

TERAPIJA PARODONTALNOG APSCESA

THE THERAPY OF PERIODONTAL ABSCESS

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Parodontalni apsces predstavlja urgentno stanje u stomatologiji, sa zastupljenošću 7-14% svih urgentnih stanja u stomatologiji. Uzroci nastanka su mnogobrojni: egzacerbacija parodontopatije, impakcija stranih tela, promena morfologije korena itd. Pri postavljanju dijagnoze treba uzeti u obzir analizu celokupnih simptoma i znakova. Mikroorganizmi izolovani iz parodontalnog apscesa nisu specifični, ali dominiraju Gram negativni striktni anaerobi. Zub sa parodontalnim apscesom ima lošu prognozu i veći je rizik za njegov gubitak.

Terapija parodontalnog apscesa je predstavljala izazov dugi niz godina. U prošlosti, parodontalni apsces kod parodontopatičnog zuba bio je glavni razlog njegove ekstrakcije. U literaturi se ne nalazi dovoljno naučnih dokaza koji bi istakli jedinstveni terapijski protokol. Danas se govori o tri terapijska pristupa u rešavanju ovog problema: drenaža i kiretaža apscesa, sistemska primena antibiotika i parodontalna hirurģija u hroničnoj fazi oboljenja.

Bitni faktori uspešne terapije su lokalizacija akutnog parodontalnog apscesa i mogućnost postizanja drenaže. Antibiotici se propisuju u slučaju prisutnih opštih simptoma ili ako postoji povećan rizik za nastanak komplikacija. Lekovi izbora su metronidazol, tetraciklini i klindamicin. Penicilin je tradicionalno bio lek izbora, pa i njegov značaj ne treba zanemariti.

Nakon smirivanja akutne faze potrebno je uraditi adekvatnu mehaničku obradu i ispiranje antiseptičnim rastvorom. U slučaju prisutnog hroničnog parodontalnog apscesa pristupa se parodontalnoj hirurģiji.

Ključne reči: parodontalni apsces, drenaža, antibiotici, parodontalna hirurģija

Uvod

Parodontalni apsces je česta komplikacija parodontopatije, kada dolazi do brze destrukcije tkiva. Akutni parodontalni apsces je jedna od nekoliko retkih kliničkih situacija u par-

Summary

The periodontal abscess is the third most frequent dental emergency, representing 7–14% of all dental emergencies. Numerous etiologies are possible: exacerbations of the existing disease, post-therapy abscesses, impaction of foreign objects, factors altering root morphology, etc. The diagnosis should take into account the analysis of signs and symptoms. The microflora related with periodontal abscesses doesn't seem to be specific and is dominated by gram-negative strict anaerobe, rods. A tooth suffering from a periodontal abscess has a worse prognosis and is at a higher risk of being lost.

The treatment of the periodontal abscess has been a challenge for many years. In the past, the periodontal abscess in periodontal diseased teeth was the main reason for tooth extraction. There is not enough scientific evidence in the literature to provide a unique treatment regime for periodontal abscesses. Today, three therapeutic approaches have been discussed, including: drainage and debridement; systemic antibiotics and periodontal surgery procedures applied in chronic phase of disease.

The localization of the acute periodontal abscess and the possibility of obtaining drainage are essential considerations for successful treatment. Antibiotics should be prescribed in case of general symptoms or if complications can be suspected. Metronidazole, tetracyclines and clindamycin are drugs of choice. Penicillin was traditionally the drug of choice and its importance should not be neglected.

Proper mechanical debridement and local antiseptic irrigation should be carried out after resolution of the acute inflammatory phase. In the case of chronic periodontal abscess periodontal surgery procedures should be considered.

Key words: periodontal abscess, drainage, antibiotics, periodontal surgery

Introduction

The periodontal abscess is a frequent periodontal condition during periodontal disease in which periodontal tissues may be rapidly destroyed. The acute periodontal abscess is one of the few clinical situations in periodon-

odontopatiji u kojoj je pacijentu neophodna urgentna pomoć stomatologa. Njegov značaj nije samo u prognozi parodontopatičnog zuba, već i u postojanju opasnosti od širenja infekcije.¹ Parodontalni apsces se opisuje kao lezija sa izraženim razaranjem parodontocijuma u kratkom vremenskom periodu sa lako uočljivim kliničkim znacima i simptomima, kao što je lokalizovana akumulacija purulentnog sadržaja unutar parodontalnog džepa.²⁻⁴

Cilj ovog preglednog rada je da kritički sagleda raspoloživu literaturu vezanu za terapiju parodontalnog apscesa.

Učestalost

Parodontalni apsces je po učestalosti na trećem mestu čineći 7-14% urgentnih stanja u stomatologiji, a javlja se kod 6-7% pacijenata koji dolaze u stomatološku kliniku.⁴ Prema ovome, parodontalni apsces je značajan zbog svoje relativno visoke učestalosti i to uglavnom, kod pacijenata sa parodontopatijom. Kod ovih pacijenata veća je verovatnoća da će se javiti u već postojećem parodontalnom džepu,⁴ a njegova značajnost leži ne samo u učestalosti već i u tome kako utiče na prognozu zuba. U prošlosti, zubi sa apscesom su obično smatrani beznadežnim⁵ i pojava apscesa bila je jedan od glavnih razloga njihove ekstrakcije u toku terapije parodontopatije.^{6,7}

Etiologija

U toku parodontopatije mogući uzroci pojave parodontalnog apscesa su:

- postojanje dubokih i serpiginoznih parodontalnih džepova,⁴
- marginalno zatvaranje parodontalnog džepa (dovodi do širenja infekcije u okolna parodontalna tkiva usled pritiska izazvanog supuracijom unutar zatvorenog parodontalnog džepa),^{3,8,9}
- promena u sastavu mikroflora, virulencije bakterija ili odbrambenih sposobnosti domaćina (otežava drenažu džepa i povećava supuraciju),⁸
- terapija sistemskim antibioticima bez subgingivalne kiretaže kod pacijenata sa uznapredovanom parodontopatijom.¹⁰⁻¹²

tics where patients may seek immediate care. Its importance lies not only with the prognosis of the periodontitis affected tooth, but also with the possibility of infection spreading.¹ The periodontal abscess has been defined as a lesion with an expressed periodontal breakdown, occurring during a limited period of time, and with easily detectable clinical symptoms and signs such as a localized accumulation of pus, located within the periodontal pocket.²⁻⁴

The aim of the present review was to critically evaluate the available literature regarding the therapy of periodontal abscess.

Prevalence

The periodontal abscess is the third most frequent dental emergency, representing 7–14% of all dental emergencies, and affecting 6–7% of all patients seen in a dental clinic.⁴ Consequently, the periodontal abscess is important, due to its relatively high prevalence, mostly in patients with periodontitis. In these patients, a periodontal abscess is more likely to occur in a preexisting periodontal pocket,⁴ and its importance lies not only on its occurrence, but also how this abscess affects the prognosis of the tooth. In the past, teeth with an abscess were usually considered hopeless,⁵ and therefore the occurrence of an abscess may be one of the main reasons for tooth extraction during periodontal maintenance.^{6,7}

Etiology

Different etiologies of periodontal abscess in periodontitis are possible:

- the existence of deep and tortuous periodontal pockets⁴
- the marginal closure of a periodontal pocket may lead to an extension of the infection into the surrounding periodontal tissues due to the pressure of the suppuration inside the closed pocket^{3,8,9}
- changes in the composition of the microflora, bacterial virulence, or in host defenses could also make the pocket lumen inefficient to drain the increased suppuration⁸
- treatment with systemic antibiotics without subgingival debridement in patients with advanced periodontitis may also cause abscess formation.¹⁰⁻¹²

Parodontalni apsces se takođe može javiti i u odsustvu parodontopatije i to iz sledećih razloga:

- impakcija stranih tela⁸ (kao što su konac za čišćenje zuba, ljuspice od kokica, deo čačkalice za zube, riblje kosti, ili nepoznatog stranog tela,^{4,13-15}
- perforacija korena endodontskim instrumentima,^{4,16}
- infekcija lateralnih cista⁸ i
- promena morfologije korena zuba izazvana dejstvom lokalnih faktora (prisustvo otkinutih parčića cementa u predelu vrata zuba).¹⁷⁻¹⁹

Mikrobiologija

U literaturi se nalazi podatak da su purulentne oralne infekcije polimikrobne i izazvane endogenim bakterijama.²⁰ Topoli i saradnici¹² i Sims⁹ su objavili da su oko 60% kultivisanih bakterija striktni anaerobi. Iako nisu specifični za ovo oboljenje, najučestaliji mikroorganizmi su poznati parodontopatogeni *Porphyromonas gingivalis*, *Prevotella intermedia* i *Fusobacterium nucleatum*.

Dijagnoza

Dijagnoza parodontalnog apscesa se zasniva na simptomima koje sam pacijent otkriva i znacima koji se utvrđuju kliničkim pregledom i rentgen snimkom. Kliničkim pregledom se može uočiti ovalan otok gingive pored korena zuba.⁴ Ipak, ako je apsces lokalizovan duboko u parodontijumu teže je uočljiv. Simptomi variraju po intenzitetu od blage nelagodnosti do jakog bola, osećaja da je zub „razlabavljen“ i „duži od ostalih“, osetljivosti zuba na palpaciju.^{21,22} Čest klinički nalaz je supuracija, bilo spontana ili nakon pritiska u predelu apscesa,⁴ uz prisutnu brzu destrukciju tkiva i formiranje dubokog parodontalnog džepa.²¹ Rendgenološki snimak može otkriti normalan nalaz ili određen stepen gubitka kosti. U nekim slučajevima javlja se i poremećaj opšteg stanja sa povišenom telesnom temperaturom, leukocitozom i regionalnom limfadenopatijom.^{4,21}

Komplikacije i posledice nelečenog ili neadekvatno lečenog parodontalnog apscesa su gubitak zuba i širenje infekcije.

Periodontal abscesses can also develop in the absence of periodontitis, due to the following causes:

- impaction of foreign bodies⁸ (such as a piece of dental floss, a popcorn kernel, a piece of a toothpick, fishbone, or an unknown object),^{4,13-15}
- perforation of the tooth wall by an endodontic instrument,^{4,16}
- infection of lateral cysts,⁸
- local factors affecting the morphology of the root may predispose to periodontal abscess formation. (The presence of cervical cemental tears has been related to rapid progression of periodontitis and the development of abscesses).¹⁷⁻¹⁹

Microbiology

Review articles have pointed out that purulent oral infections are poly-microbial, and caused by endogenous bacteria.²⁰ Topoll et al¹² and Newman & Sims⁹ reported that around 60% of cultured bacteria were strict anaerobes. It does not seem to be specific, but known periodontal pathogens such as *Porphyromonas gingivalis*, *Prevotella intermedia* and *Fusobacterium nucleatum*, are the most prevalent bacterial species.⁴

Diagnosis

Diagnosis of a periodontal abscess is based on the symptoms revealed by the patient, and the signs found during the oral examination, and radiographic examination. The current sign on examination is an ovoid elevation of the gingiva along the lateral part of the root.⁴ However, abscesses located deep in the periodontium may be less evident. Symptoms range from light discomfort to severe pain, tooth mobility and elevation, sensitivity of the tooth to palpation.^{4,21,22} Another common finding is supuration, either spontaneous or after pressure on the abscess,⁴ combined with rapid tissue destruction and deep pocket formation.²¹ The radiographic examination may reveal a normal appearance, or some degree of bone loss. Systemic involvement has been reported in some severe cases, including fever, leukocytosis and regional lymphadenopathy.^{4,21}

Complications and consequence of untreated or inadequate treated periodontal abscess include tooth loss and spreading of infection to other body sites.

Terapija

Terapija parodontalnog apscesa predstavlja izazov dugi niz godina. Ona obično obuhvata dva stadijuma: saniranje akutne lezije i adekvatnu terapiju rezidualnog procesa kada je situacija stavljena pod kontrolu.^{4,23} Ako je zub jako oštećen i ako je njegova prognoza loša, najefikasnija terapijska procedura je ekstrakcija zuba.²⁴

Protokol terapije parodontalnog apscesa preporučuje drenažu kroz parodontalni džep, uklanjanje kamenca i konkremenata, kiretažu i kompresiju mekog zida parodontalnog džepa uz ispiranje rastvorom antibiotika. Pacijent se zakazuje na kontrolni pregled nakon 24–48 sati. U određenim slučajevima, za nedelju dana, potrebno je sprovesti definitivnu terapiju. U ovim slučajevima pristupa se režanj operaciji uz ispiranje antiseptičnim sredstvom.⁴

Još uvek ne postoji čvrst stav o sistemskoj primeni antibiotika u terapiji parodontalnog apscesa. Njihova primena ima za cilj sprečavanje širenja infekcije i nastanak ozbiljnih komplikacija.²⁵⁻²⁷ Koncentracija ovako aplikovanih antibiotika je mnogo niža u apscesu nego u krvi, a zbog slabe snabdevenosti apscesa krvlju postizanje maksimuma koncentracije antibiotika u parodontalnom apscesu kasni u odnosu na krvotok. Iako se primene antibiotici u terapiji parodontalnog apscesa ne sme izostati mehanička obrada ili mehanička obrada sa hirurškom terapijom.^{28,29} Neki autori primenjuju sistemski antibiotike samo u slučaju poremećaja opšteg stanja ili ako infekcija nije ograničena.³¹ Drugi autori ipak, preporučuju sistemsku primenu antibiotika samo kao početni tretman u slučajevima kada se ne može postići adekvatna drenaža. Na primer, u slučaju velikog apscesa sa difuznim otokom i jako izraženim bolom.³⁰

Dužina aplikacije i vrsta antibiotika često su predmet polemisanja. Neki autori preporučuju kraću upotrebu antibiotika tvrdeći da je ona jednako efikasna kao i standardni režim aplikacije.^{30,31} Drugi autori savetuju kombinovanje konzervativne-bazične terapije (incizija, drenaža i kiretaža) sa antibiotskom terapijom.^{4,32} Dugo se „uspešnom“ smatrala kombinacija incizije i ispiranja uz sistemsku aplikaciju penicilina. U Velikoj Britaniji antibiotici iz grupe penicilina bili su dugo prvi lek izbora u terapiji parodontalnog apscesa i koristilo ih je 57% sto-

Treatment

The treatment of a periodontal abscess has been a challenge for many years. The treatment of the acute periodontal abscess usually includes two stages: the management of the acute lesion and the appropriate treatment of the original and/or residual lesion, once the acute situation has been controlled.^{4,23} If the tooth is severely damaged, and its prognosis is bad, one of the most effective treatments could be tooth extraction.²⁴

For the treatment of periodontal abscesses, a protocol has been recommended: drainage through the pocket, scaling of the tooth surface, compression and debridement of the soft tissue wall and irrigation with antibiotic solutions. After therapy, the patient should be examined for the abscess resolution after 24–48 hours. In some cases one week later, the definitive treatment should be carried out. In these cases flap surgery and topical antiseptics may be applied.⁴

The addition of systemic antibiotics to the treatment regime of the periodontal abscess is not a well defined issue. Systemic antibiotic treatment of dental abscess aims at preventing bacterial spreading and serious complications.²⁵⁻²⁷ The concentration of antibiotics in the abscess is considerably lower than in the blood, and because of poor blood supply the concentration peaks latter in the abscess than in the blood. In addition to antibiotics, a periodontal abscess should always receive mechanical, or mechanical and surgical therapy.^{28,29} Some authors exclude systemic antibiotics, unless a clear systemic involvement is present or when the infection is not well localized.³¹ Other authors, however, recommend the use of systemic antibiotics as the only initial treatment, in cases when initial adequate drainage can not be established. For example, in cases of large abscesses with diffuse swelling, or extreme pain.³⁰

The duration and the type of the antibiotic therapy is also a matter of discussion. Some authors have recommended shorter antibiotic regimes, claiming that they are as effective as conventional regimes.^{30,31} Some authors recommend the combination of basic treatments (incision, drainage, debridement) and antibiotic therapies.^{4,32} The combination of incision and drainage with the systemic administration of penicillins has been considered as „often suc-

matologa, njih 21% je koristilo amoksisilin, a 14% metronidazol.¹ Na žalost, anaerobni mikroorganizmi pokazuju različitu osetljivost na penicilin. Prema Eicku i saradnicima³³ 41% Gram pozitivnih bakterija je rezistentno na penicilin. Kod pacijenata alergičnih na penicilin lek izbora je eritromicin.³⁴ Ipak, sve veći broj značajnih anaeroba je rezistentan na eritromicin.³⁵ Danas, metronidazol i drugi nitroimidazoli (ornidazol i tinidazol) i klindamicin su dokazano efikasni kod striktno anaerobnih bakterijskih vrsta.²⁸

Hafström i saradnici² preporučuju konzervativnu terapiju sa ciljem postizanja što veće regeneracije epitelnog pripoja. Drenaža se postiže kroz parodontalni džep uz ispiranje sterilnim fiziološkim rastvorom. Ukloni se supragingivalni kamenac, a tetraciklini se prepisuju u trajanju od dve nedelje (1 gram dnevno). Ovaj terapijski protokol je klinički i mikrobiološki ispitan na grupi od dvadeset apscesa, trinaest ih je praćeno 180 dana, a sedam 42 dana. Dobijeni rezultati su bili zadovoljavajući sa prosečnim smanjenjem dubine džepa od 4.3 mm. Autori ističu sledeće zaključke: prvo, veliki značaj drenaže (prva 4 apscesa su tretirana antibioticima, ali bez drenaže, i dva od njih su se ponovo javila za oko 40 dana); i drugo, sklonost ka recidiviranju apscesa se češće javlja ako se ne uklone konkrementi i obradi džep.

Smith i Davies²⁴ su proučavali ponašanje apscesa nakon sprovedene terapije. Oni su pratili 62 parodontalna apscesa. Kod 22 od njih, u akutnoj fazi urađena je incizija i drenaža, uz primenu metronidazola sistemski (200 mg, 5 dana). Kasnije, urađena je parodontalna terapija koja je obuhvatala održavanje oralne higijene uz pomoć hlorheksidina, uklanjanja kamenca i konkremenata, kiretažu parodontalnih džepova, i u indikovanim situacijama parodontalnu hirurgiju. Od 22 tretirana zuba, 14 je ekstrahirano iz parodontoloških razloga u toku tri godine, dok je preostalo samo 8 zuba.

Fine³⁶ je pratio 3 pacijenta kod kojih su se javljala 3 do 6 apscesa godišnje. Savetovao je uklanjanje kamenca i konkremenata sa kiretažom parodontalnih džepova svih zuba uz sistemsku aplikaciju antibiotika nakon mikrobiološke analize subgingivalne mikroflore. Sva tri slučaja su uspešno sanirana.

Palmer¹⁵ je opisao slučaj akutnog lateralnog parodontalnog apscesa koji je uspešno saniran peroralnom primenom penicilina. Postignuta je potpuna regeneracija destrukcije. U ovom

uspehu.⁴ In the United Kingdom, penicillins were the first drug of choice in the treatment of periodontal abscesses, being used by 57% of dentists, followed by amoxicillin (21%) and metronidazole (14%).¹ Unfortunately, anaerobes show variable susceptibility to penicillin. According to Eick et al.³³ 41% of the gram+ bacterial isolates were penicillin resistant. Erythromycin has been used as an alternative drug for treatment of patients allergic to penicillin.³⁴ However, an increasing number of important anaerobes are resistant to erythromycin.³⁵ Today, metronidazole, other nitroimidazoles (ornidazole and tinidazole) and clindamycin are proven to be effective against strictly anaerobic bacterial strains.²⁸

Hafström et al.² proposed a conservative treatment, aiming to get as much attachment gain as possible. Drainage was established through the periodontal pocket, and irrigation with sterile saline was performed. Only supragingival scaling was done, tetracycline was prescribed for 2 weeks (1 g/day). The protocol was tested clinically and microbiologically in a group of 20 abscesses, 13 followed for 180 days, and 7 for 42 days. The results were considered satisfactory, with a mean reduction of probing pocket depth of 4.3 mm. Two conclusions were suggested: firstly, the importance of the drainage (the first 4 abscesses were treated with antibiotic but without drainage, and 2 of them reappeared within 40 days); and secondly, the potential of regeneration demonstrated by the abscesses, which was supposed to be enhanced by avoiding subgingival scaling.

Smith & Davies²⁴ also studied the behaviour of abscesses after therapy. They studied 62 periodontal abscesses. In 22 of them, the acute phase was treated surgically by incision and drainage, along with the administration of systemic metronidazole (200 mg, tid, 5 days). At a later stage, periodontal therapy was carried out, including oral hygiene procedures with the help of chlorhexidine, scaling and root planing, and if necessary, periodontal surgery. Out of the 22 treated teeth, 14 were extracted for periodontal reasons within the 3 years of follow-up, while only 8 teeth were still in place.

Fine³⁶ reported 3 patients who suffered from 3 to 6 abscesses per year. The proposed therapy was to treat the patient with full-mouth scaling and a systemic antibiotic selected after microbi-

slučaju sumnjalo se da je uzrok nastanka apscesa impakcija stranog tela i da je njegovom eliminacijom uz primenu antibiotika došlo do potpune eliminacije procesa.

Neki autori sugerišu da se uz konzervativnu terapiju parodontalnog apscesa može kao pomoćno sredstvo koristiti soft laser za smanjenje bola i otoka gingive.²²

U terapiji hroničnog parodontalnog apscesa, preporučuje se hirurška terapija (gingivektomija ili režanj operacija), uglavnom kod apscesa u dubokim infrakoštanim džepovima kod kojih se eliminacija apscesa i ne može postići na drugi način.^{4,8} Režanj operacija se preporučuje i u slučajevima kada zbog nepristupačnosti apscesa konzervativnom terapijom nije moguće ukloniti sve konkremete. Glavni cilj ovakve terapije je ukloniti preostale konkremete i istovremeno uspostaviti drenažu.³⁷ U literaturnim podacima ukazuje se na terapiju koja se sastoji od kombinacije režanj operacije koja omogućava pristup, uklanjanja duboko lokalizovanih konkremenata i ispiranja doksiciklinom. Autori su izneli dobre rezultate kod više od 50 pacijenata.³⁸

Zaključak

Dugi niz godina uspešna terapija parodontalnog apscesa predstavlja pravi izazov. U prošlosti, pojava parodontalnog apscesa kod parodontopatičnih zuba bila je glavni razlog za ekstrakciju zuba.

Ne postoji dovoljno naučnih dokaza u literaturnim podacima koji bi obezbedili postojanje jedinstvene doktrine u lečenju parodontalnog apscesa. Danas se govori o tri terapijska pristupa u rešavanju ovog problema: drenaža i kiretaža apscesa, sistemska primena antibiotika i parodontalna hirurgija u hroničnoj fazi oboljenja. Antibiotike treba primeniti u slučaju pojave opštih simptoma ili kod postojanja sumnje na moguć razvitak komplikacija. Lek izbora su metronidazol, tetraciklini i klindamicin. U slučaju postojanja hroničnog parodontalnog apscesa treba razmotriti i primenu parodontalnih hirurških procedura. Smatra se da su lokalizacija procesa i mogućnost postizanja drenaže glavni preduslovi uspešne terapije.

ological analyses of the subgingival microflora. Both 3 cases were treated successfully.

Palmer¹⁵ reported a case of an acute lateral periodontal abscess treated successfully with a course of oral penicillin, with complete regeneration of the destruction. In this case a foreign object impaction was suspected, and its elimination, with the help of the antibiotic, led to the complete resolution.

Some authors suggested that adjunct to conservative treatment, soft laser therapy could be used to decrease pain and swelling of gingival.²²

In the treatment of chronic periodontal abscesses, surgical therapy (either gingivectomy or flap procedures) has also been advocated,⁴ mainly in abscesses associated with deep vertical defects, where the resolution of the abscess may only be achieved by a surgical operation.⁸ Surgical flaps have also been proposed in cases in which calculus is left subgingivally after the treatment. The main objective of the therapy is to eliminate the remaining calculus and obtain drainage at the same time.³⁷ A therapy, with a combination of an access flap with deep scaling and irrigation with doxycycline, has also been proposed. The author reported good results with more than 50 patients.³⁸

Conclusions

The successful treatment of the periodontal abscess has been a challenge for many years. In the past, the periodontal abscess in periodontal diseased teeth was the main reason for tooth extraction.

There is not enough scientific evidence in the literature to provide a unique treatment regime for periodontal abscesses. Today, three therapeutic approaches have been discussed, including: drainage and debridement; systemic antibiotics and periodontal surgery procedures applied in chronic phase of disease. Antibiotics should be prescribed in case of general symptoms or if complications can be suspected. Metronidazole, tetracyclines and clindamycin are drugs of choice. In the case of chronic periodontal abscess periodontal surgery procedures should be considered. The localization of the acute periodontal abscess and the possibility of obtaining drainage are essential considerations for successful treatment.

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