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PRAKAZ SLUČAJA
CASE REPORT

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Epidermoidna cista na bukalnoj sluznici: prikaz slučaja i pregled literature

Epidermoid Cyst Arising in the Buccal Mucosa: Case Report and Literature

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Sažetak
Epidermoidne ciste dobroćudne su potkožne lezije koje uglavnom nastaju na dnu usne šupljine, a obrazna sluznica nije uobičajeno mjesto gdje se pojavljuju. Do danas je objavljeno samo pet članaka s opisom šest slučajeva epidermoidne ciste na obraznoj sluznici. Svrha ovoga rada bila je opisati klinička, histopatološka i imunohistokemijska obilježja epidermoidne ciste na obraznoj sluznici. Prema našim spoznajama ovo je prvi prikaz takve ciste s opisom gigantocelularne upalne reakcije stranog tijela na komponenti epitelnog keratina. Premda se uobičajena dijagnoza epidermoidne ciste temelji na histopatološkim nalazima, u prikazu ovog slučaja istaknute su nove informacije o imunohistokemijskim svojstvima takvih lezija.

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Ključne riječi
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Uvod

Dermoidna, epidermoidna i teratogena cista neodontogene su lezije nastale iz zametnoga epitela (1). Dermoidne ciste mogu se pojaviti bilo gdje u tijelu, posebice u područjima spoja embrionalnih elemenata (1 – 3). Obložene su epidermisom i kožnim derivatima poput lojnih i mirisnih žlijezda te folikula kose. Ako nema derivata kože, ciste se klasificiraju kao epidermoidne. Nisu povezane s dermoidnim cistama gonada koje se ubrajaju u teratome (1 – 4). Epidermoidne ciste dobroćudne su potkožne lezije i čine od 85 do 90 posto svih uklonjenih cista (5). Većina nastaje u središnjoj crti ili u podjezičnom području dna usne šupljine, a bukalna sluznica nije uobičajeno mjesto (6 – 11). Do danas je objavljeno samo pet članaka s opisom šest slučajeva epidermoidne ciste na obraznoj sluznici (1 – 3, 12, 13), pa je svrha ovoga rada istaknuti njezina klinička, histopatološka i imunohistokemijska

Introduction

The dermoid, epidermoid, and teratoid cysts are nonodontogenic lesions derived from the germinative epithelium (1). Dermoid cysts may be found in any part of the body, particularly in areas where embryonic elements are fused. The majority of cases have been reported in ovaries, testicles, hands, and feet (1-3). These lesions are lined with epidermis and contain skin appendages such as sebaceous glands, sudoriferous glands, and hair follicles. When there is an absence of these skin appendages, the cysts are classified as epidermoid or epidermal cysts. They are not related to the dermoid cysts of the gonads, which are denominated as teratomas (1-4).

Epidermoid cysts are benign subcutaneous lesions, comprising 85-90% of all excised cysts (5). Most epidermoid cysts develop in the midline or sublingual region of the mouth floor, the buccal mucosa is not the usual site of occurrence

obilježja. Prema autorovim spoznajama, ovo je prvi prikaz oralne epidermoidne ciste s opisom snažne upalne reakcije stranog tijela gigantocelularnih stanica na keratinsku epitelijalnu komponentu. Premda se uobičajena dijagnoza takve ciste temelji na histopatološkim nalazima, u ovom slučaju pronađene su dodatne informacije o imunohistokemijskim značajkama ovih lezija.

Prikaz slučaja

Na Stomatološku kliniku za vanjske pacijente Federalnog sveučilišta Ceará Sobral Campus u Brazilu, primljen je 29-godišnji muškarac. Žalio se na bezbolnu intraoralnu oteklinu obrazne sluznice uočenu prije četiri godine. Prema riječima pacijenta, lezija je traumatizirana i uzrokovala je blagi poremećaj u prehrani. Tijekom ekstraoralnog pregleda uočena je asimetrija lica na desnoj labijalnoj komisuri. Kliničkim pregledom nisu pronađeni palpabilni limfni čvorovi u području glave i vrata. Intraoralno je na obraznoj sluznici uočena osjetljiva gumasta, ulcerirana, čvorasta struktura od tri i pol centimetra (slika 1.). Na osnovi tih kliničkih nalaza postavljena je inicijalna dijagnoza – riječ je o dobroćudnoj tvorbi malih žlijezda slinovnica. Točnije, dijagnostička hipoteza bio je pleomorfni adenom. Zbog moguće rijetke zloćudnosti, zbog dugogodišnjeg razvoja lezije, obavljena je incizijska biopsija pod lokalnom anestezijom (slika 2.).

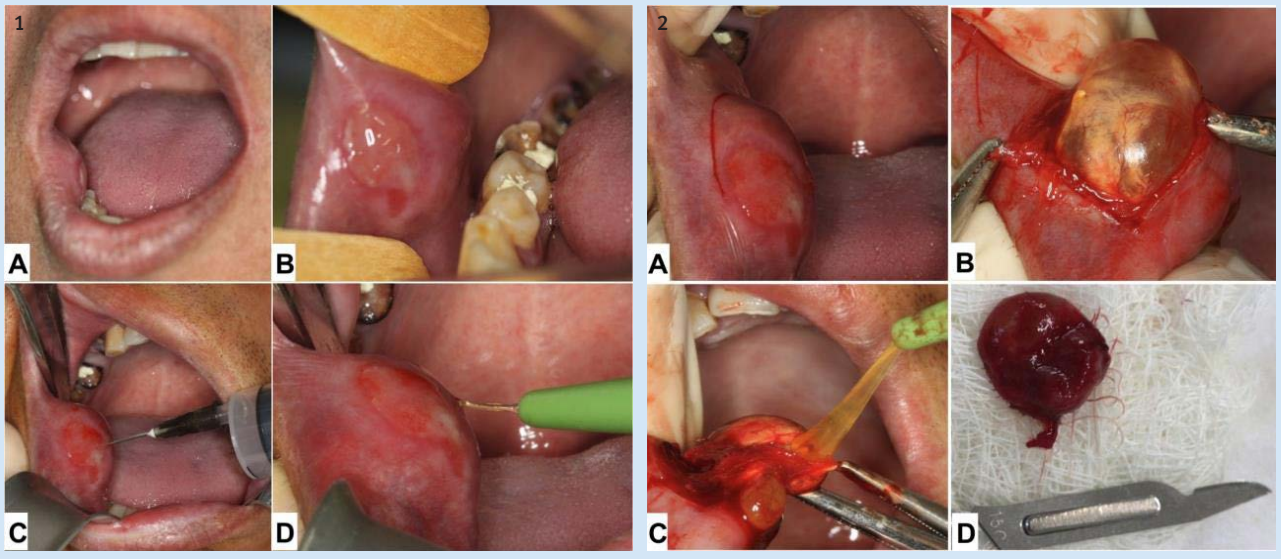
Primijenjena je anestezija mentalnog živca i infiltracijska terminalna anestezija oko lezije. Anestetik je apliciran na si-

(6-11). To date, only five articles have been published with six cases of epidermoid cysts arising in the buccal mucosa region (1-3, 12, 13). Therefore, the aim of this study was to describe the clinical, histopathological, and immunohistochemical features of a case of an epidermoid cyst located in the buccal mucosa. To the authors' knowledge, this is the first report of an oral epidermoid cyst describing an intense foreign body gigantocellular inflammatory reaction against an epithelial keratin component. Although the usual diagnosis for epidermoid cysts is based on histopathological findings, this case report addresses novel information regarding the immunohistochemical pattern that may be found in these lesions.

Case report

A 29-year-old man presented to the Dental outpatient clinic of the Federal University of Ceará, Sobral Campus, Brazil, complaining of a painless intraoral swelling in the buccal mucosa (first noticed four years earlier). According to the patient, the lesion had been traumatized and caused mild dysphagia. During the extra-oral examination, facial asymmetry was observed in the right labial commissure. During the clinical examination, there was no presence of palpable lymph nodes in the head and neck region. Additionally, a 3.5 cm nodular, sessile, and ulcerated lesion of rubbery consistency was observed in the right buccal mucosa (Figure 1).

Due to these clinical findings, the initial diagnosis was benign salivary gland lesions. More precisely, the pleomorphic adenoma was the main diagnostic hypothesis. Due to the possibility of the occurrence of low grade malignant lesions associated with a relatively long time of evolution, an incisional biopsy was performed under local anesthesia (Figure 2).

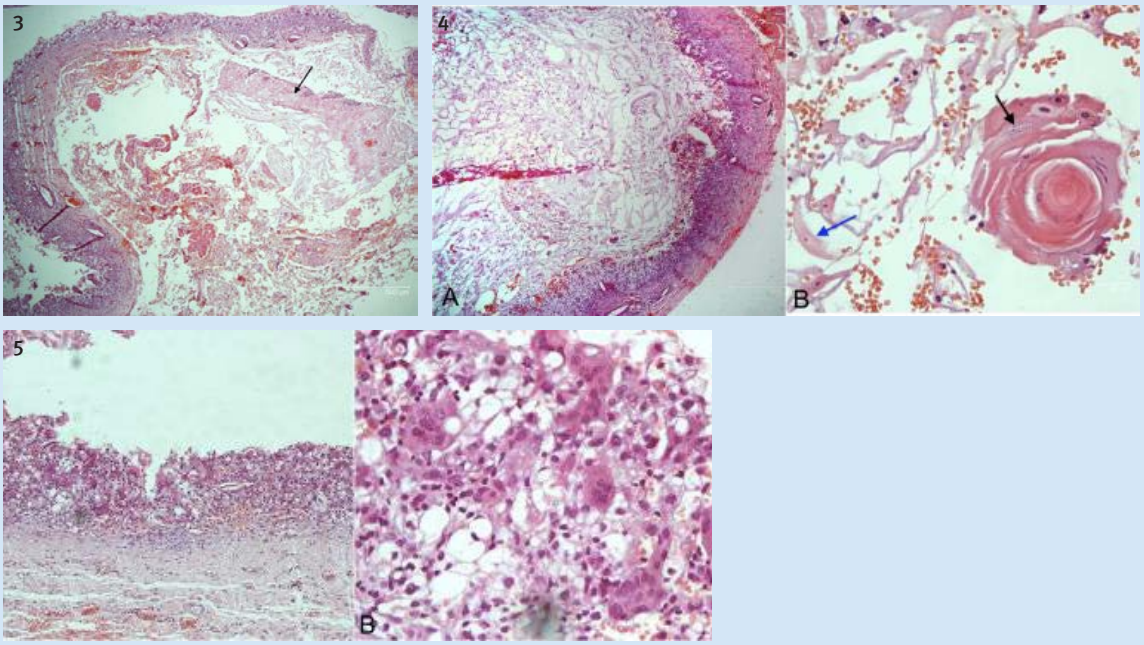


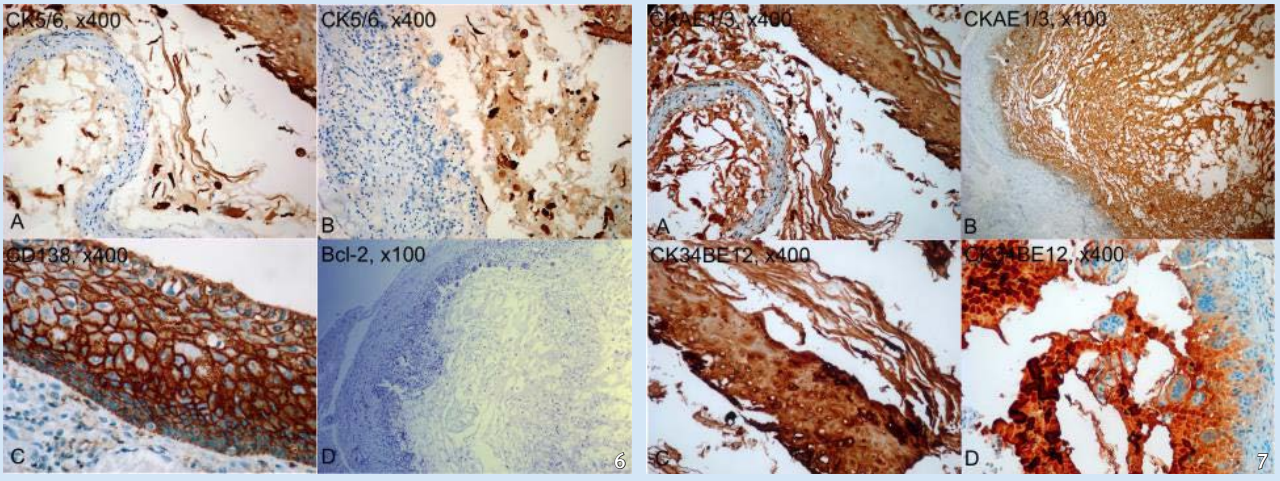
Slika 1. **a** i b: Klinički izgled desne obrazne sluznice s ulceriranom površinom; c i d) aspiracijskom punkcijom dobivena je žuta viskozna tekućina slična mucinu

Figure 1 A, B) Clinical view showing a right buccal mucosa swelling with an ulcerated surface. C, D) Aspirative puncture denoting a viscous yellow liquid similar to mucin.

Slika 2. a i b) Transoperativni izgled lezije nakon disekcije tkiva; c) žuta viskozna tekućina nakon slučajne rupture ciste; d) makroskopski pogled na kirurški uzorak

Figure 2 A, B) Transoperative view of the lesion after tissue dissection. C) Presence of a prominent viscous yellow liquid after accidental cyst rupture. D) Macroscopical view of the surgical specimen.





Slika 3. Mikroskopski uzorak s cističnom šupljinom i višeslojnim obložnim epitelom (crna strjelica); eozinofilni sadržaj u lumenu odgovara raspadnutom keratinu (HE, x 100)
Figure 3 Photomicrography exhibiting a cystic cavity partially lined with stratified pavimentous epithelium (black arrow), containing eosinophilic matter in its lumen, compatible with degenerated keratin (HE, x100).
Slika 4. a) Fotomikrografski prikaz cističnog lumena s izrazito puno degeneriranog keratina (HE, x100); b) prikaz visoke snage (HE, X400) cistične šupljine pokazuju keratinske naslage (crna strelica) i raspršenje keratinocita (plava strelica)
Figure 4 A) Photomicrography exhibiting the cystic lumen markedly filled with degenerated keratin (HE, x100). B) High power view (HE, x400) of the cystic lumen showing keratin deposits containing keratohyalin granules (black arrow) and disperses keratinocytes (blue arrow).
Slika 5. **a**) Mikroskopski uzorak s cističnom stijenkom u kojoj je snažna gigantocelularna upalna reakcija stranog tijela na keratinsku komponentu epitela (HE, x 100); b) veliko povećanje višejezgrene gigantocelularne stanice i ostalih upalnih stanica (HE, x 400)
Figure 5 A) Photomicrography showing cystic wall with intense foreign body gigantocellular inflammatory reaction against epithelial keratin component (HE, x100). B) High power view of the multinucleated giant cells and inflammatory cells (HE, x400).
Slika 6. Imunohistokemijski rezultat – a, c) snažno bojenje epitelne komponente na citokeratine; b, d) intraluminalni cistični sadržaj snažno obojen na degeneriran keratin; nema obojenja na multinuklearnoj divovskoj stanici
Figure 6 Immunohistochemical profile. A, C) Strong epithelial component marking for the cytokeratins. B, D) Intraluminal cystic component showed strong marking for the degenerated keratin and absence of marking for the multinucleated giant cells.
Slika 7. Imunohistokemijski rezultat – a i b) epitelna komponenta i raspršeni keratin u lumenu snažno obojeni na citokeratin 5/6; c) pozitivne stanice CD 138 u bazalnom spinoznom sloju skvamoznog epitela; d) odsutnost bojenja na Bcl-2 u epitelu i intraluminalnom cističnom sadržaju
Figure 7 Immunohistochemical profile. A, B) Epithelial component and dispersed luminal keratin showing a strong marking for the cytokeratin 5/6. C) CD138 marking for the cells in the basal to spinous layer of squamous epithelium. D) Absence of marking for Bcl-2 in both epithelial and intraluminal cystic components.

gurnoj udaljenosti od otekline kako bi se spriječilo da prodre u leziju, a istodobno je omogućen dobar uvid u rubove. Nakon toga obavljena je aspiracijska punkcija pri čemu je dobiven žuti tekući sadržaj sličan mucinu. To je promijenilo dijagnostičku hipotezu na mukokelu te je obavljena ekscizijska biopsija (slika 2.). Područje incizije označeno je najprije skalpelom da se tkivo može odvojiti i tako doći do lezije. Pokazalo se da je bila prozirna i žućkasta, dobro ograničena i odvojena od tkiva. Tijekom odvajanja slučajno je skliznuo kirurški instrumentarij, što je uzrokovalo djelomičnu rupturu ciste, pa je iscurila viskozna tekućina slična mucinu. Kirurška rana zašivena je svilenim koncem 4,0, a uzorak je pohranjen u 10-postotni formalin radi daljnje anatomskopatološke analize. Makroskopski je kirurški uzorak izgledao kao dobro ograničeni smećkasti čvorić meke konzistencije dimenzija 2 x 1,8 x 0,9 milimetara. Translucentni materijal uočen je nakon poprečnoga reza kirurškog uzorka. Mikroskopskim pregledom ustanovljena je cistična šupljina djelomično obložena višeslojnim epitelom (slika 3.), a eozinofilni intraluminalni sadržaj odgovarao je degeneriranom keratinu i hemoragijskim područjima (slika 4. a). U šupljini ciste nađene su, osim oljuštenih, i raspršene stanice morfologije poput keratinocita, te većinom degenerirani keratin. Neke skvamozne stanice imale su eozinofilnu citoplazmu s keratohijalinim granulama (slika 4. b). Uočena je i ruptura obložnog epitela pa je bio degeneriran keratin u neposrednom doticaju s okolnim potpornim tkivom koje pokazuje reakciju gigantocelularnog tipa. Ovaj nalaz obilježavaju multinuklearne divovske stanice te upalne stanice koje reagiraju na keratin (slika 6.). Nakon tih pretraga postavljena je konačna dijagnoza – epidermoidna cista s upalnom reakcijom gigantocelularnog tipa.

Imunohistokemijska analiza (slike 6. i 7.) obavljena je standardnom metodom streptavidin-biotin-peroksidaze na rezovima udaljenima 5 μm od uzoraka uloženih u parafin te položenih na silanizirana predmetna stakalca. Tridesetominutno deparafiniranje uzoraka za dobivanje epitopa toplinom obavljeno je u otopini EZ Prep (Ventana; Tucson, AZ, SAD). Korištena su primarna protutijela na citokeratin AE1/3, citokeratin 34βE12, citokeratin 5/6, CD138 i Bcl-2. Upotrijebljen je bio BenchMarkTM XT IHC/ISH (Ventana; Tucson, AZ, SAD), automatizirani uređaj za bojenje, a indirektna imunoperoksidaza prikazana je s pomoću sustava XT Ultraview DAB v3 (Ventana; Tucson, AZ, SAD), nakon čega je korišten dijaminobenzidin (DAB). Rezovi su nakon toga obojeni Mayerovim hematoksilinom. Za svaku pretragu korišteni su pozitivni i negativni kontrolni uzorci. S obzirom na epitelnu komponentu dobiveni su snažno obojeni svi keratinociti i CD138, ali ne i Bcl-2. Intraluminarna komponenta bila je jako obojena u slučaju analiziranih citokeratina te jako do srednje kad je riječ o CD138. Nije bilo Bcl-2. Od bojenja upalnih komponenti, samo je protutijelo na Bcl-2 pokazalo fokalnu raspodjelu upalnih stanica.

Pacijent je na kontrole dolazio godinu dana nakon operacije, no nije bilo znakova recidiva.

Initially, anesthesia of the mental nerve and infiltrative terminal anesthesia in the proximities of the lesion were performed. The anesthesia was kept a safe distance from the lesion to prevent infusion of the anesthetic into the lesion and allow preservation of its reference margins. Following this procedure, aspiration puncture of the lesion was performed, and a yellow liquid similar to the mucin was obtained. The probable presence of mucin inside the lesion changed the diagnostic hypothesis to mucocele, and an excisional biopsy was performed (Figure 2). The area of the incision was delimited with a scalpel blade so that separation of the tissues could be performed and, consequently, expose the lesion. It was shown to be translucent and yellowed, well delimited and not adhering to the tissues. During the tissue separation procedure, the slip of a surgical instrument accidentally caused a partial rupture of the lesion, revealing a yellow and viscous liquid similar to mucin. The surgical wound was closed using a 4.0 silk suture, and the specimen was stored in 10% formol for further anatomopathological study. The macroscopic aspect of the surgical specimen showed a well-delimited brownish nodule with a soft consistency and measuring 2 x 1.8 x 0.9 mm. A translucent material was observed after the transverse section of the surgical specimen.

A microscopic examination showed a cystic cavity partially lined with stratified pavimentous epithelium (Figure 3), containing an intraluminal eosinophilic material compatible with degenerated keratin and hemorrhagic areas (Figure 4A). In the cystic lumen, squamous cells, along with dispersed cells with morphology similar to that of keratinocytes, were observed in the midst of this degenrated keratin. Some squamous cells exhibited an eosinophilic cytoplasm containing keratohyalin granules (Figure 4B). Additionally, rupture of the epithelial lining was observed, leaving the degenerated keratin in direct contact with the adjacent conjunctive tissue, which stimulated a giant- cell-type reaction. This finding was characterized by a massive presence of multinucleated giant cells and inflammatory cells reacting to the keratin (Figure 5). Thus, the final diagnosis was epidermoid cyst associated with an exuberant giant-cell- type inflammatory reaction.

Immunohistochemical analyses (Figures 6 and 7) were performed using the standard streptavidin-biotin-peroxidase method in 5 μm thick tissue sections that had been obtained from paraffin-embedded blocks and mounted on silanized microscopic slides. The steps from deparaffinization to the heat-induced epitope retrieval were performed with an EZ Prep solution (Ventana; Tucson, AZ, USA) for 30 minutes. The primary antibodies used in this study included Cytokeratin AE1/3, Cytokeratin 34βE12, Cytokeratin 5/6, CD138, and Bcl-2. The BenchMarkTM XT IHC/ISH (Ventana; Tucson, AZ, USA) automated slide stainer was used, and the indirect immunoperoxidase was detected by the XT Ultraview DAB v3 system (Ventana; Tucson, AZ, USA) followed by the use of diaminobenzidine (DAB). The sections were subsequently counterstained with Mayer hematoxylin. Positive extrinsic and intrinsic control samples were used in each assay. With regard to the epithelial component, a strong marking for all the cytokeratins used and CD138 was observed, but there was no marking observed for Bcl-2. With

respect to the intraluminal cystic component, a strong marking was observed for the analyzed cytokeratins, a medium marking for CD138, and an absence of marking for Bcl-2. With regard to the inflammatory component, only the antibody Bcl-2 showed focal marking for inflammatory cells.

The patient was clinically followed for 12 months after the surgery, and has shown no signs of recurrence of the lesion.

Rasprava

U slučaju otekline na obraznoj sluznici može se postaviti više kliničkih dijagnoza jer se mnoge lezije izgledom baš i ne razlikuju, što otežava kliničku dijagnozu. Među mogućim kliničkim dijagnozama nalaze se infektivni procesi odontogenog podrijetla koji pogađaju obrazne mišiće *m. maseter* i *m. buccinator*, pleomorfni adenom, limfoepitelna i dermoidna cista, mukokela, granulomatozna reakcija stranog tijela na kozmetičke *fillere* itd. (1, 14 – 17). Kad je riječ o opisanom slučaju, nakon aspiracijske punkcije postavljena je klinička hipoteza o mukokeli, iako se rijetko pojavljuje na obraznoj sluznici. To je učinjeno zahvaljujući transoperativnim nalazima, premda su i druge dijagnoze mogle doći u obzir.

Dermoidne ciste klasificirane su u tri kategorije: epidermoidna cista (cistična šupljina obložena je epitelom bez derivata kože), dermoidna cista (cistična šupljina uključuje i derivate kože poput kose, folikula dlake, znojnih i lojnih žlijezda) i teratoidna cista (uz kožne derivate u cističnoj šupljini nalaze se i elementi mezoderma poput kostiju, mišića te probavnog i dišnog tkiva) (1).

New i Erich (18) epidemiološki su pregledali 1459 epidermoidnih cista i pronašli da je sedam posto slučajeva povezano s područjem glave i vrata, a 1,6 posto uključivalo je usnu šupljinu. Taylor i suradnici (19) istaknuli su da je 6,5 posto, od 541 dermoidne ciste glave i vrata, bilo smješteno intraoralno. Rijetko su bile na jeziku, usnama i intraosealno unutar mandibule i maksile (2). Većina tih lezija pojavljuje se u središnjoj liniji ili u podjezičnom području dna usne šupljine te se može topografski klasificirati kao sublingvalno ili submentalno, ako se izme u obzir anatomski odnos s milohioidnim mišićem (1). Etiologija tih tumora je nepoznata. Smatra se da su nastali ili zbog sekvestracije epitela na mjestu spajanja tijekom embrionalnog procesa, ili se epitelno tkivo traumatski implantiralo u tkivo (1, 2, 20). Tradicionalno stajalište o postupku spajanja epitela upitno je jer ne objašnjava derivate kože u slučaju dermoidne ciste ili odsutnost dermoidne ciste u poznatim područjima spajanja poput nepca. Ozan i suradnici (1) te Rajayogeswaran i njegovi kolege (2) ne vjeruju u ta tradicionalna objašnjenja o nastanku lezija na obraznoj sluznici. Postoje dva oblika epidermoidne ciste: prirođeni i stečeni (3, 4, 20). Prirođeni se razvija pri bilo kojem spajanju u razvoju tijela dok se epidermoidno tkivo ne zaglavi u crti spajanja tijekom razvoja embrija. Posttraumatski, stečeni tip, ili implantacija keratinirane epidermoidne ciste, prema mišljenju većine autora, nastaje zbog traume određenog područja. Posttraumatski, stečeni oblik, ili implantacijsku keratiniziranu epidermoidnu cistu, većina autora opisuje kao rezultat neke prijašnje traume. Obično se

Discussion

Swellings in the buccal mucosa may lead to a series of clinical diagnoses, since some conditions may present in a similar manner making the diagnostic process difficult. Among the oral alterations compatible with the clinical condition presented in the present study, the following may be mentioned: infectious processes of odontogenic origin affecting the facial spaces of the masseter and buccinator muscles, pleomorphic adenoma, lymphoepithelial cysts, dermoid cysts, mucocele, and foreign body granulomatous reactions to cosmetic fillers (1, 14-17). With regard to the present case, after the aspiration puncture had been performed, the clinical hypothesis of mucocele was strongly supported, in spite of it being atypical in the buccal mucosa, particularly due to the transoperative features, although other diagnoses could also have been suggested.

Dermoid cysts have been classified into three categories: epidermoid cysts (the cystic cavity is lined with epithelium without skin appendages), dermoid cysts (the cystic cavity includes skin appendages such as hair, hair follicles, sebaceous, and sudoriferous glands), and teratoid cysts (in addition to the skin appendages in the cystic cavity one could observe elements of the mesoderm such as bone, muscle, gastrointestinal, and respiratory tissue), (1).

Epidemiologically, New and Erich (18) reviewed 1459 epidermoid cysts and found 7% of the cases related to the head and neck region and 1.6% involved the oral cavity. Taylor et al. (19) observed that 6.5% of 541 dermoid cysts of the head and neck region were located intraorally. Rare cases have been observed in the tongue, lips, and in interosseous sites in the mandible and maxilla (2). The large majority of these lesions affect the midline or sublingual region of the floor of the mouth, and may be topographically classified as sublingual or submental, taking into consideration their anatomic relationship with the mylohyoid muscle (1).

The etiology of these tumors is considered unknown. A suggested theory is that either the epithelium is sequestrated in lines of fusion during the embryonic process or the epithelial tissue is implanted in the tissues in a traumatic manner (1, 2, 20). However, the traditional view of the process of fusion of the epithelium has been contested because it does not explain the presence of skin appendages in dermoid cysts or the absence of dermoid cysts in known zones of fusion such as the palate. Ozan et al.1 and Rajayogeswaran et al. (2) do not believe in these traditional explanations for the appearance of the lesion in the buccal mucosa.

There are two types of epidermoid cysts: the congenital and the acquired (3, 4, 20). The congenital type develops at

stvara zbog pritiska tupog instrumenta ili predmeta koji potisne epitel u dermis. Kada počne cijeljenje, epitelne se stanice ponašaju kao kožni presadak u kojemu se stanice umnažaju pa se stvara centralna masa keratina koja nastavlja polako rasti. Posttraumatske ciste pojavljuju se ispod kožnog epitela, neposredno ispod ožiljka. Klinički je njihov nalaz vidljiv kao bezbolna izraslina koja sporo raste, s čvrstim i dobro ograničenim edemom koji se može palpirati ispod normalne površine epitela (3, 20). Prema povijesti bolesti, u opisanom slučaju nije poznato je li se dogodila bilo kakva trauma prije pojave lezije. Prema našem istraživanju (tablica 1.), u literaturi je opisano samo šest slučajeva epidermoidne ciste obrazne sluznice (1 – 3, 12, 13). Suprotno od našeg slučaja, dobiven je blagi omjer za pojavu na lijevoj obraznoj sluznici od 2 : 1 u *korist* žena (1 – 3, 12, 13). Obično je lezija pomična u tkivu (1 – 3), a razvija se od šest mjeseci do tri godine. Čini se da lokalna trauma s bolnim simptomima usmjerava pozornost pacijenata na lezije u oralnoj šupljini (tablica 1.) (2, 3).

Prvi slučaj epidermoidne ciste obrazne sluznice opisali su Schneider i Mesa 1978. godine. Radilo se o ženi od četrdesetak godina. Autori su bili uvjereni da njihov slučaj podupire teoriju implantacijske hipoteze površinskog epitela (12). Gutmann i suradnici povezali su atipični slučaj intradermalnog nevusa koji se pojavio u stijenki epidermoidne ciste (13). Lezija je opisana kao bolni edem na desnoj obraznoj sluznici dodatno traumatiziran ugrizima koji su istiskivali tvar sličnu gnoju. Autori smatraju da je veći dio lezije bila cista i da

any point of fusion in the development of the body where the ectodermal tissue becomes included in the line of fusion of the body during the embryonic process. The post-traumatic, acquired type, or implantation keratinizing epidermoid cyst, is characterized, by the majority of the authorities, as the result of some previous trauma at the site. It is generally produced by a blunt instrument or object, which may have driven epithelial cells into the dermis. When healing occurs, the epithelial cells may behave as a cutaneous graft, multiplying and producing a central mass of keratin that continues to grow slowly by expansion. Post-traumatic cysts are found under the epithelium of the skin, immediately below the site of the scar. Clinically, their presence is characterized by a slow, painless growth, with firm and well circumscribed edema, which is palpable below the normal surface of epithelium (3, 20). In the clinical history of the present case, it is not known for sure if any trauma occurred before the appearance of the lesion.

According to this study (Table 1), only six cases of epidermoid cysts arising in the buccal mucosa have been described in the literature (1-3, 12, 13). In contrast with this study's findings, a slight predilection for the female sex and for the left buccal mucosa has been observed at a ratio of 2:1 (1-3, 12, 13). Free mobility of the lesion in the tissues1-3 has been observed in the majority of cases. Moreover, the time of evolution ranged from 6 months to 3 years, and local trauma along with painful symptomatology appears to be the factor

Tablica 1. Pregled literature o epidermoidnim cistama iz obrazne sluznice
Table 1 Review of the literature about oral epidermoid cysts arising in the buccal mucosa.

Autor • Author	N	Spol • Gender	Dob (godine) • Age (years)	Strana • Side	Simptomatologija • Symptomatology	Trauma • Trauma	Veličina • Size	Trajanje • Onset	Terapija • Treatment
Schneider, Mesa 1978[12]	1	Ž • F	36	Desno • Right	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Ne • No	10 mm	NI	Kirurška ekscizija • Surgical excision
Schneider, Mesa 1978[12]	1	Ž • F	30	Lijevo • Left	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Ne • No	30 mm	3 god. • years	Kirurška ekscizija • Surgical excision
Gutmann et al., 1978[13]	1	Ž • F	48	Desno • Right	Bolno na pritisak • Painful to pressure	Da • Yes	15 mm	1 god. • year	Kirurška ekscizija • Surgical excision
Rajayogeswaran, Eveson 1989[2]	1	M	25	Lijevo • Left	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Da • Yes	20x15 mm	1 god. • year	Kirurška ekscizija • Surgical excision
Ozan et al., 2007[1]	1	Ž • F	38	Lijevo • Left	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Ne • No	20x30x40 mm	6 mj. • months	Kirurška ekscizija • Surgical excision
Kini et al., 2013[3]	1	M	25	Lijevo • Left	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Ne • No	15x15x15 mm	2 god. • years	Kirurška ekscizija • Surgical excision
Present study	1	M	29	Desno • Right	Asimptomatska intraoralna oteklina • Asymptomatic intraoral swelling	Da • Yes	35 mm	4 god. • years	Kirurška ekscizija • Surgical excision

Ž • F - žensko • female; M - muško • male; NI - nema informacija • not informed.

je nevus nastao neovisno o njoj (13). Rajayogeswaran i suradnici opisali su slučaj 25-godišnjeg pacijenta koji je došao s vidljivim edemom na lijevom obrazu, a otkriven je slučajno nakon okluzalne traume (2). Taj slučaj sličan je našemu jer je pacijent potražio pomoć stomatologa tek nakon što je trauma stvorila bolno stanje. Ozan i suradnici objavili su slučaj 38-godišnjeg pacijenta s vidljivim edemom u području lijevoga obraza iza komisure (1). Pacijent se pojavio s oteklinom nastalom prije šest mjeseci kada je bio podvrgnut neuspjeloj antibiotskoj terapiji. Nijekao je bilo kakav kirurški zahvat i/ili raniju traumu. Autori istraživanja vjeruju da se ipak dogodila neopažena trauma tijekom žvakanja, što je uzrokovalo ulceraciju pokrovne sluznice. Naime, traumu može objasniti strano tijelo i gigantocelularnu upalnu reakciju u vezi s prikazanim slučajem te djelomično obloženu stijenku ciste. Nakon traume možda se dogodio kontakt između keratinskog epitela i spojnog tkiva pa je stimulirao upalnu reakciju gigantocelularnog tipa i degeneraciju obložnog epitela. Prema autorovim spoznajama, još nije objavljen slučaj epidermoidne ciste s upalnom gigantocelularnom reakcijom na strano tijelo. Slično našem slučaju, Orozco-Covarrubias i suradnici (21) opisali su 75 slučajeva pedijatrijskih pacijenata s ekstraoralnim lokacijama dermoidnih cista, od kojih je 17 pokazivalo reakciju gigantskih stanica na strano tijelo. Malo je informacija o mogućem imunološkom profilu epidermoidne ciste. Nakamura (22) je opisao svojstva tih cista na temelju deset slučajeva kožnih lezija i pronašao je negativnu imunoreaktivnost na molekule vezane za apoptozu (ssDNA, odlomak lamin A, gama-H2AX, i odlomak caspase-3). CD138 bio je imunohistokemijski izražen u skvamoznom epitelu (većinom u bazalnom i spinoznom sloju), ali ne u keratiniziranim komponentama. Ti nalazi potvrđeni su u našem slučaju u kojemu je korišteno signalno protutijelo (Bcl-2) za apoptozu također bilo negativno. Molekula se smatra onkogenom ako inhibira programiranu staničnu smrt. Slično tomu je, u našem slučaju, otkriven imunosni izražaj CD138 u slojevima skvamoznog epitela, osim u gornjim dijelovima spinoznoga sloja (22, 24). Taj antigen površinska je molekula koja se obično nalazi u bazalnom i suprabazalnim slojevima te djeluje kao medijator stanične adhezije (22, 25). Terada je u svojem istraživanju (26) uočio pozitivna obilježja citokeratina CK5/6 i CK34BE14 u slučaju epidermoidne ciste kože povezane s karcinomom skvamoznih stanica. Taj isti imunosni profil pronađen je u našem istraživanju – naime, snažnu imunoreaktivnost pokazivali su skvamozni epitel i raspršeni keratin u cističnoj šupljini. Citokeratini odgovaraju velikoj grupi filamentoznih proteina povezanih s najmanje 54 humana funkcionalna gena u svim epitelnim stanicama (27, 28). U opisanom slučaju, epitel oralne sluznice u histološkim rezovima, koji je korišten kao unutarnja pozitivna kontrola, pokazao je obilnu i homogenu imunoreaktivnost za CK5/6 i CK34BE14.

Međunarodna znanstvena literatura jedinstvena je u vezi s terapijom epidermoidne ciste. Svi se slažu da je treba kirurški ukloniti i uzorke poslati na histopatološku analizu (1 – 5, 13, 17, 20). Dermoidna i epidermoidna cista rijetko su maligne. Prema istraživanju Ozana i suradnika, pronađeni su samo izolirani slučajevi malignosti ili premalignosti povezani s

that draws the patient's attention to the presence of the lesion in the oral cavity (Table 1), (2, 3).

The first two cases of epidermoid cyst in the buccal mucosa related in the literature were published by Schneider, Mesa in 1978 and involved women in the fourth decade of their lives. The authors believed that the cases were supported by the theory of implantation of the histogenesis of surface epithelium (12). Gutman et al. reported on an atypical case of intradermal nevus which appeared to involve the wall of an epidermoid cyst (13). The lesion presented as a painful edema in the right buccal mucosa and was traumatized by biting it, which eventually drained material similar to puss on the surface of the mucosa. The authors believed that the cyst comprised the major portion of the lesion, and originated independently of the associated nevus (13). Rajayogeswaran et al. described the case of a 25-year-old patient who presented a visible edema in the left cheek, which was discovered accidentally after an occlusal trauma (2). This may be similar to the present case, since the patient only sought dental treatment after trauma in the region which produced painful symptomatology. Ozan et al. published the case of a 38-year-old patient who presented a visible edema in the left cheek posterior to the commissure (1). The patient presented a swelling six months before and underwent an unsuccessful antibiotic therapy. The patient denied any history of surgery and/or previous trauma in the region. However, the authors of this study believe that a non-noticeable trauma had occurred during masticatory activity and caused the ulceration of the covering mucosa.

The presence of a trauma may explain the presence of the foreign body gigantocellular inflammatory reaction associated with the present case and the partially lined cystic wall. After the trauma, the contact between the epithelial keratin and the conjunctive tissue may have occurred, stimulating an intense giant-cell type reaction followed by degeneration of the epithelial lining. To the authors' knowledge, no cases of oral epidermoid cysts associated with intense foreign body gigantocellular inflammatory reaction have been published. Similarly to the present case, Orozco- Covarrubias et al. (21) reported a case series of 75 pediatric patients with extra-oral dermoid cysts. Of these cases, 17 lesions showed foreign body giant-cell reactions.

There is scarce information about the immunoprofile of oral epidermoid cysts. Nakamura (22) described the epidermoid cyst features in 10 cases of skin lesions. Negative immunoreactivity to apoptosis-related molecules (ssDNA, cleaved lamin A, gamma-H2AX, and cleaved caspase-3) was observed. CD138 was immunohistochemically expressed in the squamous epithelium (mainly in the basal and spinous layers) but not in the keratinizing components. These findings were observed in the present case, in which the apoptosis-signaling antibody (Bcl-2) used was also negative. This molecule is considered an oncogene that inhibits programmed cell death, and, similarly, CD138 immunoexpression was detected in the present case in the squamous epithelium layers, except in the upper part of the spinous layer (22, 24). This antigen is a cell surface molecule usually expressed in basal and suprabasal layers, functioning as a mediator of cell adhe-

podlogom epidermoidne ciste. Bhatt i njegovi kolege opisali su karcinom skvamoznih stanica u sklopu obložnoga epitela epidermoidne ciste dna usne šupljine povezane s podjezičnom žlijezdom slinovnicom. Devine i Jones (29) uočili su karcinomatoznu transformaciju podjezične dermoidne ciste. Svi ti autori ističu da, iako je maligna preobrazba tih lezija rijetka, liječnici dentalne medicine moraju oprezno ocijeniti svaki podjezični edem koji ne prolazi i poslati uzorak na histopatološku analizu (5).

Prema kliničkim znakovima i obilježjima prikazanog slučaja, premda rijetka na obraznoj sluznici, epidermoidna cista mora se uključiti u diferencijalnu dijagnostiku oteklina toga anatomskog područja. Ta lezija može biti slična različitim uobičajenim oralnim patološkim pojavama, poput mukokela. Dodatno treba obaviti imunohistokemijske pretrage zbog boljeg razumijevanja bioloških aspekata tih lezija, posebice fenomena u vezi sa shvaćanjem stanične smrti.

sion (22, 25). In another study, Terada (26) observed positive marking for the cytokeratins CK5/6 and CK34BE14 in an epidermoid cyst of the skin associated with a squamous cell carcinoma. The same immunoprofile was shown in the present report, in which both squamous epithelium and dispersed keratin in the cystic lumen showed strong immunoreactivity. Cytokeratins correspond to a vast group of filamentous proteins related to at least 54 human functional genes that are expressed in all epithelial cells (27, 28). The epithelium of the oral mucosa present in the histological cuts of the present case, which served as an internal positive control, showed abundant and homogeneous immunomarking for both CK5/6 and CK34BE14.

International scientific literature is unanimous with regard to the treatment modality for epidermoid cysts, which consists of a complete surgical removal of the lesion and afterwards sending the specimen for histopathological analysis (1-5,13,17,20). Dermoid and epidermoid cysts rarely undergo malignant transformation. According to Ozan et al, only the isolated cases of malignancy or pre-malignancy have been associated with the lining of epidermoid cysts. Bhatt et al. described the case of a squamous cell carcinoma that appeared in the epithelium of an epidermoid cyst in the floor of the mouth, associated with the sublingual gland. Devine, Jones (29) reported a case of carcinomatous transformation of a sublingual dermoid cyst. In conclusion, the previous authors emphasized that although the malignant transformation of these lesions is rare, dentists must be more careful with every persistent sublingual edema and have a low threshold for the excision of specimens for histopathologic examination (5).

According to the clinical characteristics observed in the present case, although relatively uncommon in the buccal mucosa, the epidermoid cyst must be included in the differential diagnosis of swellings in this anatomic site. This lesion may be similar to various common oral pathological entities, such as the mucocele. In addition, further immunohistochemical studies should be conducted in order to gain better understanding of the biologic aspects relative to this lesion, especially the phenomena related to the process of cell death.

Sukob interesa:

Ne postoji

Competing interests

None declared

Abstract
Epidermoid cysts are benign subcutaneous lesions, and the large majority of these cysts affect the floor of the mouth; however, the buccal mucosa is not the usual site of occurrence. To date, only 5 articles have been published with 6 cases of epidermoid cysts arising in the buccal mucosa. Therefore, the aim of this study was to describe the clinical, histopathological and immunohistochemical features of a case of an epidermoid cyst located in the buccal mucosa. To our knowledge, this is the first report of an oral epidermoid cyst describing an intense foreign body gigantocellular inflammatory reaction against epithelial keratin component. Although the usual diagnosis for epidermoid cysts is based on histopathological findings, this case report addresses novel information regarding the immunohistochemical pattern which may be found in these lesions.

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Epidermal Cyst; Mouth Mucosa, immunohistochemistry

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