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REVIEW

Internal Hypopharyngeal Cyst: A Review of Literature

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Abstract
Detailed information on the hypopharyngeal cyst presentation, terminology, classification, diagnosis, management, and possible complication is scarce though it would lead to life-threatening symptoms. This review article, therefore, meticulously presents and analyzes the majority of the pertaining literature. In this context, a particular emphasis has been placed on the embryological development of the branchial arches while discussing each entity that would improve the current understanding of different pharyngeal cyst's pathologies.

Keywords Foregut-derived choristoma · Bronchogenic · Retention · Lymphoepithelial · Deglutition · Deglutition disorders

Introduction

Cysts of the pharynx and, particularly, of the hypopharynx are tremendously rare. The patient's complaints are directly related to the cyst's size and location, and they range from asymptomatic to life-threatening symptoms. Three different types of pharyngeal cysts had been documented according to their locations, namely nasopharyngeal, oropharyngeal, and hypopharyngeal. The first two types (nasopharyngeal, oropharyngeal) were frequently addressed and classified in the literature, but detailed information about hypopharyngeal cyst is rather limited. Thus, the aim of the current review is to meticulously present and analyze the majority of literature pertaining to different types of hypopharyngeal cysts, terminology, presentation, classification, diagnosis, management, and possible complications. Special concern has been devoted in this article to the embryological development of the branchial arches and the anatomical structures of the head and neck derive from each arch, a discussion that would lead to better understanding of different pharyngeal cyst's pathologies.

Embryological development of the pharynx

Hypopharynx is a striated muscular tube with a stratified squamous epithelium which has clear cell appearance due to the high glycogen content. At the pyriform fossa, lymphocytes located immediately beneath the epithelium occasionally form lymphoid follicles with rich lymphatic vessel plexus. The submucosa contains glands made up of both mucous and serous acini that open on the surface by occasional ducts [1].

In fact, the human pharynx development is complex. It arises embryologically from the branchial apparatus. The primitive pharynx tissue has five branchial arches lined externally by four ectodermal recesses, referred to as branchial clefts, and internally by five internal endodermal branchial pouches. The branchial arch is a core of mesenchyme derived from a combination of lateral plate mesoderm, somite, and neural crest cells [2, 3] (Figure 1). Each arch is associated with a cranial nerve, a muscle or a group of muscles, an artery, and a group of skeletal or cartilaginous derivatives. These clefts and pouches are

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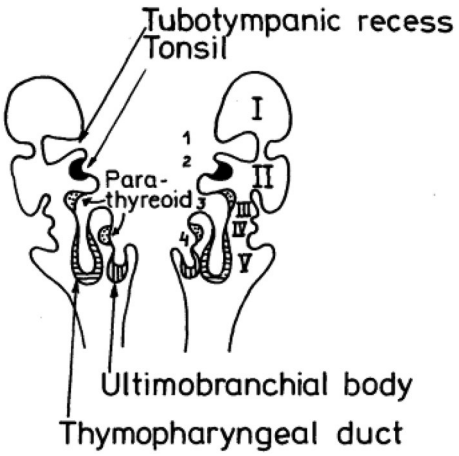

Fig. 1 Schematic view of the pharyngeal arches and pouches and their derivates. I–V denote the arches and 1–4 the endodermal pouches (Adapted from Langman J. Medical embryology. 3rd ed. Baltimore: Williams & Wilkins, 1975; 234-236.) [3]

gradually obliterated by invasion of mesenchyme to form a variety of essential structures (e.g., the ear drum, thymus and parathyroid glands) [4].

Except for the first cleft, the branchial clefts begin to obliterate after the fifth week of development. The first branchial cleft persists as an adult structure providing the epithelium of the external auditory canal and the other clefts, including the cervical sinus of His, are obliterated as the neck develops. However, abnormally persistence of branchial clefts may present as cysts, fistulas, and sinuses [5].

Each pharyngeal pouch gives rise to important head and neck structures. Derivatives of dorsal part of the first pharyngeal arch are pharyngotympanic tube and middle ear cavity. The second pharyngeal pouch gives rise to tonsillar fossa, palatine tonsils, stapes, lesser horn of the hyoid, adjacent muscles of facial expression, and floor of the mouth. The third pharyngeal pouch gives rise to the greater horn of the hyoid, thymus, and pyriform fossa. The thymic gland precursors migrate inferiorly and ventral to the thyroid to fuse in the midline, forming a bilobed structure [6]. The lumen of the thymus primordia derived from the third pouch is initially patent and usually closes after the fusion of the thymic tissues from either side and failure of the closure may result in the persistence of thymopharyngeal duct leading to a branchial sinus in communication with the pharynx [2]. The inferior parathyroid glands also develop from the third pharyngeal pouch; the superior parathyroid glands, paradoxically, arise more inferiorly from the fourth pharyngeal pouch and the rudimentary fifth pouch. The fourth pharyngeal pouch also contributes to the apex of the pyriform fossa, as well as laryngeal cartilages and muscles [6, 7].

Pharyngeal Cysts

This pictorial review presents different types of hypopharyngeal cysts based on an anatomical, clinical, pathological, and treatment. The types of hypopharyngeal cyst in question in this article are listed below:

- Hypopharyngeal retention cyst
- Hypopharyngeal Foregut-derived choristoma
- Hypopharyngeal bronchogenic cyst
- Hypopharyngeal lymphoepithelial cyst (LEC)
- Branchial cyst (Bailey's type IV)

Hypopharyngeal Retention Cyst

Retention cysts are the most common benign lesions in the pharynx. They often detected in the valleculae, less frequently in pyriform sinuses, post-cricoid, and aryepiglottic folds. Mucus retention cyst, mucocele, duct cyst, and oncocytic ductal cyst are synonyms to retention cysts. These cysts developed as dilatation and obstruction of the mucous gland duct in the lamina propria or deeper layers of the pharynx secondary to retained secretions and or chronic inflammation [8]. Histopathologically, the epithelium-lined cyst wall consists of a uniform layer of cuboidal, columnar, or non-keratinizing squamous epithelium. It is filled with serous or proteinaceous fluid, barely hemorrhagic features. Uncommonly, retention cysts neither ulcerated nor secondarily infected. Spontaneous resolution and malignant degeneration have never been reported [9].

Thirteen cases only reported in the previous literature as shown in Table 1. The number of cases may be more than the reported as endoscopy fails to reveal about 50% of cases since their submucosal origin and normal overlying mucosa. In addition, some cysts are not reported on otolaryngologic examinations because of the misconception of that these lesions are not clinically important.

These cysts are painless slow-growing circumscribed and often fluctuant swelling. Mostly, they discovered accidentally. However, cysts ≥ 1 cm may cause globus sensation, deglutition disorders, and respiratory symptoms as coughing, choking, or aspiration [10–21].

The cyst is well visualized by a double contrast pharyngograms and frontal views of the pharynx. It appears as a small, round or ovoid, well-circumscribed, smooth-contour submucosal masses etched in white [18]. CT and MRI are useful in distinguishing it from malignant tumors and determining its extent and location.

Treatment is size dependent; the large symptomatic pharyngeal retention cysts should be removed. Relatively smaller cyst can be excised by endopharyngeal

Table 1 Hypopharyngeal retention cyst reported cases

Author/reference	Sex/age	Symptoms	Endoscopic picture	Treatment
Dinolt [10]	F/52 years	Deglutition disorders	Pedunculated smooth cystic swelling arising from right pyriform	Endoscopic marsupialization
Borgström et al. [11]	NAD	GORD Symptoms	NAD	NAD
Junger and Wright [12]	F/29 years	Globus pharyngeus	Left aryepiglottic cyst	Endoscopic excision
Yasutaka et al. [13]	M/10 years	Snoring	Pedunculated yellow cyst from the right pyriform sinus extending to oropharynx	Endoscopic Marsupialization
Kawaida et al. [14]	M/59 years	Globus pharyngeus	A pale red hemispherical cyst 1 cm in diameter arising from antero-medial region in the right pyriform sinus	Endoscopic excision using a side-opened direct laryngoscope
	M/51 years	Globus pharyngeus	A pale red cyst arising from the antero-medial region in the left pyriform sinus	
Watanabe et al. [15]	M/54 years	Incidentally discovered	Cystic lesion in right pyriform sinus	NAD
Guo et al. [16]	M/77 years	Intermittent cough and deglutition disorders for solid	Smooth lobulated intraluminal mass arising from the posterior aspect of the left side of the hypopharyngeal wall	Transoral CO2 laser excision
Woodfield et al. [17]	F/47 years	Deglutition disorders	Whitish, smooth, translucent submucosal cyst	NAD
Takwoingi et al. [18]	NAD	Three cases with globus sensation	Cystic mass in the hypopharyngeal region.	NAD
Ozlugedik et al. [19]	M/75 years	Progressive difficulty in breathing, dysphonia, and deglutition disorders	Mass with regular mucosal surface in post-cricoid region obstructing laryngeal inlet	Endoscopic excision with radiofrequency
Choi et al. [20]	M/64 years	Globus sensation.	An ovoid smooth submucosal mass in the left pyriform sinus	Endoscopic surgical excision
Cadena et al. [21]	F/73 years	Progressive foreign body sensation	Pedunculated smooth cyst arising from the medial wall of pyriform sinus	Transoral robotic surgery (TORS)

NAD no available data

microsurgery through a direct laryngoscope using (CO2) laser, radiofrequency device, or electrosurgery using microdissection electrodes. Larger cyst, on the other hand, should be reduced in size by puncturing and draining before a complete removal or marsupialization. The recurrence after complete or partial excision is uncommon [10–21].

Hypopharyngeal Foregut-Derived Choristoma

Foregut-derived choristoma is a rare benign congenital and developmental anomaly while it is the commonest reported hypopharyngeal cyst in the literature. It represents the heterotrophic foregut derivatives with a histological mature normal tissue that is not indigenous to the present site or surrounding region [22, 23]. There is diverse terminology used for describing these lesions according to the epithelial lining (sometimes mixed with one predominant type), location and nature of the lesion which may be cystic or solid or mixed. The cystic form is referred to as choristomatic cyst, foregut duplication cyst, enterocystoma, gastrointestinal duplication cyst, heterotopic gastrointestinal cyst, heterotopic large bowel cyst, and alimentary tract cyst. The solid form is titled as gastrointestinal heterotopias, heterotopic, and ectopic gastrointestinal mucosa [24]. The exact mechanism remains unclear. There are diverse theories addressing the pathogenesis. One theory explanation was incomplete squamous epithelization from the stratified columnar epithelium during development forming a heterotopic rest of gastric mucosa that varies from microscopic foci to grossly visible lesions. Their origin is either heterotropic (congenital) or metaplastic (acquired like Barrett's esophagus) [25]. Nevertheless, this theory cannot explain cases with mixed foregut mucosa. Another postulated theory by Veeneklass [26] suggested that failure of separation between notochord and foregut and hence the adherent part of the esophagus

might separate and form a cyst or duplication. Qi et al. demonstrated the failure of foregut to detach from the notochord at the normal time in Adriamycin-injected rats that could contribute to cyst development [27]. Alternatively, theories include foregut tissue trapping during descent; dual-lumen formation due to errors in recanalization; a faulty fusion of different and incorrect portions of the alimentary tract on the "organizer" part; and primitive endothelial cell differentiation by various local inductive factors [28].

The direct consequence of these variations has resulted in diverse terminology, classification, embryogenesis, and failure to identify their correlation. Thus, some authors support unifying the used term to foregut malformations, since they are all sharing common foregut origin, which gives rise to the pharynx and its associated structures as well as the lower respiratory tract, esophagus, stomach, duodenum, and hepatobiliary tract [29]. According to the reported cases, gastric heterotopias are the commonest throughout the gastrointestinal tract [30]. Most of the cases located within the thorax and abdomen; fewer were in the head and neck. The commonest location in head and neck is oral cavity especially tongue (representing approximately 60% of oral cavity lesion and 0.3% of all foregut duplication cysts) followed by the floor of the mouth and less frequently the hypopharynx [22, 24].

Of the 20 hypopharyngeal foregut-derived choristoma cases, 9 were 9 adults and 11 pediatric cases with female predominance as shown in Table 2. Age ranges of adult cases were 16–70 years old, while pediatric cases were 0–5 years old [23, 25, 28, 31–43]. Most of the cases were solid (85%; 17/20) and cystic (15%; 3/20). Only 10% (2/20) cases were patchy lesion and 10 % (2/20) ulcerative lesion not exceeding few millimeters. Hypopharyngeal and esophageal lesions are mostly solid in contrast to intraoral which are cystic [28]. Clinical presentations vary depending upon the size and location of the lesion. Table 3 shows the differences between adult and pediatric patients. Pediatric patients are mainly symptomatic due to the smaller aerodigestive tract. They presented with life-threatening symptoms as stridor, cyanosis, respiratory distress, deglutition disorders, failure to thrive, and recurrent aspiration. However, adult patients showed incidentally or presented with mild symptoms, such as globus pharyngeus, and dysphonia. The differential diagnosis for hypopharyngeal submucosal masses include other congenital masses as teratoma and other choristoma, and other benign neoplasms such as lipoma, hemangioma, neurofibroma, chondroma, papilloma, hamartoma, granular cell tumor, oncocytoma and soft-tissue sarcoma. In adult group, malignancy should be excluded.

Endoscopy and biopsy are considered the gold standard for diagnosis. In spite variable endoscopic presentations, any erythematous or salmon well-demarcated velvety patches notable in the hypopharyngeal or esophageal mucosa in adult should increase the suspicious [44]. Complementary MRI and CT are invaluable for accurate assessment of the mass, defining the extent of the lesion and surgery planning. Moreover, prenatal imaging to detect such a fetal anomaly especially in the case of Polyhydramnios decreased swallowing "deglutition" and tongue protrusion. Early prenatal diagnosis may improve the outcome with a planned ex utero intrapartum treatment procedures [45].

All reported cases are gastric heterotopias and only three cases were mixed foregut lining. There are three histopathologic criteria to confirm the diagnosis: (1) the cyst is covered by a well-developed smooth muscle layer, (2) the epithelial lining derived from the foregut with patches of normal stratified squamous epithelium, and (3) an intimate attachment to a portion of the foregut [29]. Moreover, the cyst may be lined by one or more of gastric mucosa, ciliated respiratory, stratified squamous, simple cuboidal, pigmented ciliated epithelium, or even pancreatic acini and islets. Cysts may show squamous metaplasia, mucosal ulceration, inflammation, and necrosis making the cyst type distinction sometimes impossible.

The affirmed complications were airway obstruction, aspiration, pharyngeal scarring, and stenosis following excision. Malignant transformation has been reported to occur in long-standing foregut-derived choristoma of the head and neck. There are two cases reported of malignant transformation in adenocarcinoma and squamous metaplasia [46, 47]. Thus, routine surveillance for malignant transformation should be performed for any lesion with dysplasia [25].

Treatment varies according to age, symptoms, and location. For adult with small patchy lesion and acid-related symptoms, a trail for acid-suppressing medication to relief symptoms is suggested [31]. If medical treatment fails to relieve the symptoms, excisional biopsy, electrocautery, or CO2 laser ablation may be beneficial. However in pediatric, surgical excision is essential because of the high risk of airway compromise and feeding problem. Complete surgical excision is more recommended to avoid the delayed complications. Preservation of a functional hypopharyngeal anatomy through mucosal edge re-approximation and mucosal flap to cover the raw area is mandatory. The solid type has poorly defined margins that make complete excision more difficult than cystic. Staged excision or de-bulking for a big lesion is required to relieve the symptoms. Follow-up by endoscopy in the first-year post-operative to detect any residual or recurrence as described in 6 cases is recommended [28].

Hypopharyngeal Bronchogenic Cyst

Bronchogenic cysts are rare ventral foregut-derived congenital malformations. They originate from an abnormal budding of the primitive foregut and tracheobronchial tree

Table 2 Adult and pediatric hypopharyngeal Foregut-derived choristoma reported cases in the hypopharynx

Author/reference	Sex/age	Symptoms	Endoscopic picture	Histopathology	Treatment/recurrence
Adult					
Stout [42]	M/44 years	Incidentally discovered while pyriform sinus cancer excision	NAD	GH	Excision with pyriform sinus cancer surgery
Wolff and Rankow [43]	M/31 years	Incidentally discovered with hiatal hernia symptoms	Small mucosal polyp	GH	Excision No recurrence within 7 years follow-up
	M/70 years	Incidentally discovered with dysphonia due to left Vocal fold paralysis caused by lung cancer	Small fungating mass in left post-cricoid area	GH	Transoral excision
Frenkiel and Remsen [36]	F/16 years	Incidentally discovered during tonsillectomy	Submucosa tubular mass arising from right posterior pharyngeal wall curled up in pyriform sinus	GH	Transoral excision
Lancaster et al. [39]	F/51 years	Globus pharyngeus	1×1 cm erythematous mucosal area in posterior cricoid extending into cervical esophagus	GH	PPI with no change in endoscopic picture after 3 months
Chang et al. [32]	F/32 years	Globus pharyngeus	Pedunculated mass attached to the left posterior oropharyngeal wall and its inferior portion filled the left pyriform sinus	GH with intestinal metaplasia	Transoral excision
Alaani et al. [31]	F/53 years	Globus pharyngeus and GORD symptoms	Post-cricoid ulcer and Hiatus hernia	GH	PPI No improvement of the globus symptoms
	F/50 years		Raised mucosa in post-cricoid area		
	F/58 years		Post-cricoid ulcer		NAD
Pediatric					
Picard et al. [40]	F/13 days	Stridor	Mass in the glosso-epiglottic fold	GH	Tracheotomy Transoral surgical excision. One month later re-excision
Hüttenbrink and Stoll [37]	F/New born	Recurrent respiratory distress and deglutition disorders	A grape like tumor in the oral cavity affixed like a pendulum in the hypopharynx	GH	Transoral surgical excision
Johnston et al. [23]	M/4 months	Airway obstruction, chocking and FTT	2-cm pale polypoid mass at the right posterior hypopharyngeal wall	GH	Transoral CO2 laser excision. 1 month later CO2 laser ablation for residue small nodule
	F/2 months	Stridor since birth and FTT	Mass arising from right posterior hypopharyngeal wall	GH	Transoral CO2 laser excision. 1 month later, removal of residual granulation tissue
Hsu et al. [25]	F/8 weeks	Aspiration, emesis, and FTT	Mass arising from the right postero-lateral hypopharyngeal wall	GH	Transoral CO2 laser excision. 1 year later, excision of small residual lesion. Scar band vaporized by CO 2 laser with edges approximation

Table 2 (continued)

Author/reference	Sex/age	Symptoms	Endoscopic picture	Histopathology	Treatment/recurrence
Edwards et al. [34]	F/2 days	Stridor and cyanosis	Mass arising from posterior hypopharynx	GH, respiratory epithelium, and pancreatic tissue	Transoral surgical excision with mucosal edges approximation. One month later, excision of residual mass
Daher et al. [33]	F/8 months	Stridor, deglutition disorders, and regurgitation	3×2-cm mucosal fold originating from the posterior pharyngeal wall	GH	Tracheostomy and gastrostomy feeding tube. Transoral surgical excision
Fraser et al. [35]	F/28 days	Respiratory distress	Cystic swelling involving the lateral wall of the pharynx and tongue	GH, small intestinal mucosa, and pancreatic tissue	Surgical excision
Roy et al. [41]	M/5 years	Stridor, weak voice, deglutition disorders, and FTT	First view, the lesion was cystic swelling arising from the posterior pharyngeal wall. At age of 5 year, a lobulated mass arising from the posterior pharyngeal wall obscuring the larynx	GH	Endoscopic radiofrequency marsupialization. At age of 5 year, transoral excision with mucosal flaps approximation
Van Abel et al. [28]	F/7 weeks	Progressive deglutition disorders, FTT, and intermittent stridor	Broad-based lesion attached to midline of the posterior pharyngeal wall obstructing glottis and esophageal inlet	GH	Transoral CO2 laser excision
Steineger and Brondbo [38]	F/5 days	Respiratory distress with inspiratory stridor	Cystic swelling arising from the anterior and lateral walls of the left pyriform sinus	GH	Endoscopic CO2 laser marsupialization. No complication with 14 months follow-up

GH gastric heterotropia, *FTT* failure to thrive, *PPI* proton pump inhibitors, *NAD* no available data

Table 3 Comparisons between adult and pediatric Hypopharyngeal Foregut-derived choristoma are shown

Pediatric type Foregut duplication cyst	Adult type
Airway obstruction commonest symptoms	Incidentally discovered or globus pharyngeus are commonest presentation
Congenital etiology is more suspected	Reflux was suspected as etiology
Bigger size	Size smaller and sometimes small patch or ulcer
Scar formation common after excision so careful mucosal edge approximation are needed	Risk of cancer so careful follow-up is essential.

which develop at day 24–36 of gestation as an initial median bulge on the ventral wall of the pharynx [48]. They can be located anywhere along the developmental pathway of the foregut. Frequently, they are detected in the mediastinum or intrapulmonary area and rarely in the cervical area. Cervical bronchogenic cysts are mainly recorded in the suprasternal region [49]. 75 % of published cases were in the midline particularly the upper third and 25% of cases detected in the lateral cervical region mostly in the lower third. Generally, bronchogenic cysts are classified according to the site into paratracheal, carinal, hilar, para-esophageal, and atypical (diaphragmatic, abdominal, subcutaneous tissues, neck area, hypopharyngeal, etc.) [50].

Cervical bronchogenic cysts are mainly symptomatic that vary according to the site, size, and occurrence of infection. They were discovered mainly in the pediatric age group representing < 1% of all pediatric neck cysts. On the other hand, fewer cases were reported in adults predominantly in paratracheal region and a very few cases were reported in lingual, oropharynx, hypopharynx, retropharyngeal, and larynx [51]. Cervical bronchogenic cysts are commonly presented by swelling, stridor, dyspnea, and deglutition disorders [52], and this should be accounted for in situation where pediatric patients undergoing endoscopic evaluation for airway compromise.

There are only five reported cases in hypopharynx (Table 4). Endoscopic examination of these cases showed smooth cystic mass either attached to the posterior pharyngeal wall or pyriform with laryngeal encroachment or smooth submucosal bulge on the posterior pharyngeal wall [53–56]. CT and MRI are mandatory for better pre-operative planning to reveal the extent and the relationship between the cyst and the adjacent structures. However, it is essential to exclude other anomalies that may co-exist as bronchopulmonary atresia and intralobar pulmonary sequestration [57]. None of such anomalies are documented in the reported hypopharyngeal cases. McAdams et al. declared a CT diagnosis guideline as thin, smooth, and well-defined cyst with homogenous areas of high attenuation that are not enhanced with contrast. On the other hand, MRI

Table 4 Reported cases of bronchogenic cyst in the hypopharynx

Author/reference	Sex/age	Symptoms	Endoscopic picture	Treatment/recurrence
Canty and Hendren [53]	F/new born	Severe respiratory distress	Cystic swelling arising from the right posterior hypopharyngeal wall	Tracheostomy Endoscopic marsupialization. Tracheostomy closed 26 days post-operation.
	M/10 days	Respiratory distress	Cystic mass arising from left pyriform sinus covering glottic inlet	Endoscopic marsupialization. Recurrence 5 and 6 months later and another endoscopic marsupialization
Sedwick and Giannoni [54]	F/new born	Severe respiratory distress after birth	Right-sided hypopharyngeal mass pushing the epiglottis posteriorly, poor right Vocal fold mobility, and laryngomalacia.	Transcervical Surgical excision
Jacob et al. [55]	M/38 years	Globus pharyngeus	Submucosal bulge on right posterior pharyngeal wall extending from soft palate to level of the epiglottis	Transoral surgical excision
Kim and Park [56]	M/new born	Stridor	Cystic swelling arising from posterior aspect of the right arytenoid contagious to right pyriform sinus	Endoscopic marsupialization. Recurrence 5 months later and endoscopic excision

demonstrates enhancement on T2-weighted images due to mucinous and proteinaceous debris [58].

Histopathological confirmation is essential for the diagnosis as there are no specific clinical or radiological criteria for differentiation from other cysts. Characteristically, histopathological findings of bronchial elements are the definitive diagnosis. Bronchogenic cysts are lined by ciliated cuboidal or pseudostratified columnar ciliated respiratory epithelium. One or more bronchial fibroelastic tissues (hyaline cartilage, smooth muscle, and seromucinous glands) can be detected and often filled with mucoid material. The mucosal lining may show chronic inflammatory infiltrates, necrosis, ulceration, and focal areas of squamous metaplasia making the classic features hard to be identified. The presence of cartilage plate in the wall of the cyst promotes the diagnosis of bronchogenic cysts and differentiates it from the branchial cyst (Bailey's type IV). However, the absence of cartilage plates does not exclude bronchogenic cyst diagnosis especially in the presence of other criteria [59, 60].

Malignant transformations have been reported in adults and once in an eight-year-old girl. Hence, histopathological study of the cyst wall is pivotal to confirm the diagnosis and to rule out malignancy transformations [61, 62]. Generally, a complete surgical excision is the treatment of choice since recurrence has been reported after incomplete resection [63].

Hypopharyngeal Lymphoepithelial Cyst (LEC)

Lymphoepithelial cysts (LEC) are rare, benign, slowly growing uniloculated, or multiloculated lesion. Virtually, they occur in any organ as submandibular gland [64], thymus [65], pancreas [66], lung [67], thyroid gland [68], parotid gland and oral cavity (intraoral LEC) [69, 70], esophagus [71], hypopharynx [72, 73], and larynx [74]. They are most frequently reported in the neck (benign cervical lymphoepithelial cyst (BCLC)).

King, was the first who adopted the "lymphoepithelial cyst" term stemmed from the histological characteristic of the lateral neck branchial cyst [75]. Histopathologically, these cysts were lined by stratified squamous epithelium with desquamated keratin in the lumen, a variable amount of complete (with germinal centers) or incomplete surrounding lymphoid tissue, resembling a lymph node and fibrous connective tissue capsule [70].

It is worth to mention that the controversy over the etiology and used terms makes the studying of these lesions more difficult [76]. Some authors stated that lymphoepithelial cysts are the same as branchial cysts, branchial cleft cyst, branchiogenic cyst, or pseudocyst. They proposed that lymphoepithelial cysts arise from the cystic degeneration of epithelium close to lymph nodes or tonsilar tissue, and for this reason the cyst is surrounded by lymphoid tissues [76–79]. Otherwise, Burkhardt judged the term 'lymphoepithelial cyst' to be unspecific due to the multiplicity of entities that might give rise to this lesion. Moreover, other authors favor cystic cervical lymph node or salivary gland inclusion theory [77]. Consequently, alternative terms were suggested such as benign cystic lymphoid aggregates. However, it is not widely used and the authors still preferring usage of LEC or branchial cleft cyst [76, 80].

According to the most accepted etiological hypothesis, the etiology of these cysts could be varying according to the organ location (branchial arch and non-branchial arch organs). Thus, lymphoepithelial cyst may occur where it is hard to explain the presence of a lymphoepithelial cyst, e.g., esophagus. Since the esophageal gland is similar to the parotid gland, obstruction and cystic dilatation of an esophageal gland may lead to lymphocytic infiltration of the ductal epithelium [72].

Only six cases have been detected in the previous literature in the pyriform fossa (five cases in left pyriform and one case in right pyriform). Five patients were complaining from throat discomfort (3 males and two females, age between 50 and 81 years old). One infant boy of 11 months old presented with stridor [72–74, 81]. The etiopathology of these cases could be explained by entrapment theory, i.e., cystic degeneration of the ectopic entrapped epithelium within nodal aggregates since pyriform fossa epithelium is rich in lymphocytes that occasionally form lymphoid follicles [76–79]. Liao et al. suggested the mucosal injury, especially after an endotracheal intubation, to correlate with the occurrence of hypopharyngeal lymphoepithelial cysts [81].

Endoscopic examination shows a small painless well-circumscribed yellow or white submucosal nodule or cystic lesion covered by normal overlying mucosa. Occasional cysts are transparent. Surgical excision by endopharyngeal microsurgery was limited to symptomatic cyst or malignancy exclusion. Unfortunately, LEC may be associated with HIV as a part of diffuse infiltrative lymphocytosis syndrome. About 3–10% of HIV-positive patients developed HIV-associated salivary gland disease. Salivary gland diseases usually develop before AIDS and sometimes it is the first manifestation of HIV infection. It is usually bilateral and accompanied by cervical lymphadenopathy [64]. However, hypopharyngeal lymphoepithelial cysts are extremely rare; we should keep it in mind as one of the differential diagnoses of the submucosal hypopharyngeal cyst.

Branchial Cyst (Bailey's Type IV)

Pharyngeal Branchial cysts are extremely uncommon. The second branchial cyst (Bailey's type IV) was reported in nasopharyngeal [82], oropharyngeal [83, 84], parapharyngeal [85], and retropharyngeal [86]. Moreover, branchial cyst (Bailey's type IV) was reported once in hypopharyngeal [87]. Branchial cyst is a subepithelial cyst

without sinus tract. It is derived mainly from the remaining branchial plate without mesodermic arch interposition or from the plate breaking down to ectodermic–endodermic apposition without a fistula that could explain the absence of sinus [84].

Patient compliant varies according to the lesion size and location. The diagnosis is mainly based on the anatomic location and histopathological features. CT scan demonstrates a well-circumscribed cystic lesion, and MRI shows a hyposignal cyst on T1 and hypersignal on T2, with enhancement of the wall after injection of contrast material if it is an infected cyst [82, 84].

Histopathologically, the lining epithelium of the branchial cyst is derived from branchial cleft ectoderm or branchial arch/pouch endoderm (pseudostratified columnar epithelium) or both epithelial types as in case of a long-standing cyst and lacks mesodermal component in its wall. This lining is resting on a complete or incomplete band of lymphoid tissue with part of the cyst wall. The cystic contents may be clear, mucinous, or seromucinous fluid [88]. Treatment includes either endoscopic marsupialization or laser surgical excision.

Conclusion

Although the existing literature on hypopharyngeal cysts is rather limited, available data on congenital (Foregut-derived choristoma, bronchogenic, and branchial) and acquired (retention and lymphoepithelial) hypopharyngeal cysts were addressed and classified in this review article. Based on the detailed presentation of the hypopharyngeal cysts in the current study, the following conclusions can be withdrawn:

1. Signs and symptoms that characterize the hypopharyngeal cysts are non-specific.
2. Compared to adult patients, the pediatric patients are usually presented with life-threatening symptoms and quite large cysts.
3. The diagnosis is based on clinical findings, radiological examination, and histopathological findings which is essential for establishing the final diagnosis.
4. Surgical excision is the main treatment of the hypopharyngeal cysts. However, surgery is challenging to excise the lesion and avoid later scarring and stenosis.
5. Malignancy exclusion is a mainstay in adult.

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