Acta Scientific Paediatrics (ISSN: 2581-883X)

Volume 5 Issue 7 July 2022

Clinical Review

The Lymphatic Bursa - Oral Lympho-Epithelial Cyst

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Received: May 25, 2022

Published: June 14, 2022

Abstract

Lympho-epithelial cyst is a rare, non-odontogenic, benign, soft tissue developmental cyst emerging within the oral cavity. Oral lympho-epithelial cyst predominantly appears within ventral surface or posterolateral lingual margin, floor of mouth, soft palate, buccal mucosa, hard palate, labial mucosa, palatoglossal fold, tonsillar pillar, lip, glossodesmus fold or retro-molar region. The asymptomatic lesion can represent as a miniature, painless lump or a yellowish white, soft to firm, submucosal nodule of around ~one centimetre magnitude. Cyst cavity is layered with attenuated, para-keratinized, ortho-keratinized or non-keratinized stratified squamous, pseudo-stratified columnar, respiratory metaplastic, ciliated pseudostratified or ciliated columnar epithelium with mucous or goblet cells and intensely infiltrated by mature, small lymphocytes configuring germinal centres..

Keywords: Lympho-Epithelial Cyst; Lymphocytes; Lymphoid Tissue

Introduction

Lympho-epithelial cyst is an infrequently discerned, non-odontogenic, benign, soft tissue developmental cyst of the oral cavity. Initially scripted by Gold in 1962 as a "branchial cleft cyst", the cyst emerges within sites enriched by lymphoid tissue [1]. The uncommon, benign, lympho-epithelial cyst occurs due to epithelial entrapment or proliferation in concurrence with lymphoid tissue. Additionally designated as branchiogenic cyst, tonsillar pseudo-cyst, intra-oral lympho-epithelial cyst or benign lympho-epithelial cyst, the lesion is characteristically constituted of stratified squamous epithelium encased by lymphoid tissue. Lympho-epithelial cyst or pseudo-cyst may represent as a yellowish nodule imbued with retained, desquamated keratin. The lesion is situated within specific sites as the palatine tonsil. On morphological grounds, a cystic cavity layered by stratified squamous epithelium, incorporated by keratin and enmeshed within lymphoid tissue rich stromal fibro-connective tissue is exemplified. Essentially asymptomatic, lympho-epithelial cyst may be discerned as an incidental finding. Majority of lympho-epithelial cysts can be misinterpreted as a mucus cyst, normal anatomic structures as foliate papilla, sebaceous gland, sublingual gland or lymphoid tissue aggregate. Conservative surgical extermination of the cyst is usually adequate and lesion reoccurrence is undocumented.

Disease characteristics Commonly, lympho-epithelial cyst is exemplified in the pancreas, mediastinum, stomach, oesophagus or sites within head and neck as the thyroid, parotid gland, oral cavity or lateral cervical region where the lesion is designated as branchial cyst. Besides, no site of lesion emergence is exempt. The cyst denominates below < 1% of oral cavity lesions [2,3]. Although oral lympho-epithelial cysts are devoid of the concurrence, lesions emerging within major salivary glands are associated with infection with human immunodeficiency virus (HIV) [3,4]. Oral lympho-epithelial cysts predominantly appear within the ventral surface or posterolateral lingual margin followed in frequency by floor of mouth, soft palate, buccal mucosa, hard palate, labial mucosa, palatoglossal fold, tonsillar pillar, lip, glossodesmus fold and retro-molar area. Lympho-epithelial cyst is exceptionally discerned within the palatine tonsil [3,4]. Multiple lesions may be discerned and an oral lympho-epithelial cyst may concur with an epithelial inclusion cyst. Generally, lympho-epithelial cyst measures below < one centimetre magnitude. A female predilection is observed with a female to male proportion of 2 :1 [3,4]. Mean age of emergence of adult-onset lympho-epithelial cyst is 44.1 years although the cyst is commonly delineated within second decade to fifth decade and may arise up to seventh decade [3,4]. Cogent tissue sampling following surgical excision is recommended to adequately confirm the diagnosis of oral lympho-epithelial cyst [3,4].

Disease pathogenesis of Debatable pathogenesis, oral lympho-epithelial cyst is denominated to be a pseudocyst which emerges from submucosal lymphoid tissue aggregated upon floor of the mouth, soft palate or ventral surface or posterolateral lingual perimeter [4,5]. It is posited that oral lympho-epithelial cysts are not

true cysts, are constituted of epithelial proliferation and manifest as pseudocysts which originate from a distended, obstructed, tonsillar crypt with accumulated purulent material or desquamated stratified squamous epithelium [4,5]. Nevertheless, oral lympho-epithelial cyst may be contemplated as a pseudocyst and is hypothesized to arise from submucosal aggregates of lymphoid tissue situated upon floor of the mouth, ventral lingual surface or soft palate [4,5]. Thus, lympho-epithelial cysts are posited to arise from obstruction of oral or palatine tonsillar crypts with consequently distended, squamous epithelium layered cavity. The cyst cavity is imbued with keratin and desquamated squamous epithelial cells and communicates with extraneous cutaneous surface or oral cavity wherein the communication may be challenging to ascertain [4,5]. Theory of "embryologic entrapment" or "epithelium enclavement" posits the entrapment of squamous epithelium within oral mucosal lymphoid tissue subsequent to proliferation initiated by trauma or chronic inflammation of the cyst. The entrapped epithelium emerges as a remnant of branchial arches situated upon floor of mouth, oral mucosa or salivary gland ducts [4,5]. Lympho-epithelial cyst may be contemplated as a developmental lesion. Epithelial islands and duct-like structures enmeshed within or abutting the lymphoid tissue may undergo cystic change. Besides, a columnar epithelial layer appearing contiguous with the cystic epithelium or salivary gland ducts may be discerned [5,6]. "Obstruction theory" indicates the occurrence of a traumatic event or microbial invasion with an accompanying inflammatory reaction. Aforesaid modifications may activate para-keratinization of non keratinized crypt epithelium. Also, factors such as incomplete desquamation, para-keratinized squamous epithelial cells, bacteria and purulent substances accumulate and obstruct the crypt orifice with consequent configuration of a lympho-epithelial cyst or a pseudocyst. Frequent occurrence of oral lymphoid tissue or "oral tonsils" upon floor of mouth, tongue and soft palate, concurrence of an intraepithelial inflammatory cell infiltrate and contiguity of cystic epithelium within superficial oral mucosa contribute to emergence of oral lympho-epithelial cyst. Nevertheless, mucosal contiguity may be absent in advanced stages of developmental lympho-epithelial cyst [5,6]. Oral tonsil situated upon floor of the mouth may simulate a lympho-epithelial cyst devoid of cystic cavity. Thus, an oral tonsil may be contemplated as a preceding stage of lympho-epithelial cyst. Aforesaid aggregates of ectopic lymphoid tissue or oral tonsils may be designated as "new tonsils" and appear as an addendum to "regular tonsils" exemplified upon posterior segment of oral cavity, oropharynx and nasopharynx [5,6]. Possibly, stratified squamous epithelium and lymphocytes are incriminated in genesis of lympho-epithelial cysts [5,6]. It is postulated that proliferation of glandular epithelium within lymph nodes of parotid gland or cervical region may engender the lesion. Additionally, abdominal lymph nodes may be contemplated as a source of pancreatic lympho-epithelial cysts [5,6]. Besides, lympho-epithelial cysts of parotid gland may commence from ductal dilatation occurring due to epithelial hyperplasia, probably stimulated by lymphocytic infiltration as encountered with focal sialadenitis [5,6].

Clinical elucidation

Generally, oral lympho-epithelial cyst can be asymptomatic or represent as a miniature, painless lump in the throat or a yellowish white, soft to firm, submucosal nodule of around ~one centimetre magnitude. Nevertheless, majority of lesions are below < 1 centimetre diameter and persist for an extensive duration [6,7]. The soft to firm, nodular lympho-epithelial cyst manifests with a smooth, granular or exceptionally ulcerated surface superimposed with normal, yellowish or whitish mucosa. Enlarged, ulcerated cysts may be accompanied by clinical symptoms such as pain, discomfort or dysphagia [6,7]. Yellowish mucosal hue occurs due to keratin or purulent content of the cystic cavity. Transparent, translucent oral cysts with purple or grey overtones are exceptional. Surface ulceration may arise due to secondary trauma [6,7]. Upon intraoral examination, a well-circumscribed, yellowish, soft nodule traversed with superficial vascular articulations may be observed [6,7].

Histological elucidation

Oral lympho-epithelial cyst represents as a thickened, well defined, submucosal nodule delineating a cystic cavity imbued with viscous fluid, desquamated epithelial cells, keratin and inflammatory cells [7,8]. The cystic cavity is layered with para-keratinized stratified squamous epithelium which exemplifies a smooth interface with adjoining lamina propria. Circumscribing dense cyst capsule and wall is intensely infiltrated by mature, small lymphocytes configuring germinal centres. Upon microscopy, the ruptured cystic cavity may be imbued with few squamous epithelial cells and absence of keratin and is coated with attenuated, para-keratinized, ortho-keratinized or non-keratinized stratified squamous, pseudostratified columnar, respiratory metaplastic, ciliated pseudostratified or ciliated columnar epithelium with constituent mucous or goblet cells. Epithelial layer exhibits lymphoid tissue pressure-induced flattening of rete ridges and a flat interface with subjacent connective tissue [7,8]. Para-keratinized cystic epithelium exemplifies prominent hyperplasia of para-keratin layer. Focal transition from squamous epithelium to pseudostratified columnar epithelium may be observed. Besides, the cyst may be coated by non-keratinized squamous epithelium with intermingled cuboidal cells [7,8]. Cystic cavity is inundated with desquamated squamous epithelial cells, amorphous eosinophilic material, keratin and inflammatory cells as polymorphonuclear leukocytes, lymphocytes or plasma cells [7,8]. Exceptionally, subgemmal neurogenous plaques may appear adjacent to the cyst [7,8]. Sub-epithelial or sub-mucosal cyst wall is thickened, encased within minimal to moderate, loose to dense fibrous connective tissue, appears infiltrated by innumerable lymphocytes and may occasionally display islands of epithelial

cells or minor salivary glands. Cystic epithelium may appear contiguous with superimposed oral mucosa or epithelial layer [7,8]. Typically, encompassing lymphoid tissue configures germinal centres and exhibits a follicular pattern. Focal intraepithelial infiltration of lymphocytes may be discerned [7,8]. Circumscribing lymphoid tissue with follicular configuration, prominent germinal centres and fibro-connective tissue may incorporate islands of epithelial cells, mucous glands, duct-likes articulations, microorganisms or calcified material [7,8]. Usually, mucous cell or goblet cell metaplasia is absent. Focal infiltration of inflammatory cells occurs within the cystic epithelium. Partial or complete encasement of cystic cavity by lymphoid tissue with a follicular pattern and prominent germinal centres is observed [7,8]. Epithelial layer of the cyst is immune reactive to p40. Lymphoid stroma is predominantly immune reactive to CD20 and minimally immune reactive to CD3 [7,8].

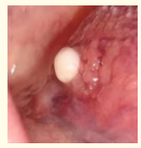

Figure 1: Oral lympho-epithelial cyst depicting a yellowish pouch imbued with keratin and desquamated epithelium [12].

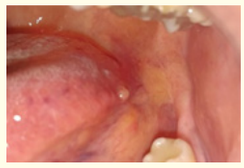

Figure 2: Oral lympho-epithelial cyst delineating a tiny, yellowish, submucosal nodule with impacted keratin, epithelial and inflammatory cells [13].

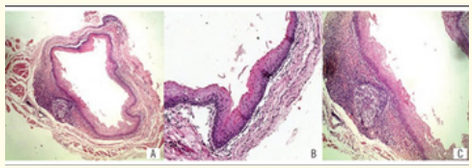

Figure 3: Oral lympho-epithelial cyst demonstrating a cystic cavity layered with stratified squamous epithelium along with constituent keratin debris and desquamated epithelium [13].

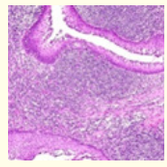

Figure 4: Oral lympho-epithelial cyst exhibiting a cystic cavity layered with pseudo-stratified squamous epithelium and a circumscribing lymphoid stroma [14].

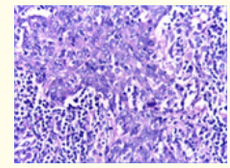

Figure 5: Oral lympho-epithelial cyst exemplifying islands of stratified squamous epithelium surrounded by extensive lymphoid tissue [15].

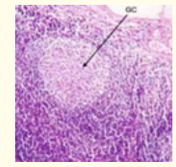

Figure 6: Oral lympho-epithelial cyst enunciating a follicular arrangement along with germinal centres appearing in lymphoid tissue circumscribing a cystic cavity [16].

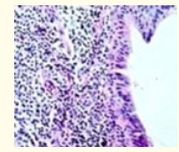

Figure 7: Oral lympho-epithelial cyst lined by pseudo-stratified tall columnar epithelium with encompassing lymphoid tissue and prominent vascular articulations [17].

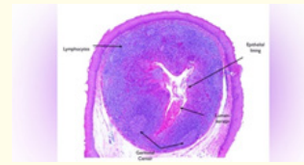

Figure 8: Oral lympho-epithelial cyst demonstrating a submucosal nodule lined with stratified squamous epithelium, circumscribing lymphatic tissue with germinal centres and keratinous debris in the cyst cavity [18].

Differential diagnosis

Lesions situated upon palatine tonsil require a segregation from conditions such as tonsillar cyst, tonsillolith, tonsillitis, papilloma, lipoma, streptococcal sore throat, infectious mononucleosis, oropharyngeal candidiasis or peri-tonsillar abscess [7,8]. Demarcation on clinical grounds is required from pathological conditions and benign neoplasms such as lipoma, mucous extravasation cyst or mucocoele, irritation fibroma, inflammatory fibrous hyperplasia, squamous papilloma, granular cell tumour, hyperplastic foliate papilla, ectopic lympho-glandular tissue, dermoid cyst, inclusion cyst, abscess, sialolithiasis, sialadenitis, nevus, leukoplakia or minor salivary glands [7,8]. Distinction is necessitated from epidermal inclu-

sion cyst which is composed of a cystic cavity layered by stratified squamous epithelium. However, circumscribing lymphoid tissue stroma is absent [9,10].

- Sebaceous cyst is constituted of a cystic cavity layered by stratified squamous epithelium accompanied by cutaneous adnexal structures. However, encompassing lymphoid stroma is absent [9,10].
- Fordyce's granules are essentially composed of aggregates of mature sebaceous glands [9,10].
- Sialolith is constituted of calcified material encompassed within ductal epithelium and foci of squamous metaplasia.
- Mucocoele is exemplified by a pseudocyst impacted with mucin. Cyst cavity is layered by histiocytes and lymphocytes [9,10].
- Foreign body giant cell reaction enunciates several inadequately configured epithelioid cell granulomas admixed with innumerable multinucleated giant cells and impacted foreign bodies, crystals or bacterial organisms [9,10].
- Squamous cell carcinoma exhibits proliferation of nests of squamous epithelial cells which configure and infiltrate surrounding stroma as irregular, anastomosing tumour cell nests, cords or singular cells. Tumour cells depict enlarged, hyperchromatic nuclei, coarse chromatin and inconspicuous nucleoli. Enveloping stroma can be desmoplastic or invaded with inflammatory cells. Foci of stromal dehiscence or desmoplastic reaction can be observed. Superficial stromal invasion, lymphoid tissue infiltration and vascular invasion may be delineated. Tumour grading is contingent to features such as nuclear pleomorphism, nucleolar magnitude, mitotic activity and tumour cell necrosis. Keratin pearls, abundant keratohyaline granules and intercellular bridges may be exemplified [9,10].

Therapeutic Options

Miniature, asymptomatic, oral lympho-epithelial cyst can be appropriately managed with conservative measures and periodic monitoring. Generally, oral lympho-epithelial cysts spontaneously resolve within few months and may be accompanied by rupture of obstructed segment of tonsillar crypt. Miniature lesions may rupture or disappear spontaneously and cogent surgical procedures are unnecessary [10,11]. Alternatively, comprehensive surgical excision of the cyst can be adopted contingent to factors such as medical history, clinical symptoms or magnitude and location of lesion. Conservative measures as simple excision or marsupialization of an asymptomatic cyst can be adopted. The procedure is accompanied by superior therapeutic outcome and minimal proportionate lesion reoccurrence [10,11]. Enlarged cysts engendering dysphagia or possible airway obstruction mandate surgical extermination in order to circumvent life-threatening complications and ameliorating quality of life [10,11]. However, enlarged lesions associated with clinical symptoms require rapidly alleviation with minimalistic surgical procedures [10,11]. Oral lympho-epithelial cyst is accompanied by a favourable prognosis. Generally, lesion reoccurrence is absent [10,11].

Conclusion

Oral lympho-epithelial cyst requires a segregation from lesions such as lipoma, mucous extravasation cyst or mucocoele, irritation fibroma, inflammatory fibrous hyperplasia, squamous papilloma, granular cell tumour, hyperplastic foliate papilla, ectopic lymphoglandular tissue, epidermal inclusion cyst, dermoid cyst, inclusion cyst, abscess, sialolithiasis, sialadenitis, nevus, leukoplakia, Fordyce's granules, minor salivary glands, foreign body giant cell reaction or oral squamous cell carcinoma. Generally, oral lympho-epithelial cysts resolve spontaneously within few months. Comprehensive surgical cyst excision is adopted contingent to clinical symptoms or magnitude and location of lesion.

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12. Image 1 Courtesy: Facebook.com

13. Image 2 and 3 Courtesy: Scielo Brazil.com

14. Image 4 Courtesy: Webpathology.com

15. Image 5 Courtesy: Wikiwand.com

16. Image 6 Courtesy: Semantic scholar

17. Image 7 Courtesy: Scielo.sid.cu

18. Image 8 Courtesy: RDH magazine