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PRIKAZ SLUČAJA
CASE REPORT

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Epidermoidna cista nastala na bukalnoj sluznici: prikaz slučaja i pregled literature

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

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Sažetak
Epidermoidne ciste benigne su supkutane lezije vrlo česte u dnu usne šupljine, a rijetke na bukalnoj mukozi. Do danas je objavljeno pet članaka o samo šest slučajeva epidermoidnih cista na tom mjestu. Svrha ovoga članka je opisati klinička, histopatološka i imunohistokemijska obilježja epidermoidne ciste na bukalnoj sluznici. Prema našim spoznajama, ovo je prvi slučaj oralne epidermoidne ciste koja izaziva upalnu reakciju gigantocelularnog tipa prema epitelnom keratinu. Iako se uobičajeni dijagnostički postupak u slučaju epidermoidne ciste temelji na histopatološkom nalazu, u ovom prikazu nalaze se nove informacije o imunohistokemijskim uzorcima u ovakvim lezijama.

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Ključne riječi
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Uvod

Dermoidna, epidermoidna ii teratoidna cista neodontogene su lezije nastale iz zametnog epitela (1). Dermoidna cista može se pojaviti bilo gdje na tijelu, posebice tamo gdje se spajaju zametni slojevi. Uglavnom nastaje na jajnicima, testisima, rukama ii nogama (1 – 3). Lezije su prekrivene epidermisom i sadržavaju kožne elemente kao što su žlijezde lojnice, znojnice i folikuli. Ako nema kožnih elemenata, klasificira se kao epidermoidna ili epidermalna cista. Nije povezana s dermoidnim cistama gonada koje su klasificirane kao teratomi (1 – 4).

Epidermoidne ciste benigne su supkutane lezije i čine 85 do 90 posto cista (5). Većina nastaje u središnjoj liniji ili u sublingvalnoj regiji. Na bukalnoj sluznici ne pojavljuju se če-

Introduction

The dermoid, epidermoid, and teratoid cysts are non-odontogenic 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

sto (6 – 11). Do danas je objavljeno pet članaka o šest slučajeva epidermoidnih cista u području buklane sluznice (1– 3, 12, 13). Svrha ovog istraživanja bila je opisati klinička, histopatološka ii imunohistokemijska obilježja epidermoidne ciste nastale na bukalnoj sluznici. Prema autorovim riječima, ovo je prvi prikaz oralne epidermoidne ciste koja izaziva upalnu reakciju gigantocelularnog tipa prema epitelnom keratinu. Iako se uobičajeni dijagnostički postupak u slučaju epidermoidne ciste temelji i na histopatološkom nalazu, ovaj prikaz otkriva nove informacije o imunohistokemijskim uzorcima u ovakvim lezijama.

Prikaz Slučaja

U Stomatološku kliniku Federalnog sveučilišta Ceará u Sobral Campusu u Brazilu primljen je 29-godišnji pacijent. Žalio se na bezbolnu intraoralnu oteklinu na bukalnoj sluznici (prvi put je bila uočena prije četiri godine). Prema njegovim riječima, lezija je bila traumatizirana nekoliko puta i uzrokuje mu blagu disfagiju. Tijekom ekstraoralnoga pregleda uočena je asimetrija lica u području desnog spoja usana. Na kliničkom pregledu nisu zapaženi povećani limfni čvorovi glave i vrata, nego samo kvrgava ulcerirana izraslina gumene konzistencije promjera 3,5 centimetara na desnoj strani bukalne sluznice (slika 1. a – d).

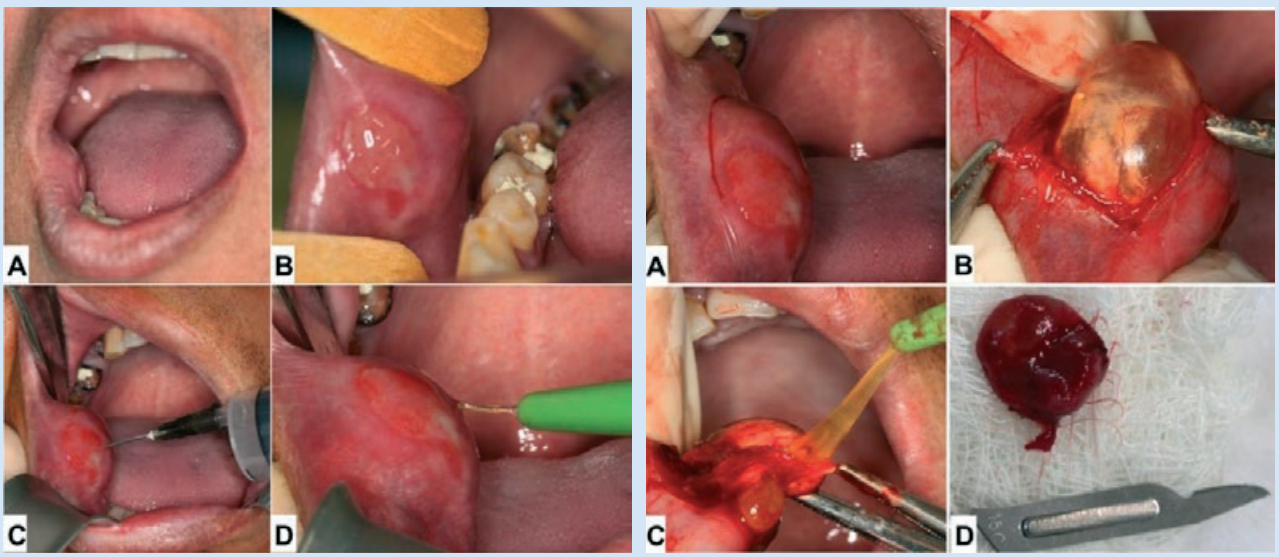
Prema kliničkim nalazima, početna dijagnoza bila je benigna lezija žlijezde slinovnice, odnosno pleomorfni adenom. Zbog moguće pojave maligne lezije povezane s dugim

cysts develop in the midline or sublingual region of the mouth floor, the buccal mucosa is not a usual site of occurrence (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 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 new information regarding the immunohistochemical pattern that may be found in these lesions.

Case Report

A 29-year-old man visited the Stomatology outpatient clinic of the Federal University of Ceará, Sobral Campus, Brazil, complaining of a painless intraoral swelling in the buccal mucosa (firstly 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 1a-d).

Due to these clinical findings, the initial diagnosis was benign salivary gland lesions. More precisely, the pleomor-

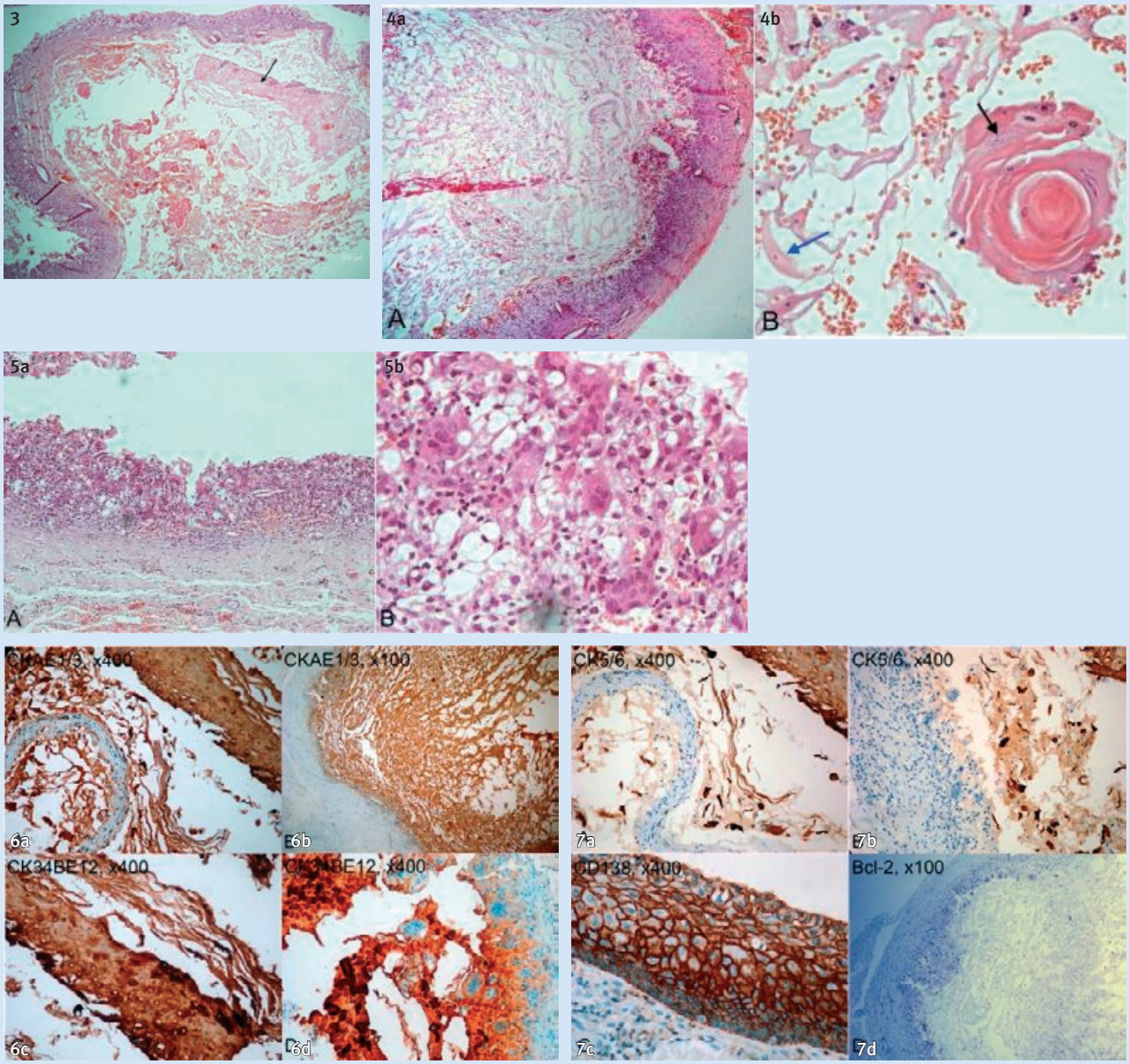


Slika 1. a i b) Kliničkim pregledom otkrivena je oteklina desne strane bukalne sluznice s ulceriranom površinom; c,d) Aspirativnom punkcijom dobivena je žuta viskozna tekućina slična mucinu

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

Slika 2. **a** i b) Transoperativni pogled na leziju nakon disekcije tkiva; c) Prisutnost viskozne žute tekućine nakon slučajne rupture ciste; d) Makroskopski pogled kirurškog uzorka

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. Fotomikrografija – cistična šupljina djelomično je obložena višeslojnim epitelom (crna strelica) koji sadržava eozinofilnu tvar u lumenu kompatibilnu s degeneriranim keratinom (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**) Fotomikrografija – cistični lumen ispunjen degeneriranim keratinom (HE, x 100), pogled pod većim povećanjem (HE, x 400) cističnog lumena koji pokazuje depozite keratina koji sadržavaju granule keratohijalina (crna strelica) i disperzne keratinocite (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) Fotomikrografija – cistični zid s intenzivnom gigantocelularnom uplanom reakcijom na komponentu epitelnog keratina (HE, x 100); b) Veliko povećanje multinuklearnih orijaških stanic i 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 profil – a,c) Snažan odgovor epitalnog makera na citokeratine; b i d) Intraluminalna cistična komponenta pokazuje snažan odgovor markera za degenerirani keratin te izostanak markera za multinuklearne orijaške stanice

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 profil – a i b) Epitelna komponenta i disperzni luminalni keratin pokazuju snažan odgovor markera za citokeratin 5/6; c) Marker CD138 za stanice u bazalnom i spinoznom sloju pločastoga epitela; d) Izostanak markera za Bcl-2 u epitelnoj i intraluminalnoj cističnoj komponenti

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.

razvojem inicijalne otekline, obavljena je incizijska biopsija u lokalnoj anesteziji (slika 2. a – d).

Anesteziran je *N. mentalis* te je anestetik perilezijski injiciran pazeći pritom da su ubodna mjesta dalje od lezije kako bi se prevenirao ulazak anestetika u oteklinu i održao integritet njezinih rubova. Zatim je obavljena punkcijska aspiracija sadržaja iz lezije iz koje je izvučena žuta tekućina slična mucinu. Moguća prisutnost mucina u punktatu promijenila je dijagnozu u mukokelu, pa je obavljena ekscizijska biopsija (slika 2. a – d). Područje incizije određeno je skalpelom te je omogućeno razdvajanje tkiva kako bi se odvojila lezija. To je pokazalo da je lezija prozirna i žućkasta, dobro ograničena i rahlo spojena s okolnim tkivom. Tijekom zahvata je, zbog nespretnoga rukovanja instrumentom, nastala ruptura pa je iscurila žuta viskozna tekućina slična mucinu. Nakon toga je rana je zašivena svilom 4,0, a ekscidirani uzorak pohranjen je u 10-postotni formaldehid radi daljnjeg istraživanja. Makroskopskim pregledom ustanovljen je dobro ograničeni smećkasti nodul meke konzistencije, dimenzija 2 x 1,8 x 0,9 milimetara. Prozirni materijal uočen je nakon što je što je transverzalno prerezan kirurški uzorak.

Mikroskopskim pregledom ustanovljena je cistična šupljina obložena višeslojnim epitelom (slika 3.) koja je sadržavala eozinofilni materijal sličan degenerativnom keratinu s područjima krvarenja (slika 4. a). U cističnom lumenu nalazile su se pločaste stanice i razbacane stanice morfološki slične keratinocitima pomiješane s degenerativnim keratinom. Poneke pločaste stanice imale su eozinofilnu citoplazmu s granulama keratohijalina (slika 4. b). Uočena je i ruptura epitelne ovojnice pa je degenerirani keratin bio u izravnom kontaktu s vezivnim tkivom, što je stimuliralo gigantocelularnu reakciju. Ovaj nalaz obilježavaju multinuklearne orijaške stanice te upalne stanice koje su reagirale na keratin (slika 5. a, b). Stoga je krajnja dijagnoza glasila epidermoidna cista povezana s burnom upalnom reakcijom gigantocelularnih stanica.

Imunohistokemijska analiza (slika 6. a – d i 7. a – d) obavljena je standardnom metodom streptavidin-biotin-peroksidaze na 5 µm debelim preparatima tkiva koji su dobiveni iz parafinskih blokova i preneseni na silanizirana predmetna stakalca. Postupci deparafinizacije toplinom induciranoga epitopa provedeni su 30 minuta otopinom EZ Prep (Ventana; Tuscon, AZ, SAD). Primarna antitijela korištena u ovom istraživanju uključivala su citokeratin AE1/3, 4βE12 i 5/6, zatim CD138 i Bcl-2. Kao automatizirani bojač preparata korišten je Bench Mark TM XT IHC/ISH (Ventana; Tucson, AZ, SAD). Indirektna imunoperoksidaza detektirana je sistemom XT Ultraview DAB v3 (Ventana; Tucson, AZ, SAD) te upotrebom diaminobenzidina (DAB). Preparati su zatim obojeni Mayerovim hematoksilinom. Pozitivni vanjski i unutarnji kontrolni uzorci korišteni su u svakom testu. Kod epitelne komponente uočeno je snažno obilježavanje svih citokeratina i CD138, ali ne Bcl-2. Kod intraluminalne komponente zabilježeno je snažno obilježavanje svih citokeratina, srednje jako za CD138, a za Bcl-2 uopće ga nije bilo. Upalne stanice žarišno su reagirale jedino na antitijela Bcl-2.

Pacijent je klinički praćen 12 mjeseci nakon kirurškoga zahvata te u tom razdoblju nije uočen recidiv lezije.

phic 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 development, an incisional biopsy was performed under local anesthesia, (Figure 2a-d).

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 2a-d). 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 adhered 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 exam 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 5a, b). Thus, the final diagnosis was epidermoid cyst associated with an exuberant giant-cell-type inflammatory reaction.

Immunohistochemical analyses (Figures 6a-d and 7a-d) 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 surgery, and has shown no signs of recurrence of the lesion.

Rasprava

Oteklina bukalne sluznice može rezultirati nizom kliničkih dijagnoza zato što su neka stanja slična, što uvelike otežava ispravno dijagnosticiranje. Osim dijagnoze za ovaj slučaj, diferencijalna dijagnoza može uključivati upalni proces odontogenog podrijetla koji zahvaća područje masetera i obrazne mišiće (1), pleomorfnni adenom (14), limfoepitelijalnu cistu (15), dermoidnu cistu (1), mukokelu (16) i granulomatoznuu reakciju na strano tijelo, kao što su estetski fileri (17). U ovom slučaju, nakon punkcije otekline, hipotetska klinička dijagnoza upućivala je na mukokelu, iako je lokacija bila atipična pa su u obzir mogle doći i diferencijalne dijagnoze.

Dermoidnu cistu možemo klasificirati u tri kategorije – kao epidermoidnu (cistična šupljina obložena epitelom bez kožnih elemenata), dermoidnu (u cističnoj šupljini kožni su elementi kao što su dlake, folikuli, lojne i znojne žlijezde) te teratoidnu (osim kožnih elemenata mogu se naći i elementi mezoderma, kao što su kost, mišić te gastrointestinalno i respiratorno tkivo) (1).

New i Erich (18) pripremili su pregled literature s epidermiološkog stajališta pa su pregledali 1459 zabilježenih slučajeva cista i pronašli da je sedam posto svih povezano s regijom glave i vrata, a samo 1,6 posto s oralnom šupljinom. Taylor i suradnici (19) uočili su da je 6 posto od 541 dermoidne ciste glave i vrata nastalo u usnoj šupljini. Rijetki slučajevi zabilježeni su u području jezika, usnice te intraosealno u maksili ili mandibuli (2). Velika većina intraoralnih lokacija uključuje središnju liniju ili bilo koje sublingvalno područje te se topografski može klasificirati kao sublingvalna ili submentalna cista, uzimajući u obzir njihov anatomski odnos prema milohioidnom mišiću (1).

Etiologija ovih tumora je nepoznata. Teorije o nastanku ciste navode mogućnost zaostaloga epitela kod spajanja tijekom embrionalnog razvoja ili inserciju epitelnog tkiva zbog nekog traumatskog događaja (1, 2, 20). Klasična teorija o nastanku, koja podupire mogućnost zaostaloga epitela tijekom razvoja, osporena je jer ne objašnjava pojavu kožnih elemenata u dermoidnoj cisti ni izostanak dermoidnih cista u poznatim zonama fuzije kao što je nepce. Ozan i suradnici. (1) te Rajayogeswaran i njegovi kolege. (2) ne vjeruju u tradicionalno objašnjenje o nastanku tih lezija u bukalnoj sluznici.

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 (1), pleomorphic adenoma (14), lymphoepithelial cysts (15) dermoid cysts (1), mucocele (16), and foreign body granulomatous reactions to cosmetic fillers (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 related in the tongue, lips, and in intraosseos 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

Dvije su vrste epidermoidnih cista – kongenitalne i stečene (3, 4, 20). Kongenitalne nastaju u bilo kojem trenutku razvoja organizma tijekom spajanja kada je ektoderm uključen u liniju spajanja tijela za vrijeme embriogeneze. Kako smatraju stručnjaci, stečene posttraumatske ciste, ili implantirana keratinizirana epidermoidna cista, rezultat su traume na mjestu nastanka. Najčešće nastaju tupim instrumentom ili nekim drugim predmetom koji utisne epitelne stanice u dermis. Kada cijeljenje završi, epitelne se stanice mogu ponašati kao kožni presadak čije se stanice umnožavaju i proizvode središnju masu keratina koji raste i širi se. Posttraumatske ciste mogu se pronaći i u kožnom epitelu, odmah ispod lokacije ožiljka. Cista se klinički očituje kao tvrd, ograničen i bezbolan edem koji sporo raste i može se palpirati ispod normalne površine epitela (3, 20). U opisanom slučaju nije poznato je li se prije nastanka lezije dogodila kakva trauma.

U pregledu literature (tablica 1.) zabilježeno je samo šest slučajeva epidermoidne ciste na obraznoj sluznici (1 – 3, 12, 13). U kontrastu s tim rezultatima jest blaga sklonost prema pojavnosti cista kod žena i to na lijevoj strani obrazne sluznice u omjeru 2 : 1 (1, 12, 13). U gotovo svim slučajevima lezija je u mekom tkivu sluznice bila pomična (1 – 3). Vrijeme razvoja iznosilo je od šest mjeseci do tri godine. Glavni simptomi zbog kojih su pacijenti obratili pozornost na leziju bili su lokalna trauma i bol (tablica 1.) (2, 13).

Prve epidermoidne ciste u bukalnoj sluznici opisali su 1978. Schneider i Mesa (12). Pronađene su kod žena u dobi između četrdeset i pedeset godina. Autori su smatrali da su

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 ones (3, 4, 20). The congenital type develops at 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 authors, 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, its 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 bucal 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,

Tablica 1. Pregled literature o oralnim epidermoidnim cistama nastalima na bukalnoj sluznici
Table 1 Review of the literature about oral epidermoid cysts arising in the bucal mucosa.

Autor • Author	N	Rod • Gender	Dob • Age (years)	Strana • Side	Simptomatologija • Symptomatology	Trauma	Promjer • Size	Trajanje • Onset	Tretman • Treatment
Schneider, Mesa 1978[12]	1	F	36	Desna • Right	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Ne • No	10 mm	Nema podataka • NI	Kirurški uklonjena • Surgical excision
Schneider, Mesa 1978[12]	1	F	30	Lijeva • Left	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Ne • No	30 mm	3 godine • 3 years	Kirurški uklonjena • Surgical excision
Gutmann i sur., 1978.[13] • Gutmann et al., 1978[13]	1	F	48	Desna • Right	Bolna na pritisak • Painful to pressure	Da • Yes	15 mm	1 godina • 1 year	Kirurški uklonjena • Surgical excision
Rajayogeswaran, Eveson 1989[2]	1	M	25	Lijeva • Left	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Da • Yes	20x15 mm	1 godina • 1 year	Kirurški uklonjena • Surgical excision
Ozan i sur., 2007.[1] • Ozan et al., 2007[1]	1	F	38	Lijeva • Left	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Ne • No	20x30x40 mm	6 mjeseci • 6 months	Kirurški uklonjena • Surgical excision
Kini et al., 2013[3] • Kini i sur., 2013.[3]	1	M	25	Lijeva • Left	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Ne • No	15x15x15 mm	Dvije godine • 2 years	Kirurški uklonjena • Surgical excision
Prezentirane studije • Present study	1	M	29	Desna • Right	Asimptomatska intraoralna oteklina • Asymptomatic intra-oral swelling	Da • Yes	35 mm	4 godine • 4 years	Kirurški uklonjena • Surgical excision

F, female • feminum; M, male • masculinum; NI, not informed.

uzroci ili implantacija epitela tijekom histogeneze ili insercija površinskog epitela. Gutman i suradnici (13) uočili su atipičnu pojavu intradermalnog madeža u epitelnoj ovojnici epidermoidne ciste. Lezija se očitovala kao bolna oteklina na desnoj strani bukalne sluznice iz koje je, nakon traumatiziranja zagrizom, iscurio sadržaj sličan gnoju. Autori su smatrali da je cista činila veći dio lezije te da je nastala neovisno o madežu (13). Rajayogeswaran i njegovi kolege (2) opisali su slučaj 25-godišnjeg pacijenta s oteklinom na lijevom obrazu koja je slučajno otkrivena nakon okluzalne traume. Taj slučaj sličan je našemu – pacijent je zatražio stomatološku pomoć tek nakon što je trauma lezije izazvala bol. Ozan i suradnici (1) objavili su slučaj pacijenta u dobi od 38 godina kod kojega je otkriven edem lijeve strane obraza posteriorno od komisure. Naveo je da je šest mjeseci prije bio neuspješno liječen antibioticima. Negirao je bilo kakav kirurški zahvat ili traumu u području lezije. Unatoč tomu autori su uočili okluzalnu traumu koja je uzrokovala ulceraciju pokrovne sluznice.

Trauma u ovom slučaju može objasniti upalnu gigantocelularnu reakciju povezanu sa stranim tijelom te djelomično obloženu cistu. Naime, nakon traume kontakt epitelnog keratina i vezivnog tkiva stimulira intenzivnu gigantocelularnu reakciju praćenu degeneracijom epitela. Prema riječima autora, u literaturi nije opisan slučaj epidermoidne ciste povezane s intenzivnim gigantocelularnim upalnim odgovorom na strano tijelo. Orozco-Covarrubias i suradnici (21) opisali su 75 pedijatrijskih slučajeva s ekstraoralnim dermoidnim cistama. Među njima je 17 lezija bilo zahvaćeno gigantocelularnim upalnom reakcijom.

Vrlo je malo informacija o imunoprofilu oralnih epidermoidnih cista. Nakamura (22) je opisao značajke epidermoidnih cista na temelju deset slučajeva kožnih lezija. Zabilježen je negativan imunološki odgovor na molekule povezan s apoptozom (ssDNK, rascijepljeni lamin A, gama-H2AX te rascijepljena kaspaza-3). CD138 imunohistokemijski je izražen u pločastom epitelu (uglavnom u bazalnom i nazubljenom sloju), ali ne i u keratiniziranom sloju. Isti rezultati dobiveni su i u ovom istraživanju – korišteno je antitijelo koje signalizira apoptozu (Bcl-2), a dalo je negativni rezultat. Ova molekula je onkogen koji inhibira programiranu smrt stanice (22 – 14) te slično kao i kod CD138, u ovom je slučaju imunoekspresija detektirana u sloju pločastog epitela, ali ne i u gornjem spinoznom sloju. Ovaj antigen je molekula s površine stanice koja se obično nalazi u bazalnom i suprabazalnom sloju te djeluje kao medijator adhezije stanica (22, 25). Tekada (26) je u svojem istraživanju uočio pozitivne markere za citokeratine CK5/6 i CK34BE14 u epidermoidnoj cisti povezanoj s karcinomom pločastih stanica. Isti imunoprofil bio je i u ovom slučaju – pločasti epitel i raspršeni keratin u lumenu ciste pokazali su jaki imunosni odgovor. Citokeratini se ubrajaju u veliku grupu proteina povezanih s najmanje 54 funkcionalna gena u epitelnim stanicama (27, 28). Epitel oralne sluznice u histološkim preparatima u ovom je slučaju poslužio kao pozitivna kontrola te je pokazao izrazito homogeno markiranje za CK5/6 i CK34BE14.

U znanstvenoj literaturi istaknuta je suglasnost kad je riječ o načinu liječenja epidermoidnih cista. Postupak se sastoji od potpunoga kirurškog uklanjanja lezije i histopatološke

(1, 12, 13). Free mobility of the lesion in the tissues has been observed in the majority of cases (1-3). Moreover, the time of evolution ranged from 6 months to 3 years, and local trauma along with painful symptomatology appears to be the factor that draws the patient's attention to the presence of the lesion in the oral cavity (Table 1), (2, 13).

The two first cases of epidermoid cyst in the buccal mucosa described in the literature, were published by Schneider, Mesa in 1978 (12), 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. Gutman et al. (13) related an atypical case of intradermal nevus which appeared to involve the wall of an epidermoid cyst. 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.[2] 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. This fact 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. (1) published the case of a 38-year-old patient who presented a visible edema in the left cheek posterior to the commissure. The patient presented a swelling six months previously and had submitted to 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 accurred, 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 current 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 current case, in which the used the apoptosis-signaling antibody (Bcl-2) used was also negative. This molecule is considered an oncogene that inhibits programmed cell death (22-14), and, similarly, CD138

analize (1 – 5, 13, 17). Dermoidna i epidermoidna cista rijetko postaju maligne. Prema mišljenju Ozana i suradnika, samo su izolirani slučajevi maligniteta ili predmaligniteta povezani sa staničnim slojem epidermoidnih cista. Bhatt i njegovi kolege opisali su slučaj karcinoma pločastih stanica koji je nastao u epitelnom sloju epidermoidne ciste locirane na dnu usne šupljine povezane sa sublingvalnom žlijezdom (1, 5). Devine i Jones (29) zabilježili su karcinogenu transformaciju sublingvalne dermoidne ciste. Svi su autori istaknuli da stomatolozi moraju, iako su maligne alteracije rijetke, vrlo detaljno pregledati svaki perzistentni sublingvalni edem te imati stroge kriterije za eksciziju lezije i naknadnu histopatološku obradu (5).

Prema svim kliničkim obilježjima u ovom slučaju, iako vrlo rijetkom zbog lokacije u bukalnoj sluznici, epidermoidna cista mora biti uključena u diferencijalnu dijagnozu svake otekline na tom anatomskom mjestu. Ova lezija slična je ostalim patološkim entitetima u oralnoj šupljini, kao što je mukokela. Treba istaknuti da je potrebno daljnje imunohistokemijsko istraživanje kako bismo bolje razumjeli biološke aspekte povezane s ovom lezijom, posebice proces povezan sa staničnom smrti.

Sukob interesa

Nije prijavljen.

immunoexpression was detected in the present case in the squamous epithelium layers, except in the upper part of the spinous layer. This antigen is a cell surface molecule usually expressed in basal and suprabasal layers, functioning as a mediator of cell adhesion (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 samples of the present case, which functioned as 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 complete surgical removal of the lesion and afterwards sending the specimen for histopathological analysis (1-5, 13, 17). Dermoid and epidermoid cysts rarely undergo malignant transformation. According to Ozan et al. only 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 (1, 5). Devine, Jones (29), reported a case of carcinomatous transformation of a sublingual dermoid cyst. To sum up, 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.

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 a 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 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 to the immunohistochemical pattern that may be found in these lesions.

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Key words
Epidermal cyst; Mouth Mucosa; Immunohistochemistry

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