharyngeal pouches are endodermal out-pockets occurring between the pharyngeal arches. The pouches give rise to several tissues responsible for the formation of permanent structures. Of six pairs of pouches, only four give rises to a structure since the 5th and 6th pouch blends within the 4th pharyngeal pouch. See Table 2 regarding the structure associated with each pharyngeal pouch. Pharyngeal pouches produce tissue necessary for hearing, calcium homeostasis and adequate immune response.

Table 2. Pharyngeal Pouches.

Pouch	**Structure**
1st	Eustachian tube and middle ear cavity, inner layer tympanic membrane
2nd	Palatine tonsil and middle ear
3rd	Dorsal – inferior parathyroid glands Ventral – thymus
4th	Dorsal – superior parathyroid glands Ventral – Ultimobranchial body (parafollicular C cell thyroid gland)

Failure of branchial arches to properly develop may result in a congenital malformation. Anomalies of the branchial arches are the second most common congenital lesions of the head and neck in children. Thyroglossal duct cyst is the most common congenital lesion of the neck in children. Pharyngeal arch anomalies may present as cysts, sinus tracts, fistula, or cartilaginous remnants and present with typical clinical and radiological patterns dependent on which arch is involved. Most branchial cleft malformations in children involve the 1st and 2nd arches. Second branchial arch anomalies are the most common, accounts for 95% of cases and most commonly present as cysts. 1st branchial anomalies occur 4% of cases and 3rd and 4th branchial arch anomalies are very rare. Branchial cysts present in older children/young adults, while fistulas present in infants/young children. Surgical management involves complete surgical excision encompassing the external sinus opening with dissection of the sinus tract. First branchial anomalies present as cystic masses adjacent to the external auditory canal and submandibular area, are often misdiagnosed, and often managed inadequately. Since they have propensity for infection, surgical excision is definitive treatment. There is potential risk to the facial nerve during resection. Third branchial cleft anomalies are associated to the superior laryngeal nerve, arise from the rostral end of the pyriform fossa, usually present as fistula/sinus tract in the posterior cervical space, posterior to the sternocleidomastoid muscle (posterior triangle of the neck).

Fourth branchial cleft fistula/sinus tracts arise from the pyriform sinus apex, are left-sided, and most often present as sinus tract coursing from the apex of the pyriform fossa to the upper aspect of the left thyroid lobe. They are a cause of purulent thyroiditis. Cleft lip and palate, auricular atresia and micrognathia are examples of 1st branchial arch malformation. A branchial cleft cyst is an example of a 2nd branchial arch malformation.

References:
1- Waldhausen JH: Branchial cleft and arch anomalies in children. Semin Pediatr Surg. 15(2):64-9, 2006
2- Miles B, Srinivasan VN: Embryology, Pharyngeal Pouch. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.2022 Apr 5.
3- Shen LF, Zhou SH, Chen QQ, Yu Q: Second branchial cleft anomalies in children: a literature review. Pediatr Surg Int. 34(12):1251-1256, 2018
4- Bajaj Y, Ifeacho S, Tweedie D, et al: Branchial anomalies in children. Int J Pediatr Otorhinolaryngol. 75(8):1020-3, 2011
5- Li W, Xu H, Zhao L, Li X: Branchial anomalies in children: A report of 105 surgical cases. Int J Pediatr Otorhinolaryngol. 104:14-18, 2018
6- Adams A, Mankad K, Offiah C, Childs L: Branchial cleft anomalies: a pictorial review of embryological development and spectrum of imaging findings. Insights Imaging. 7(1):69-76, 2016
7- Li Y, Lyu K, Wen Y, et al: Third or fourth branchial pouch sinus lesions: a case series and management algorithm. J Otolaryngol Head Neck Surg. 48(1):61, 2019

Electromagnetic Navigation Bronchoscopy

Electromagnetic navigation bronchoscopy (ENB) is a promising technology that increases the diagnostic accuracy of peripheral lung and mediastinal lesion, and is taken as a supplement to traditional bronchoscopy, endotracheal ultrasound, and endotracheal biopsy techniques into consideration. ENB has been designed as a localizing and guide endoscopic tool through the airway to a target lesion. The system consists of an electromagnetic tracking system that detects a position sensor incorporated within a flexible catheter which can be advanced through a bronchoscope. An electromagnetic field is generated by a localization system which consists of a processor, amplifier, and location board. When the sensor is placed within the electromagnetic field, its position and orientation can be identified. This information is superimposed on a previously acquired high-resolution CT data creating a 3-dimensional virtual bronchoscopic image. ENB-guided transbronchial needle aspiration or biopsy has shown high accuracy and lower complication rate, such as a pneumothorax or hemothorax, than the conventional percutaneous core needle biopsy. The rate of successful ENB-guided biopsy can reach 92%. Transbronchial ENB-guided lung biopsy is feasible and safe, provides larger samples and has a higher diagnostic yield than transbronchial lung biopsy only. The advantages of this method are no pain with localization procedure, complete control of ventilation, simplified workflow, high accuracy, and immediate transition to operation, which eliminates the consequences of complications. Small, deep or subsolid pulmonary nodules can be difficult to find during either thoracoscopy or even thoracotomy. Larger lung resections are performed when the nodule is hard to find or the need to convert to thoracotomy to do bimanual palpation. Criteria for using ENB preoperative localization include nodule diameter of 5 mm or less, ratio of maximum diameter of nodule to minimum distance between pleural space and inferior border of nodule of 0.5 mm or less, and for nodules with low density on CT. Small

pulmonary nodules can be identified using ENB-guided transbronchial dye-marking. Dye utilized include methylene blue, indigo carmine or Indocyanine green. Indigo carmine can be visible at least three days after marking. While fluorescein is dissipated after several hours of staining. This localization technique can help resect the pulmonary lesion during thoracoscopic exploration. An accurate localization is very important for these sublobar or non-anatomical resections. Nodules should be resected with negative resection margins. There are several potential benefits to applying ENB for the preoperative localization of pulmonary nodules prior to thoracoscopy. It can be safely and effectively implemented in the same OR, and VATS resection can be performed immediately following the localizing procedure. Long delay after staining results in difficult to locate nodule due to excessive diffusion and fading of methylene blue. No concern after immediate surgery for developing pneumothorax or hemothorax. The ENB localization success rate is around 79-100%. ENB has been recently utilized in pediatric oncology patients needing a lung biopsy or resection for nodule and found to be safe and efficacious. The technique is performed in the same operating room as the biopsy. It can be able to localize lesions as small as 2-3 mm identified on CT. ENB can be used for multiple biopsies as well as for bilateral biopsies. There are reports that ENB can interfere with cardiac monitoring.

References:

1- Abbas A, Kadakia S, Ambur V, Muro K, Kaiser L: Intraoperative electromagnetic navigational bronchoscopic localization of small, deep, or subsolid pulmonary nodules. J Thorac Cardiovasc Surg. 153(6):1581-1590, 2017

2- Cho HJ, Roknuggaman M, Han WS, Kang SK, Kang MW: Electromagnetic navigation bronchoscopy-Chungnam National University Hospital experience. J Thorac Dis. 10(Suppl 6):S717-S724, 2018

3- Qian K, Deng Y, Shen C, Feng YG, Deng B, Tan QY: Combination of electromagnetic navigation bronchoscopy-guided biopsy with a novel staining for peripheral pulmonary lesions. World J Surg Oncol. 17(1):158, 2019

4- Wang LL, He BF, Cui JH, et al: Electromagnetic navigational bronchoscopy-directed dye marking for locating pulmonary nodules. Postgrad Med J. 96(1141):674-679, 2020

5- Harris K, Schaefer E, Rosenblum J, Stewart FD, Arkovitz MS: Intraoperative electromagnetic navigation bronchoscopy (IENB) to localize peripheral lung lesions: A new technique in the pediatric oncology population. J Pediatr Surg. 57: 179-182, 2022

6- Song JW, Park IK, Bae SY, et al: Preoperative electromagnetic navigation bronchoscopy-guided one-stage multiple-dye localization for resection of subsolid nodules: A single-center pilot study. Thorac Cancer. 13(3):466-473, 2022

PUCAI

The Pediatric Ulcerative Colitis Activity Index (PUCAI) is a non-invasive objective measure of clinical outcome developed to standardize the reporting of ulcerative colitis disease activity in children. PUCAI is based on six quantifiable items obtained from the child history without need for an abdominal exam, blood testing or endoscopy results. The six items recollected within the activity index include the presence of abdominal pain, rectal bleeding amount, stool consistency, number of stools, whether there are nocturnal stools and the activity bedrest of the child. The highest score is 85, with 65 or above used as an assessment of severe disease. Moderate disease is between 35-64 and mild disease is between 10 and 34 points score. Less than 10 means the child is probably in remission.

Clinically significant response is defined by a PUCAI change of at least 20 points. PUCAI has been mostly used to characterized disease activity and effect of medical therapy. The high feasibility and validity of the PUCAI score in clinical practice provide strong support for the use of this instrument as a clinical tool serving as a basis for inpatient and outpatient care algorithms. PUCAI is not an objective measure of inflammation. PUCAI can be used with confidence as the sole outcome measure in pediatric UC without the need for endoscopy. Several colitis from UC is initially managed with systemic steroids. Effectiveness of steroid can be measured using PUCAI on day 3 and day 5 of treatment. Should the score be above 45, steroid-refractory disease should be considered, and second-line treatment should be started. Second-line medical management includes agents such as infliximab, tacrolimus, and cyclosporine. Infliximab is a monoclonal antibody to human TNF-alpha which has been shown to be effective in modulating intestinal inflammation in UC. Infliximab has a short-term response rate of 75%, and a long-term response rate of 64%. Infliximab has significantly reduced the colectomy rate in children with acute colitis. Tacrolimus is a macrolide immunosuppressant that inhibits calcineurin, which subsequently prevents the production of pro-inflammatory cytokines such as interleukin-2. Most restorative proctocolectomy children has received tacrolimus as a bridge to surgery and there is a significant improvement in the PUCAI score of patients receiving preoperative tacrolimus therapy. There is a strong correlation between the preoperative PUCAI score and the likehood than an ulcerative colitis patient needs a staged restorative proctocolectomy. Children with severe UC, bowel dilatation, uncontrolled pain, toxic appearance, significant anemia, or hypoalbuminemia should be hospitalized and started in systemic steroids. The mortality of acute severe UC is 1%, mainly from perforation, toxic megacolon, and infectious complications. Ominous signs in UC include severe abdominal pain or tenderness, vomiting, fever, significant weight loss and bowel dilatation. PUCAI scores in days 3 and 5 of corticosteroid therapy can predict patients failing therapy with steroid in need of salvage therapy with infliximab. PUCAI score does not significantly correlate with the likehood of developing surgical complications. Emergent colectomy is performed infrequently with medical therapy constituting first-line therapy in severe UC. If an infectious etiology is suspected (i.e., C Difficile) antibiotics should be used empirically. Oral feedings should be held if toxic megacolon is suspected. Persistency elevated PUCAI score in the face of steroid therapy is a call for second-line treatment. Therapeutic options include surgical intervention, infliximab and calcineurin inhibitors. Second-line medical therapy can induce a response in 70% of children. Surgical options can be elective or emergent. Children with UC more often undergo colectomy for medically refractory disease. Elective surgery is done in children unresponsive to medical management, in those with active, or steroid-dependent, UC despite optimized medical therapy or with evidence of dysplasia or malignancy on endoscopy. Restorative proctocolectomy with ileal pouch-anal anastomosis (J pouch) and a covering loop ileostomy is the recommended elective surgery for pediatric UC. Emergent surgery is indicated in children with colonic perforation, massive hemorrhage, toxic megacolon, or sepsis. Children with fulminant disease without adequate control and PUCAI > 65 despite intense medical therapy should be referred for surgery. In the emergent situation a subtotal colectomy, end-ileostomy and blind rectal pouch stump is recommended (Three-stage procedure). A minimally invasive laparoscopic approach is recommended in children as there are equivalent outcomes to open surgery both for urgent

and elective cases, and possibly superior outcomes regarding fertility in girls. Functional outcomes and surgical complications are comparable after hand-sewn and stapled anastomosis. Colectomy should be preferably performed 4-6 weeks after the last infliximab infusion if it can be safely postponed. Children that undergo emergent surgery have a higher incidence of postoperative complications compared with those undergoing elective colectomy.

References:

1- Turner D, Hyams J, Markowitz J, et al: Pediatric IBD Collaborative Research Group. Appraisal of the pediatric ulcerative colitis activity index (PUCAI). Inflamm Bowel Dis. 15(8):1218-23, 2009

2- Gray FL, Turner CG, Zurakowski D, et al: Predictive value of the Pediatric Ulcerative Colitis Activity Index in the surgical management of ulcerative colitis. J Pediatr Surg. 48(7):1540-5, 2013

3- Siow VS, Bhatt R, Mollen KP. Management of acute severe ulcerative colitis in children. Semin Pediatr Surg. 26(6):367-372, 2017

4- Turner D, Ruemmele FM, Orlanski-Meyer E, et al: Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care-An Evidence-based Guideline From European Crohn's and Colitis Organization and European Society of Paediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 67(2):257-291, 2018

5- Turner D, Ruemmele FM, Orlanski-Meyer E, et al: Management of Paediatric Ulcerative Colitis, Part2: Acute Severe Colitis- An Evidence-based Consensus Guideline From the European Crohn's and Colitis Organization and the Auropean Society of Paedeiatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 67(2); 291-310, 2018

6- Tan Tanny SP, Yoo M, Hutson JM, Langer JC, King SK. Current surgical practice in pediatric ulcerative colitis: A systematic review. J Pediatr Surg. 54(7):1324-1330, 2019

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