

The Use of Antimicrobial Photodynamic Therapy as a Coadjuvant in the Treatment of Rare Infectious Oral Manifestation by Actinomyces: Case Report

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ABSTRACT

Introduction: Actinomycosis is a rare and chronic disease caused by Actinomyces, gram-positive anaerobic bacteria that normally colonize the human mouth and the digestive and genital tracts. This infection is extremely uncommon in the oral mucosa membranes and the predisposing factors may be local and systemic, such immunosuppression.

Case presentation: This paper aims to report the case of a liver-transplanted patient, with ulcerated and painful lesions on the back of the tongue, buccal mucosa and lower vestibule fundus, associated to poor oral hygiene. For diagnostic purposes, the microbiological culture (oral swab) of the lesions was performed and also an incisional biopsy of the tongue lesion, confirming the clinical suspicion of Actinomyces infection. Patient was treated with specific antimicrobial coverage and solutions for mouthwash and, as an adjuvant, antimicrobial photodynamic therapy (aPDT) was used by the hospital dental service.

Results: The results of the oral care application and the PDT show an improvement in the symptoms and good clinical recovery of the oral tissue.

Conclusion: Photodynamic antimicrobial therapy (aPDT) is an adjunctive therapeutic modality in the treatment of oral bacterial infectious manifestations, with satisfactory results.

Keywords: Wound infection, Actinomycosis, Lasers, Photoch

INTRODUCTION

Actinomycosis is a rare disease caused by a microorganism called Actinomyces, gram-positive anaerobic bacteria that normally colonizes the human mouth and the digestive and genital tracts. Although Actinomyces is naturally present in the oral microbiota, in some cases it may become pathogenic [1].

This infection is anatomically and clinically divided into three types: cervicofacial, pulmonary and abdominal, the first being the most common form, but, in the oral cavity, this infection is considered rare [1,2].

When in the oral cavity, this infection can affect both soft and bone tissue and its appearance is usually associated with trauma or previous infections. In most cases, patients exhibit classic symptoms of abscess and formation of sulfur granules is indicative of actinomycosis [3].

Clinical diagnosis can sometimes be problematic as this pathology may present clinical features similar to fungal infections or malignant tumors. Among the diagnostic

methods, culture is the gold standard in the diagnosis of this condition [1,3].

Patients with actinomycosis require a prolonged antibiotic scheme (6 to 12 months) and in high doses, being Penicillin G or Amoxicillin considered the drugs of choice for the treatment of this lesion. Preventive measures, such as the reduction of alcohol consumption and the improvement of

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oral health status, may limit the occurrence of cases of actinomycosis, both in the cervicofacial and in the pulmonary form [4].

Photodynamic antimicrobial therapy (aPDT) is a promising co-adjuvant treatment method for the eradication of microorganisms in the oral cavity [5,6]. The mechanism of photosensitization of aPDT consists of the interaction of light with the photosensitizer and oxygen, generating free radicals that induce severe damage to the microbial cells, leading to its death [7].

The aPDT is not considered a substitute for antimicrobial drugs or any conventional treatment, but rather an important modality of complementary treatment of localized oral infections, especially in cases of resistant microorganisms. The sensitivity of bacteria, viruses and fungi to PDT suggests its applicability in localized shallow infections and known microbiota. Low cost, minimal side effects and reduction of the probability of recurrence are the main advantages of the therapy, besides technical simplicity and absence of risk of microbial resistance [6-9].

Health professionals should be aware of the possibility of actinomycosis, always aiming at a definitive and timely diagnosis and the implementation of an effective treatment protocol [2]. In view of this, this paper proposes to report a rare case of a patient diagnosed with actinomycosis in the oral cavity.

CASE PRESENTATION

This is a descriptive study, framed as a case report. The patient agreed to the disclosure of data and images by signing the Informed Consent Form, being aware that information is unique and exclusively for scientific purposes, while preserving the patient's anonymity in full.

Patient NJE, 69 years old, male, ex-smoker (stopped 30 years ago), ex-alcoholic (stopped 30 years ago), clinical picture of ulcerative colitis since 2000 and primary sclerosing cholangitis, submitted to liver transplantation in the year 2006 and using immunosuppressive medication since then (Tracolimus 2 mg/day). With complaint of bloody diarrhea for 4 months associated with abdominal pain and recurrent abdominal distension. He was treated with hydrocortisone, presenting improvement of the clinical picture, but with recurrence after discontinuation of the medicine. The patient was then admitted to the Oswaldo Cruz University Hospital of the University of Pernambuco (HUOC/UPE) for research and treatment/control of the clinical picture.

During the hospital stay, NJE complained of pain and wounds in the oral cavity, being requested the opinion of the dentistry team of CEON/HUOC/UPE. The presence of ulcerated lesions on the back of the tongue (**Figure 1A**), right buccal mucosa (**Figure 1B**) and lower right vestibule fundus (**Figure 1C**), as well as unsatisfactory oral hygiene, were observed. In view of the clinical findings and medical history, the diagnostic hypothesis was suggestive of oral infectious manifestation. Microbiological analysis (oral swab) of oral lesions was indicated and carried out, as well as an incisional biopsy on the tongue lesion. The clinical-surgical procedure occurred under local anesthesia, without interferences. After the procedure, the patient was advised about the importance of oral hygiene and it was prescribed the use of toothbrushes with small heads, soft bristles and non-abrasive toothpaste, and also mouthwash with sodium bicarbonate solution (8/8 h), chlorhexidine digluconate 0.12% without alcohol (12/12 h) and local application of hydrogen peroxide 10 volumes, with the aid of a gauze, on the lesions (12/12 h).

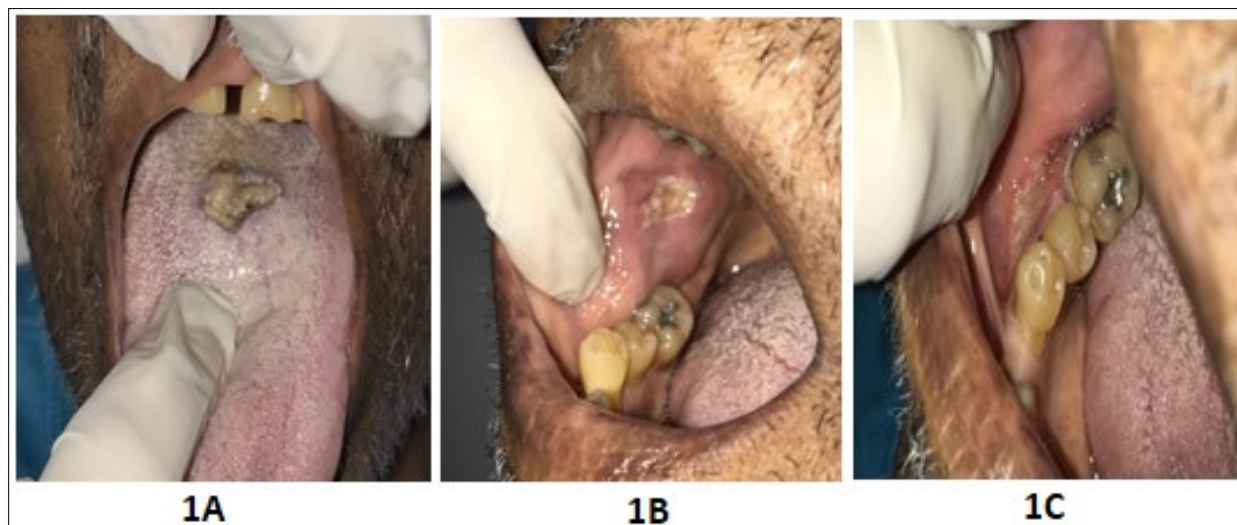


Figure 1. A) Initial clinical aspect of ulcerated lesion on the back of the tongue, it is also observed poor oral hygiene. B) Initial clinical aspect of ulcerated lesion in the right buccal mucosa. C) Initial clinical aspect of ulcerated lesion in lower right vestibule fundus.

The dental team of CEON/HUOC/UPE followed NJE daily. The patient reported, after 72 h of the institution of oral care protocol, improvement of painful symptoms in oral cavity. After 14 days of the procedure for oral diagnosis, microbiological culture of oral lesions and incisional biopsy of the tongue were conclusive for the diagnosis of infection by *Actinomyces* spp. (Report No. 172445), this microorganism was also found in biopsy and culture of ulcerated lesion in rectum (Report No. 260485-SC). With the conclusive diagnosis, specific antimicrobial coverage was established for the systemic infectious disease and, as an adjuvant in the treatment of oral lesions, photodynamic antimicrobial therapy (aPDT) was indicated. After signing

the Term of Consent and Authorization, the aPDT was performed, with a 24 h interval between sessions. The aPDT protocol consisted of the initial application of the photosensitizer (methylene blue - 0.05%) on all oral lesions and, after 5 min of interaction of the dye with the tissue, the low-level laser (GaAlAs and InGaAlP) was applied (MMOptics device, Brazil), following the manufacturer's specifications: the visible red spectrum (660 nm), with fixed power (output) of 100 mW, spot size de 0.03 cm² and energy density of 6 J/cm² and exposure time per point: 60 s. The mode of application was of the punctual type, until it contemplated all the area of the lesions (**Figures 2A-2C**).



Figure 2. A) Clinical aspect of the tongue lesion after institution of specific antibiotic therapy and after 4th session of the aPDT. B) Clinical aspect of the buccal mucosa lesion after institution of the specific antibiotic therapy and after the fourth session of the aPDT. C) Clinical aspect of lower right vestibule fundus lesion after institution of specific antibiotic therapy and after 4th session of aPDT.

With continuous use of the mouthwash with chlorhexidine digluconate 0.12% (31 days), a blackened pigmentation appeared in oral mucosa, mainly on the back of the tongue

being then suspended the use of this mouthwash solution. After suspension, the oral mucosa returned to its normal appearance (**Figure 3**).



Figure 3. Clinical aspect of tongue pigmentation after continuous use of chlorhexidine digluconate 0.12% for 31 days.

The oral clinical picture was then controlled and treated daily with satisfactory resolution of the pains symptoms in addition to good clinical tissue recovery (**Figures 4A-4C**),

but despite this, due to other systemic infectious complications, such as *Trichosporon Asahii* infection, the patient died.



Figure 4. (A) Clinical aspect of the tongue lesion showing clinical tissue recovery and normal color after suspension of the mouthwash with chlorhexidine oral solution 0.12%. (B) Clinical aspect of lesion in the right buccal mucosa showing clinical tissue recovery. (C) Clinical aspect of lower right vestibule fundus lesion showing clinical tissue recovery.

DISCUSSION

Actinomycosis is an extremely rare infectious disease in the membranes of the oral mucosa and its clinical presentation is usually characterized by suppurative granulomatous inflammation, with abscess and fistula [2,4,10]. The reported case demonstrates unusual features of the oral infectious manifestation by *Actinomyces*, with ulcerative lesions on the back of the tongue, buccal mucosa and lower vestibule fundus. However, other cases found in the literature also present a clinical manifestation that may evade the pattern [2].

Predisposing factors for the onset of this condition may be local or systemic, such as poor oral hygiene, trauma, surgical procedures, diabetes, long-term corticosteroid therapy and immunosuppression. The risk of developing the disease is also increased in smokers and alcoholics [1,3]. In the case reported, the patient presented a history of cigarette and alcohol consumption and also underwent medical treatment based on systemic corticosteroids.

Another predisposing factor presented by the patient is related to immunosuppression. Transplanted patients need to use several immunosuppressive agents throughout their post-transplant life and may present an increased risk for the development of opportunistic infections, whether of viral or bacterial origin [11]. The patient underwent liver transplantation in the year 2006 and since then makes daily use of Tacrolimus, which is an immunosuppressive medication, usually used with the aim of reducing the risk of rejection of the transplanted organ. Then, faced with this immunosuppression, the patient became more susceptible to the development of infectious processes, such as actinomycosis.

Treatment with systemic antimicrobials is the therapy of choice for bacterial infections by *Actinomyces* [3,12]. However, in the literature, the number of studies that show antimicrobial photodynamic therapy as effective in the adjuvant treatment of infectious conditions has been increasing. The aPDT presents as promising, with several applications and numerous advantages, among them, the absence of side effects and the impossibility of resistance acquired by bacteria [6,7,13].

The use of methylene blue dye has been Community-European (CE)-licensed for use in dental medicine and maxillofacial surgery in Europe since 2003 and has been used for the treatment of infected wounds. The authors have used the technique in clinical practice for medication-related osteonecrosis of the jaw lesions for at least 10 years for more than 200 patients in combination with systemic antimicrobial therapy with b-lactam antibiotics combined with b-lactamase inhibitors. They have found marked improvement especially in wounds with microbiologically proven colonization with *Actinomyces* species [13].

The first group to report the use of mouse wound infection models to investigate the effects of PDT in treating excisional wound infected with *Escherichia coli* and *Pseudomonas aeruginosa* were Hamblin et al. [14]. The experiment consisted in a single wound realized on the backs of healthy mice and infected with a suspension of bioluminescent bacteria transduced with a plasmid containing a lux gene operon, which permitted to monitor the infection in real time by a sensitive charge-coupled camera. In PDT-treated mice, the authors observed a light dose dependent loss of luminescence with a 99% reduction after the four light aliquots, which were not seen in the untreated wound.

Regarding the efficiency of bacterial inactivation by aPDT, it is known that Gram-positive bacteria are generally more susceptible to aPDT than Gram-negative species. These differences can be explained by structural differences in cell walls [15]. As the infectious disease in question is caused by Gram-positive bacteria, it is even more appropriate to perform the aPDT as a therapeutic modality associated with systemic antimicrobials.

The exact nature of the microbial killing caused by different types of lasers emitting light in the intermediate wavelength region has not yet been determined. The laser beam effect on bacterial cells depends on laser parameters (wavelength, power, time and mode of emission, beam profile and spot size) and the characteristics of each bacterium [16].

In the scientific databases, in vitro clinical studies and case reports demonstrating the use of the laser through aPDT in the microbial inactivation of several gram positive and negative bacteria can be found, for example in cases of *Pseudomonas aeruginosa*, *Fusarium* sp. and others [13,14,16]. However, the use of this therapy in actinomycosis disease with oral infections, being then a promising therapy, used in a rare oral manifestation, with few cases described in the literature.

Therefore, health professionals should be aware of the existence of infectious diseases in the mouth, which may even mimic malignant conditions. It is extremely important that the diagnosis is correctly established so that the treatment adopted is consistent with the condition exhibited by the patient [1].

CONCLUSION

Infections are the leading causes of morbidity and mortality in liver transplant patients. The clinical diagnosis associated with microbiological culture is fundamental for confirmation of the actinomycosis disease. Infectious oral lesions by actinomyces are rare and specific antibiotic therapy is the treatment of choice for these cases. Photodynamic antimicrobial therapy (aPDT) is an adjunctive therapeutic modality in the treatment of oral bacterial infectious manifestations, with satisfactory results.

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