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REVIEW ARTICLE

Naso-oropharyngeal choristoma (hairy polyps): an overview and current update on presentation, management, origin and related controversies

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Abstract This review presents a comprehensive and updated overview of bigerminal choristomas (hairy polyps) of naso-oropharynx/oral cavity, and discusses the controversies related to nosology and origin from a clinico-embryologic perspective. English-language texts of the last 25 years (January 1989–January 2014) were collected from the PubMed/MEDLINE database using the given keywords. Of the 330 records, 64 full-text articles (mostly case reports/series) were selected, incorporating clinical data from 78 patients, after screening through duplicates and the given exclusion criteria. With the available evidence, hairy polyps appear more common than generally believed, and are increasingly being recognized as an important, often-missed cause of respiratory distress and feeding difficulty in neonates and infants. Such a child without any apparent cause should be examined with flexible nasopharyngoscope to specifically look for hairy polyps which might be life-threatening, especially when small. The female preponderance as believed today has been found to be an overestimation in this review. These lesions are characteristically composed of mature ectodermal and mesodermal tissue derivatives presenting as heterotopic masses, hence termed choristoma. However, little is known about their origin, and whether they are developmental malformations or primitive teratomas is debatable. Involvement of Eustachian tube and tonsils as predominant subsites and the speculated molecular embryogenesis link hairy polyps to the development of the first and second pharyngeal arches. They are exceptionally rare in adults, but form a distinct entity in this age-group and could be explained as delayed pluripotent cell morphogenesis or focal neoplastic malformations, keeping with the present-day understandings of the expanded "teratoma family".

Keywords Choristoma · Dermoid · Hairy polyp · Congenital · Nasopharynx · Oropharynx · Oral cavity · Eustachian tube · Adult · Embryogenesis

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Introduction

Mature bigerminal lesions, the so-called hairy polyps, have continued to generate interest as well as controversy among the clinicians and developmental biologists till date. Such lesions, a choristoma according to one school of authors, have been most commonly reported in the naso-oropharynx within the head-neck region. "Choristoma" by definition is the aggregation of mature polygerminal tissue at anatomic areas where they are not destined to be. The term is often discussed in conjunction with "hamartoma" where such tissue is present in its mother organ system. Choristomas are ubiquitous in the body, yet are poorly understood and seldom explored. A classic example in the otolaryngologic purview is the hairy polyp which presents at birth or early infancy as pedunculated polypoid mass mostly from the

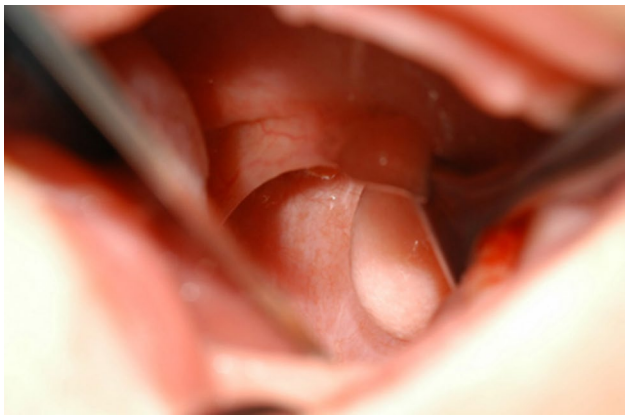

Fig. 1 Hairy polyp in the nasopharynx: a fleshy mass could be seen hanging from the nasopharyngeal surface of soft palate in this 2.5-year-old child (reproduced with permission from Elsevier, reference 43)

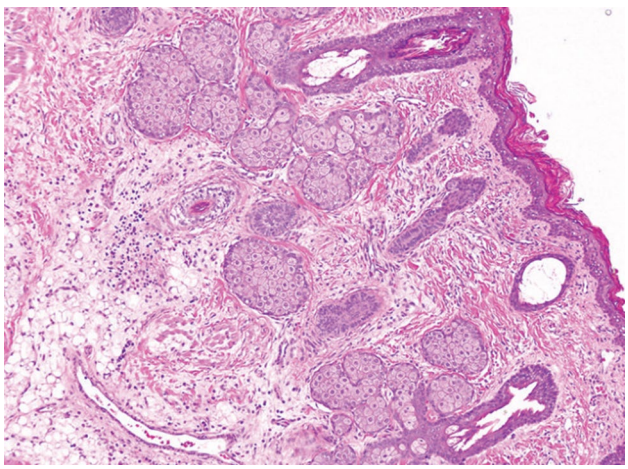

Fig. 2 A classic example of histopathology of a hairy polyp showing mature tissue elements of both ectodermal and mesodermal origin, including stratified squamous epithelium, skin adnexa (hair follicle, sebaceous glands), fibro-adipose tissue and muscle fibers [hematoxylin and eosin, ×100] (reproduced from reference 59; Hindawi Publishing Corporation; Open access)

naso-oropharynx (Fig. 1), and histologically composed of derivatives of ectoderm (epithelium, hair follicles, sebaceous and sweat glands) and mesoderm (fibro-adipose tissue, cartilage and muscle fibers) (Fig. 2). However, current literature is not unanimous on the question whether they in essence are part of the spectrum of well-described congenital defects like developmental aberrations or teratomas, or belong to the family of neoplastic disorders. Their occurrence in adults, though extremely rare, has further complicated the issue. Clinically, they present with obstructive features owing to mass effect, but may remain hidden or undiagnosed resulting in more sinister consequences that warrant a high index of suspicion from the attending clinicians. Through this review of bigerminal choristomatous lesions in the naso-oropharynx, we have attempted to present a comprehensive clinical overview and also dealt with the controversies in nosology with discussions on the plausible theories of origin from a clinico-embryologic perspective.

Methodology

Data from English-language texts (including "online first"/ahead of print) of the last 25 years (January 1989–January 2014) were collected from the PubMed/MEDLINE database using the given keywords. Only the cases of bigerminal (ectodermal and mesodermal) choristomas resembling the classic description of "hairy polyp/dermoid" [Arnold's classification [1] (Table 1)] were considered. Figure 3 provides a detailed overview on how the selection and screening were done. The keywords "hairy polyp", "dermoid" and "choristoma" were paired up with the rest, and the results recorded in each case forming a collective list. Initial search revealed 307 records which were reviewed independently by two authors. During the process, it was noticed that the Eustachian tube formed a predominant area of involvement in the nasopharynx. As the nasopharynx is anatomically and embryologically linked with the

Table 1 The Arnold's classification of the complex germ-layer lesions of the nasopharynx

	Types	Germ layer composition	Characteristics
1.	Dermoids (e. g., hairy polyps)	Bigerminal (ectoderm + mesoderm)	Skin (mucosa)-covered with epidermal appendages, with the matrix formed of predominantly fatty tissue.
2.	Teratoids	Trigerminal (ectoderm + mesoderm + endoderm)	Poorly differentiated, immature tissue derivatives.
3.	Teratomas		More differentiated, mature tissue derivatives with histologically recognizable true organoid structures.
4.	Epignathi		Tissue maturity with highly differentiated organoid presentation in gross; parasitic fetuses (fetus-in-fetu) with the same axial orientation of the host; usually incompatible with life

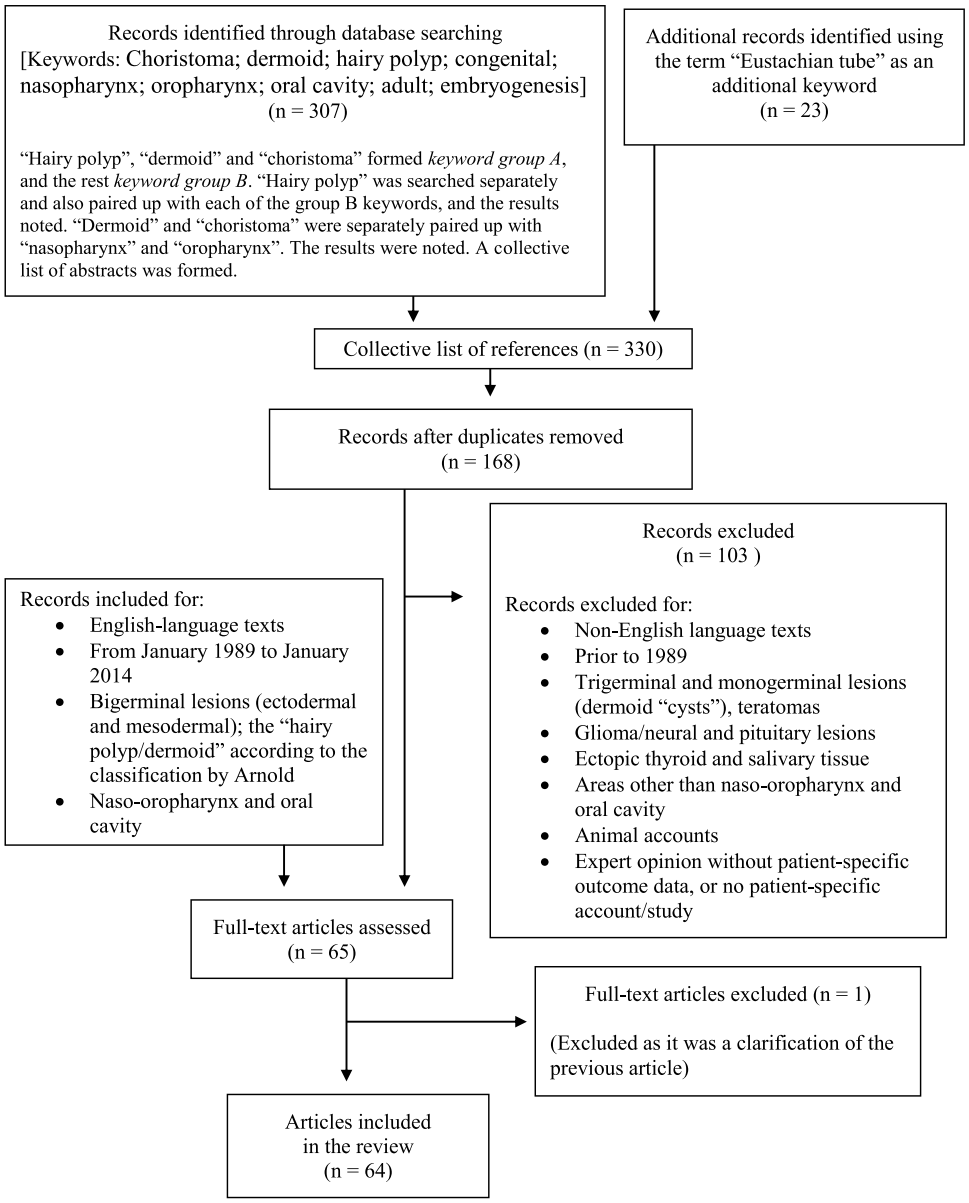

Fig. 3 Flow diagram for selection of articles in the present review

Eustachian tube and middle ear system, cases where such lesions originated within the Eustachian tube with variable extensions were also included. The search was therefore refined using "Eustachian tube" as another keyword, and 23 more citations were retrieved. Of these 330 records, 168 were selected when the duplicates from the collective list were removed. Applying the exclusion criteria (Fig. 3), 65 articles were considered for evaluation of the full text, of which one was later excluded. Bibliography of the articles reviewed was further cross-checked so that no subject was missed within the time-period under consideration. Almost all articles were case reports/series; the 4 reviews obtained were designed primarily as extensive literature search, but no well-structured systematic reviews or meta-analyses were found. Overall, 60 case reports/series and 4 review articles, with a total of 78 patients, were considered for inclusion in the present analysis (Table 2). Information from the systematic review by Muzzi et al. [2] dealing with the nosology of "tumor and tumor-like" lesions of the Eustachian tube was used in "Discussion" section of the present review, but there was no scope of its inclusion in the clinical analysis. The results were tabulated and analyzed for distribution among age-groups, sex, anatomic subsites involved, laterality and symptoms, aiming to establish a comprehensive clinical overview. Recent trends in management were also noted. Clinically relevant theoretical and molecular embryology deducible from the outcomes of the present clinical analysis along with the classification system have been discussed at appropriate places with special emphasis on adults, obtaining information from the articles

Table 2 Bigerminal choristomas of the naso-oropharynx and oral cavity reported in the last 25 years (from January 1989 to January 2014) in English-language indexed literature

No.	Year	Citation	Location/origin	Presenting age	Sex	Presentation
1.	2013	Lignitz et al. [58]	Left lateral pharyngeal wall	1 d	M	Intermittent respiratory distress, cyanosis
2.	2013	Koike et al. [24]	Posterior nasopharyngeal wall, midline	3 m	F	Intermittent respiratory difficulty, difficulty in swallowing, snoring, leading to hematemesis, cardiopulmonary arrest and hypoxic encephalopathy
3.	2013	Christianson et al. [59]	Right palatopharyngeus muscle in the superior pole of tonsil	1 d	F	Respiratory distress
4.	2013	Tariq et al. (4 cases) [13]	Two in nasopharynx, 1 in hard and soft palate, 1 in lower lip	1 m (two); 17 y, 18 y	3 M, 1 F	–
5.	2013	Seng et al. [48]	Left posterior tonsillar pillar	4 m	F	Breathing and feeding difficulties
6.	2013	Nalavenkata et al. [29]	Left PT tube, lateral nasopharyngeal wall, middle ear	2 y	F	Recurrent chronic otitis media, white mass in middle ear and in the nasopharynx
7.	2012	Vaughan et al. [32]	Left soft palate	2 d	M	Left palate mass
8.	2012	Desai et al. [33]	Hard palate, mostly in the left	6.5 m	F	Oral mass
9.	2012	Cone et al. (5 cases) [16]	Pharynx	1 d	F	Respiratory distress, cyanosis
			Nasopharynx	10 m		Gastroesophageal reflux, OSA
			Soft palate	3 m		Breathing and feeding difficulties, gagging, choking
			Nasopharynx	3 w		Upper airway compromise
			Nasopharynx	3 w		Breathing difficulty, apnea
10.	2012	Puricelli et al. [60]	Dorsum of tongue (midline), moving towards the oropharynx	3 m	F	Breathing and swallowing difficulty, vomiting, cough
11.	2011	Yilmaz et al. (2 cases) [43]	Nasopharyngeal surface of soft palate, left-side	7 d	F	Respiratory distress
			Right soft palatal wall	2.5 m	F	Intermittent respiratory obstruction
12.	2011	Zakaria et al. [61]	Nasopharynx	2 y	M	Middle ear effusion, OSA
13.	2011	Kraft et al. [40]	Left lateral wall of nasopharynx (region of the PT tube)	1 d	F	Oral mass
14.	2011	Wang et al. [62]	Left lateral wall of nasopharynx (PT tube)	1 y	M	Purulent discharge from ear
15.	2010	Russo et al. [63]	Left lateral wall of nasopharynx	3.5 y	F	Fever, cough, respiratory distress, dysphagia
16.	2010	Saliba et al. [64]	Tonsil	1 d	F	Respiratory distress
17.	2010	Fawziyah, Linder [65]	Oropharynx	2 m	F	Respiratory distress, feeding difficulty
18.	2010	Kalcioglu et al. [22]	Superior aspect of soft palate	6 m	F	Respiratory distress, feeding difficulty
19.	2009	Karabekmez et al. [52]	Left soft palate (N); incomplete cleft palate (at 9 m)	N	F	Airway obstruction
20.	2009	Agrawal et al. [28]	Eustachian tube orifice left	1 m	M	Poor feeding, respiratory distress
21.	2009	Planas et al. [14]	Oropharynx	Fetus (20 w)	F	Termination of high-risk pregnancy
22.	2008	Chang et al. [27]	Left lateral nasopharyngeal wall, and middle ear (recurrence)	6 y	F	Respiratory distress, hearing loss
23.	2008	Walker [66]	Eustachian tube Left	6 m	F	Respiratory distress

Table 2 continued

No.	Year	Citation	Location/origin	Presenting age	Sex	Presentation
24.	2008	Gambino et al. (2 cases) [67]	Left lateral oropharyngeal wall	50 d	F	Respiratory distress
			Left palatine fossa	19 d	F	Respiratory distress
25.	2008	Jang SH et al. [68]	Hard palate	1 y	M	–
26.	2007	Hemant et al. [69]	Left posterior tonsillar pillar	45 d	F	Feeding difficulty, respiratory distress
27.	2007	Shvidler et al. [70]	Superior portion of palatopharyngeus	5 w	M	Respiratory distress
28.	2007	Yossuck et al. [71]	Left pharyngeal wall	1 d	F	Feeding difficulty
29.	2006	Green, Pearl [9]	Left lateral nasopharyngeal wall	24 y	F	Earache, hearing loss, feeding difficulty, respiratory distress
30.	2006	Delides et al. [44]	Multifocal (left torus tubarius, cervical, subcutaneous)	1 y	F	Left cervical inflammatory mass, OSA
31.	2005	Budenz et al. [8]	Pharynx	1 d	F	Respiratory distress, feeding difficulty
32.	2005	Baek et al. [72]	Left PT tube, left middle ear	2 y	F	–
33.	2004	Roh [29]	Left PT tube orifice	7 m	F	Feeding difficulty, sleep apnea, snoring, blood-tinged vomiting
34.	2004	Kiroglu et al. [73]	Hard palate	1 d	F	Feeding difficulty
35.	2004	Erdogan et al. [42]	Tongue	40 d	F	Oral mass
36.	2003	Simoni et al. [56]	Left tonsillar fossa, middle ear	1 d	F	Hematemesis, hearing loss
37.	2003	Karagama et al. [74]	Right anterior tonsillar pillar	1 d	F	Respiratory distress
38.	2002	Jarvis, Bull (2 cases) [55]	Lateral nasopharyngeal wall	1 d	F	Respiratory difficulty, feeding difficulty
			Left lateral nasopharyngeal wall	1 d	F	Respiratory distress
39.	2002	De Caluwé et al. [75]	Oropharynx	11 w	F	Respiratory distress
40.	2001	Burns et al. [5]	Left tonsil	5 d	F	Feeding difficulty
41.	2000	Phansalkar et al. [76]	Left nasopharyngeal wall	12 y	F	Respiratory distress
42.	2000	Downs et al. [77]	Left lateral aspect of soft palate (superior/nasopharyngeal surface)	3 m	F	Intermittent noisy respiration
43.	1999	Gourin, Sofferman [37]	Left PT tube, left middle ear	21 m	M	–
44.	1999	Ruah et al. [78]	Right PT tube, right middle and external ear	10 w	F	Mass lesion
45.	1998	Chakravarti et al. [79]	Lateral nasopharyngeal wall	43 d	F	Feeding difficulty, respiratory distress
46.	1998	Cerezal L et al. [11]	Left lateral nasopharyngeal wall	50 y	M	Recurrent epistaxis
47.	1998	Kieff et al. [80]	Left middle ear and mastoid cavity	11 m	F	Recurrent purulent ear discharge
48.	1996	Kelly et al. [4]	Superior pole of left tonsil	1 d	F	Oral mass
49.	1996	Heffner et al. [46]	Right external auditory canal and middle ear	16 m	F	Recurrent otitis media, ear discharge
50.	1996	Franco et al. [12]	Between the palatine arches (bilateral)	58 y	F	Feeding difficulty, respiratory distress
51.	1996	Mitchell et al. [47]	Tonsil	3 w	F	Oral mass
52.	1996	Walsh et al. [81]	Superior pole of the left tonsil	1 d	F	Respiratory distress
53.	1995	Oliveres-Pakzad et al. [82]	Hard palate	1 d	M	Respiratory distress
54.	1995	Kollias et al. (2 cases) [41]	Left PT tube, left middle ear and parapharyngeal space	1 y	F	Recurrent episodes of otitis media
				15 m	F	

Table 2 continued

No.	Year	Citation	Location/origin	Presenting age	Sex	Presentation
55.	1992	Boedts et al. [83]	Left PT tube, left middle ear and mastoid	18 m	F	–
56.	1992	Vrabec, Schwaber [84]	Left PT tube, left middle ear and mastoid	14 m	F	–
57.	1991	NicklausJ et al. [30]	Right PT tube	3 w	M	Respiratory obstruction, poor feeding, snoring
58.	1990	Haddad et al. (2 cases) [6]	Nasopharynx	–	–	–
59.	1990	Kochanski et al. [39]	Nasopharynx	N	–	Respiratory distress, vomiting
60.	1990	Sexton [35]	Soft palate (uvula)	19 d	M	Intermittent respiratory difficulty (ball-valve effect)
61.	1990	Aughton et al. [85]	Hard palate, left side	1 d (30 w gestation)[a]	F	–
62.	1990	Kainz et al. [86]	Soft palate left side	3 m	F	Snoring
63.	1990	Van Haesendonck et al. [25]	Upper pole of left tonsil	3 d	M	Severe respiratory distress resulting in cerebral hypoxia
64.	1989	McShane et al.(3 cases) [87]	Nasopharynx (2), oropharynx (1)	– (one of them a neonate)	–	–

Serial numbers of the male patients have been made bold and italicized, while those of the adult cases underlined

PT tube pharyngotympanic tube, *OSA* obstructive sleep apnea, *y* year, *m* month, *w* week, *d* day, *N* neonate, *F* female, *M* male

[a] This neonate had multiple congenital anomalies and died at 2 h after birth

Female:male = 56:16 = 3.5 (data not available in 6 cases)

reviewed, and also from related textbooks chapters on embryology and other recent journal citations.

Discussion

The Arnold's classification and choristoma

The complex germ-layer lesions of the naso-oropharynx—the so-called "dysontogenetic nasopharyngeal tumors"—have been traditionally classified by Arnold in 1870 into dermoid, teratoid, teratoma and epignathi [1] (Table 1). The concept is still in vogue; however, their categorical distinction by histogenesis, tissue composition and order of cellular maturity remains controversial. The primitive pharyngeal gut develops primarily from pharyngeal arches with orderly incorporation of migrating neural crest cells from rhombomeres in the hindbrain to the intrinsic arch mesenchyme [3]. In utero alterations in the process occasionally result in persistence of histologically normal heterotopic cell-rests of one or more germ-line lineage as raised non-neoplastic masses. These lesions, erroneously separated from the mother/target tissue, have led researchers refer them as choristoma (choristo = separated). Arnold's classification was based on germ-layer composition and their maturity; these lesions when encountered in aberrant anatomic sites have often been addressed as choristoma as an alternative.

Hairy polyp as choristoma—incidence and origin in children and adults

Hairy polyps, the commonest congenital tumor of the naso-oropharynx [4, 5], was first reported in 1784 [6] and described by Brown-Kelly in 1918 [7]. With an incidence of 1 in 40,000 live births [8, 9], they mostly affect female neonates. Their occurrence beyond age 20 years is considered exceptional [10]; there have been only 5 reports in adults in the last 25 years [10–13], with 2 reports in 2013 itself (Table 2, Fig. 4). Neonates constitute almost 37 % of the cases, more than half presenting at birth or within day one (Table 3). Kelly et al. [4] in the pre-PubMed era stated that more than 50 % of such lesions presented in infancy, however, we found this to be about 36 %; with the neonates included, the figure stands at about 73 % (Table 3). This along with the fact that a fetus was once reported to harbor a hairy polyp necessitating termination of pregnancy [14] strongly suggests that they are primarily developmental aberrations. However, this does not satisfactorily explain their occurrence in adults. Though the origin of bigerminal choristomas in the naso-oropharynx is not known, theories have been put forward (Table 4). Central to the understanding is the concept that owing to an inciting factor (trauma,

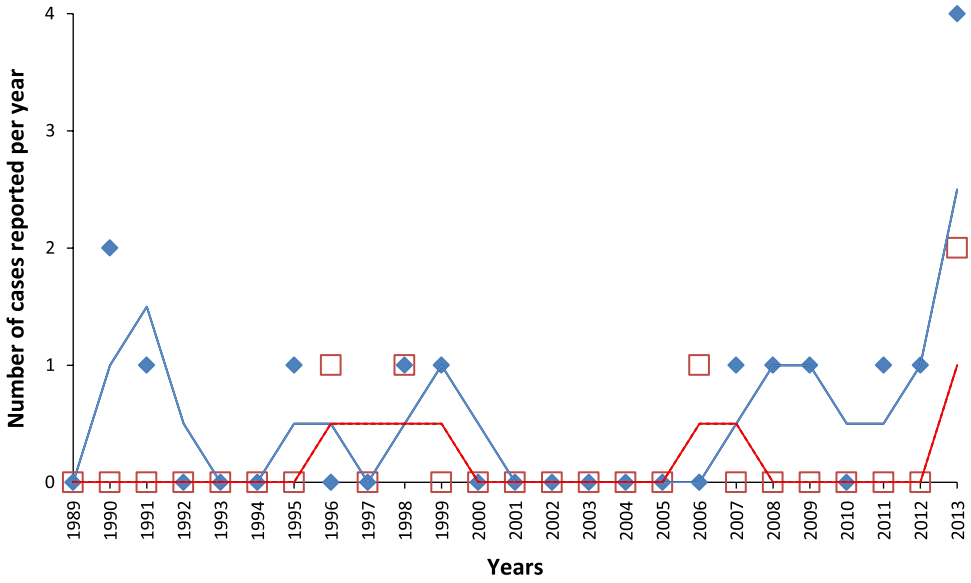

Fig. 4 Graphical representation of the reporting of male patients (*the blue rhomboids*) and adult patients (*the red squares*) with bigerminal naso-oropharyngeal choristomas with time. The *blue line* shows the moving average reporting of the male patients, and the *red line* that of the adults. It is evident that with increasing documentation, the number of male patients is consistently on the rise, especially in the last 7 years. The impression is not so clear for the adult patients due to less number of cases, but there has been 2 cases reported in 2013, the highest in the last 25 years

Table 3 Distribution (in %) of bigerminal choristomas of the naso-oropharynx and oral cavity among age-groups* (n = 78)

Age at presentation	Distribution (in %)	
Fetus	1 (1.28)	
Newborn	29 (37.18)	
29 days–2 months	9 (11.54)	Infants 28 (35.9 %)
2–6 months	11 (14.1)	
6 months–1 year	8 (10.26)	
1–6 years	10 (12.82)	Children 11 (14.1 %)
6–12 years	1 (1.28)	
Adult	5 (6.41)	

Data not available = 4

* The age-groups for neonates, infants and children mentioned here are according to the WHO model formulary for Children 2010 (http://www.who.int/selection_medicines/list/WMFc_2010.pdf; accessed 19th May, 2013)

etc.), pluripotent cells during development get released from local governing influences that would have otherwise led them to the pre-destined tissue morphogenesis [9, 15, 16], or gets misdirected or trapped during migration so that they cannot reach the targeted organ (the "missed target hypothesis") [9, 17, 18], forming heterotopic tissues. As choristomas are ubiquitous in the body, this would explain their occurrence both at the embryonal fusion points and also at sites with no plausible embryologic connection. Therefore, their occurrence in adults—Resta et al. reporting a hairy polyp in a 71-year-old man [19]—could be a delayed manifestation of pluripotent cell morphogenesis. This may further lead us to re-think whether bigerminal choristomas in the naso-oropharynx could be neoplastic—a proposition supported by earlier researchers [16] like Cadman and Kintzen [20], and by the ongoing controversy on

Table 4 Different theories proposed to explain the origin of complex germ-line lesions

Theory	Year	Proponents
Escape of pluripotent tissue from normal control mechanisms before the 4th week of gestation; failure in closure of the 2nd pharyngeal cleft; error in fusion of the epiblast of the stomodeum with the anterior foregut	1918	Brown-Kelly [7]
Inclusion dermoid cyst between two germ layers of the 1st and 2nd branchial arches	1937	New, Erich [34]
Segregation of ectodermal and endodermal germ layers during the midline fusion of the lateral palatine processes at 10th week of gestation	1947	Eggston, Wolff [88]
Accessory auricles arising from the 1st pharyngeal arch	1964	Schuring [89]
	1996	Heffner et al. [45]
Parasitic fetus; derived from misdirected pluripotent cells that have bypassed the influences appropriate for the local environment	1969	Calcaterra [17]
Incomplete resorption of the inferior aspect of buccopharyngeal membrane at 7th week of gestation	1973	Badrawy et al. [90]
Escape of pluripotential tissue as a disorganized mass	1979	Holt et al. [91]
First pharyngeal arch apparatus in germ-cell rests	1990	Sexton [35]
Developmental malformations related to the development of 1st and 2nd pharyngeal arches	2001	Burns et al. [5]

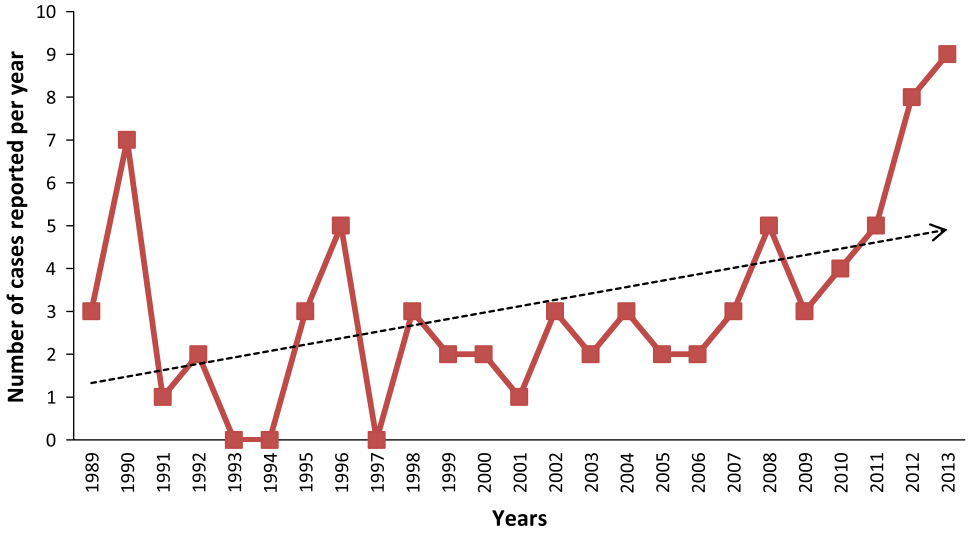

Fig. 5 Graphical representation of cases of hairy polyp reported in each of the last 25 years. The trend-line (the *black-dotted straight line*) clearly shows there has been a gradual increase in reporting of such cases in recent years

Table 5 Distribution (in %) of bigerminal choristomas of the naso-oropharynx and oral cavity according to the anatomical subsites

Involvement of anatomical subsites	Distribution (in %)	
Lateral nasopharyngeal wall (including those originating from the eustachian tube)	23 (29.49)	Nasopharynx 38
Eustachian tube	15 (19.23)	
Soft palate (nasopharyngeal surface)	3 (3.85)	
Nasopharynx (NS)	12 (15.38)	
Middle ear and mastoid (including extension from the eustachian tube)	12 (15.38)	Middle ear cleft = 18 cases (23.08 %)
Soft palate (oropharyngeal surface)	6 (7.69)	Oropharynx 26
Tonsils and tonsillar pillars	14 (17.95)	
Oropharynx (NS)	5 (6.41)	
Both soft and hard palate	1 (1.28)	
Pharynx (NS)	4 (5.13)	
Hard palate	5 (6.41)	
External auditory canal	2 (2.56)	
Tongue	2 (2.56)	
Lower lip	1 (1.28)	
Parapharyngeal space	2 (2.56)	

NS not specified

Nasopharynx: oropharynx = 1.46

nosology of the complex germ-layer lesions. Interestingly, in spite of increased reporting, the number of adult patients has still remained low (Fig. 4, 5), indicating that this age-group is affected quite exceptionally.

The female preponderance

Bigerminal choristomas of the naso-oropharynx have a definite female preponderance that still remains unexplained. Most researchers have stated the female:male ratio as 6:1 [9, 21], though it was put at 8 in the review by Kalcioglu et al. [22]. However, we found it to be 3.5—a significant deviation from earlier reports [Table 2]. Interestingly, of the 16 male patients in the last 25 years, 10 were reported within the last 7 years itself (Fig. 4). Therefore, the female preponderance as believed presently is a definite overestimation, and this could be explained from the steady rise in documentation especially in the recent years (Fig. 5). Ahmadi et al. [23] had searched for parthenogenesis to explain the origin of teratomatous lesions, but human parthenogenesis is a poorly understood, inadequately studied topic and seems not a suitable explanation for the female preponderance.

Presentation and site of involvement—the role of endoscopy

Within the naso-oropharynx and oral cavity, the lateral nasopharyngeal wall is the commonest subsite of

Table 6 Symptoms (in %) of patients presenting with bigerminal choristomas of the naso-oropharynx and oral cavity

Symptoms at presentation	Distribution (in %)
Respiratory obstruction/distress	39 (50)
Feeding/swallowing difficulties	19 (24.36)
Combined respiratory distress and feeding difficulty	15 (19.23)
Obstructive sleep apnea/snoring	8 (10.26)
Ear problems**	10 (12.82)
Termination of pregnancy	1 (1.28)
Others***	19 (24.36)

* Data were not available/provided in 14 cases

** Ear problems include discharge, decreased hearing, blocked ear and earache

*** "Others" include vomiting, hematemesis, visible mass, epistaxis, fever, cough gastro-esophageal reflux and inflammatory lesion at presentation (death resulted in 2 cases—one in a 20 week-old fetus, and the other at 2 h of life who was born with multiple congenital syndromic disorders)

bigerminal choristomas (29.49 %), followed by the tonsils/faucial pillars (~18 %) (Table 5). With the left side being 6.5 times more commonly involved than the right, they either present as visible masses, or produce symptoms due to mass effect causing respiratory obstruction (50 %), dysphagia (24.36 %), or both (~19 %) (Table 4). Most symptoms were relieved on excision of the mass, but proper diagnosis of hairy polyp in a child presenting with respiratory distress often becomes challenging. A recent study by Koike et al. [24] has shown that hairy polyps present with respiratory obstruction in 52.5 % cases and with dysphagia in 36 % cases, comparable to our findings. Interestingly, lesions $\leq$3 cm were more prone to produce symptoms because they were more liable to be missed by routine clinical examinations [24]. These lesions are not life-threatening per se, but, at least in two instances, delayed diagnosis has led to grave consequences like psychomotor retardation in older age due to cerebral hypoxia [24, 25]. Knowledge of the disease entity and a high index of suspicion would guide a clinician to search for a cause with endoscopy and imaging in a child with refractory and persistent respiratory insufficiency when other causes have been ruled out. Telescopes not only help in delineating the origin in anatomic details (Fig. 6a, b), they also ensure complete removal [26], and thereby prevent recurrences [27]. Endoscopy for excision of such masses was first described by Roh in 2004 [28], and the present consensus in published texts suggests that it is the gold standard procedure to diagnose as well as treat hairy polyps in the head-neck area. A combined naso-endoscopic and trans-oral approach has recently been emphasized by Agrawal et al. for surgical management of similar lesions [29], and it follows that careful flexible nasopharyngoscopy in a child in distress should be made considering the possibility of a nasopharyngeal mass, possibly a hairy polyp, causing upper airway obstruction.

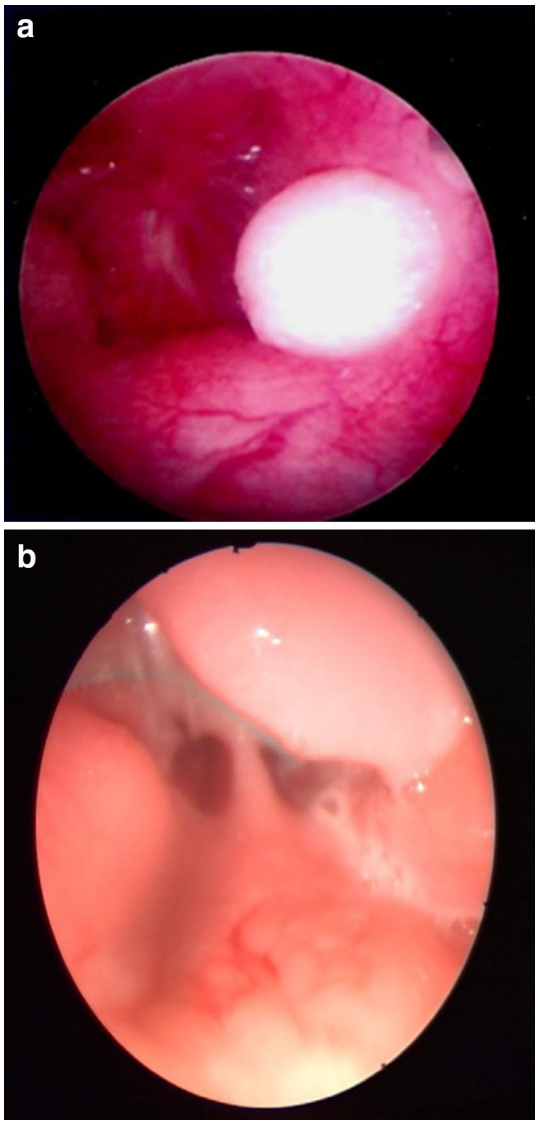

Fig. 6 **a**, **b** Diagnostic naso-endoscopy showing the mass originating from the region of the Eustachian tube orifice (reproduced with permission from Elsevier; references [26] and [29], respectively)

Eustachian tube dermoids: developmental error in the pharyngeal arch apparatus as a feasible explanation of naso-oropharyngeal choristoma

Nicklaus et al. [30] in 1991 first reported a hairy polyp originating from Eustachian tube and growing outward into the nasopharynx that was removed by trans-oral route. It appears that with widespread use of telescopes, many of these bigerminal choristomas of the lateral nasopharyngeal wall could well be found originating from Eustachian tube.

This review shows that Eustachian tube hairy polyps constitute almost two-thirds of those arising from the lateral nasopharyngeal wall (Table 5), yet it seems such incidences until recently went grossly underreported. Recent reviews by Muzzi et al. [2] and Nalavenkata et al. [26] establish Eustachian tube lesions, including teratomas and dermoid/hairy polyp complex, as a new group of "emerging disease entity". The Eustachian tube presently forms a distinctive anatomic and embryologic landmark in the classification of head-neck dermoids [2, 31].

Hairy polyps do not represent any syndromic disorder [4], but are occasionally associated with cleft palate, uvular agenesis, ankyloglossia, facial hemihypertrophy, low-set ears, osteopetrosis, hypospadias, left carotid artery atresia, agenesis of external auricle, bifurcation of tongue and branchial arch sinuses [4–6, 13, 32, 33]. There have been no such reports in adults—but they are of interest for some possible explanation of their origin. Of particular importance are the branchial arch anomalies often associated with hairy polyps of the naso-oropharynx [5, 32]. They support the ontogenetic principles laid down by Brown-Kelly [7], New and Erich [34], Sexton [35] and Burns et al. [5] (Table 4) that bigerminal choristomas in the head-neck are related to the development of the first and second pharyngeal arches. The proposition of Eustachian tube as the putative origin of bigerminal choristomas is supported by the speculation of their embryologic origin in relation to the pharyngeal arches.

During the fourth week of development, the dorsal part of the first and second arch endoderm (the pharyngeal pouch) join to form the tubotympanic recess, and with mesodermal interposition, form the middle ear cavity and Eustachian tube [36, 37]. Middle ear and mastoid account for about 15.38 % of the hairy polyps (Table 5), including one recurrence in the lateral nasopharyngeal wall [26]. Prior to Nicklaus et al., there were few reports of hairy polyps limited within the Eustachian tube that were removed by simple or modified radical mastoidectomy [31]. Overall, the middle ear cleft constitutes about 23 % of cases [Tables 2, 5]. Thus, with growing evidence of Eustachian tube as the predominant subsite for bigerminal choristomas in the nasopharynx [Fig. 6a, b], the probability of such lesions being developmental errors during pharyngeal arch morphogenesis is strengthened. This is further supported by the fact that the tonsils and faucial pillars, the commonest subsite in the oropharynx (~18 %) [Table 5], also develop from the ventral aspect of the second pharyngeal pouch.

Laterality and molecular control of pharyngeal arch morphogenesis

For reasons unknown, the left side has been found to be 6.5 times more commonly involved irrespective of the site of origin. Study on the molecular control of the development of head and neck shows that the first and second pharyngeal arches are populated by migrating NCCs from segmented regions of rhombencephalon (the rhombomeres; R1–8) in a pre-destined, programmed and regulated manner [3, 36], carrying genetic signals through the Hox and Otx2 [36] genes that convey positional information to the respective pharyngeal arches and the ultimate organogenesis of face. Expression of the Hox genes is further regulated by the sonic hedgehog (shh) genes which determine the left–right asymmetry during morphogenesis. The complex interplay between the shh gene products (coding for preferential left-sided expression [38]) and Hox in regulating the epithelial–mesenchymal interaction at the pharyngeal arches that could account for the lateral nasopharyngeal wall as the predominantly involved site, needs further exploration in determining the left-predominance of such lesions.

Expanding domain of the "teratoma family"—is naso-oropharyngeal choristoma a neoplasia or a developmental error?

Hairy polyps are diagnosed by history, clinical examination and histopathology. With the use of diagnostic endoscopy, imaging often becomes non-contributory, limited to identifying the extent and bony breach (ultrasonography, CT scan), and tissue composition ("fat within the mass") and intracranial extension (MRI) [4, 30, 39, 40]. Histopathology typically reveals ectodermal and mesodermal derivatives [Fig. 2], and grossly the surface might not always be hair-covered [41, 42]. Though characteristically bigerminal, there are reports where authors have referred them as teratoma, teratoid, or more specifically, bigerminal "teratomas" [13, 43, 44]. In contrast, they might actually originate from single germ-cell lineage, the neuroectoderm, having major contribution to the head-neck mesenchyme (the ectomesenchyme) [35]. It therefore appears that the rigidity of the classification system of complex germ-cell lesions has been acceptably approached with leniency. Thus, though hairy polyps more closely resemble dermoids (Arnold's classification [1]), they have often been referred to as "tumors", suggesting their association with teratoma, a true neoplasia [4, 10, 13, 22, 45]. With few such reports in previously asymptomatic adults, the theory of neoplasia might be pertinent.

However, unlike teratoma, hairy polyps are slow-growing [46, 47] with no malignant transformation [27], leading authors like Vaughan et al. [32] and Seng et al. [48] comment that they should not be considered a primitive teratoma but strictly as developmental malformations. Similar views were shared by Heffner et al. who proposed that cartilaginous tissue plates in such lesions morphologically resembled fetal pinna, but were unlike the orientation seen

in teratomas [46]. Yet in adults, they arise in areas so long unaffected in their life, and the theory of developmental malformation is probably inadequate to implement. Possibilities of focal neoplasm thus cannot be ruled out; Green and Pearl, while describing one of the five adult cases of hairy polyp mentioned in this review, have stated them as "neoplastic" [10], while Ferlito and Devaney [49] have placed them under the family of "benign teratoma".

With the current evidence, the definition of teratoma is seemingly experiencing a paradigm shift: a "histologically divergent differentiation" from the conventional "trigerminal" lesion [1] to a mass composed of *any two* germ layers [13, 50, 51]. The complex germ-cell lesions hence belong to a *larger* "teratoma family". Hairy polyp has therefore been denoted as a "primitive form of teratoma" by Karabekmez et al. [52], or as a subgroup of benign teratomas [53]. Weaver et al. [54] have even defined teratoma as a tumor of multiple tissues non-indigenous to their site of origin, emphasizing on the aberrant location rather than on composition. A growing group of researchers consequently are of the opinion that these bigerminal lesions of the naso-oropharynx should better be called choristomas—the heterotopic cell-rests [5, 16, 35, 42, 45, 48, 55, 56]. Though the choristoma/hamartoma group is essentially non-neoplastic, and not much is known about their origin as well, this alternative approach of classification might address the existing controversies related to the genesis of the complex germ-layer lesions.

Strengths and limitations of the review

The present review, the largest and the most comprehensive till date, deals elaborately with the clinics and present-day management of hairy polyps. It provides an up-to-date knowledge regarding the nosology and embryogenesis by analyzing the theories of origin, re-establishing the relationship between hairy polyps, the Eustachian tube system, and the development of the first two pharyngeal arches. Furthermore, the importance of a high index of suspicion of the possibility of a choristomatous mass obstructing the airway of a child in distress has been underlined. However, the review has its limitations. Non-English articles have been excluded, and being restricted to a given anatomic site, rare areas of involvement like the nose [57] could not be considered. Accordingly, time-trend of the reported cases would have been more accurate had all the cases of hairy polyps in the head-neck region be included. However, the non-English texts did not contribute significantly to the case bulk. Also, the naso-oropharynx, oral cavity and the middle ear system as an embryologically linked unit formed the most representative area for hairy polyps in the head-neck region. Therefore, the time-trend estimated should provide an unbiased view of the reporting of cases.

Conclusions and implications for practice

Naso-oropharyngeal hairy polyps mostly present in female neonates predominantly with respiratory obstruction and feeding difficulties, and with a left-sided predilection. They can be life-threatening if diagnosed late, especially when smaller. A child with refractory respiratory distress and difficulty in feeding where all possible causes have been excluded should be specifically looked for a hairy polyp in the naso-oropharynx. With increasing reports in recent years in the head-neck region, it appears that it is not as uncommon as generally believed. Flexible nasopharyngoscopy would be the best modality for estimating the size and localizing the mass. Fortunately, they have no malignant potential and symptoms are cured on surgical removal. Proper understanding of their biologic behavior requires in-depth study of embryology and molecular genetics, but an elementary idea is essential for the clinicians-in-practice, especially about their relationship with the development of the pharyngeal arches. This is because children with hairy polyps often present with pharyngeal arch anomalies, apart from other congenital stigmata. Their occurrence in adults is extremely rare and perplexing, thus might be confused with the commoner entities. The concept of focal neoplasia might be relevant, apart from the conventional theories of developmental malformations, to explain the occurrence of hairy polyps. In this review, we have highlighted the clinical characteristics of bigerminal choristomas of the naso-oropharynx and discussed about their origin and morphogenesis, as understanding their clinico-embryologic profile would help clinicians in timely diagnosis and management of similar lesions.

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