Abstract

Careful examination of the oral cavity in respiratory medicine is often neglected, although it represents sometimes a clue for clinical diagnosis and it is important in completely addressing the patient. On the other hand, the dental practitioner who treats a patient with unusual oral lesions should observe correct guidance and medical advice. Oral manifestations are of polymorphic nature, being associated with a variety of pulmonary diseases and specific therapies. Respiratory obstructive diseases, systemic diseases with pulmonary involvement, lung cancer, cystic fibrosis or tuberculosis all have clinical and/or therapeutic involvement of the oral cavity, which underlines the necessity of regular dental services and careful oral cavity exam, as well as an active collaboration between dental practitioners and pulmonologists or somnologists, for patient’s ultimate benefit.

Keywords: oral cavity, pulmonary disease, diagnosis

1. INTRODUCTION

Careful examination of the oral cavity in respiratory medicine is often neglected, although it represents sometimes a clue for clinical diagnosis and it is important in completely addressing the patient. On the other hand, the dental practitioner who treats a patient with unusual oral lesions should observe correct guidance and medical advice. The oral manifestations in this context are polymorphic, being associated with a variety of pulmonary diseases and specific therapies.

2. INHALED MEDICATION

Nowadays, inhaled medication represents the mainstay of therapy in asthma and COPD, due to its major advantages, including delivery of pharmacological agents directly to the site of action, fewer systemic adverse effects and faster onset of action. Several drug categories are used: β2-agonists, corticosteroids, anti-cholinergic agents and their combinations. The increased use of inhaled drugs and the fact that a large ratio of the inhaled substances remains in the oro-pharyngeal region has raised attention to the oral consequences of this type of medication: xerostomia, mucosal changes, ulcerations, dental cavities, halitosis, taste disturbances, oropharyngeal candidiasis, gingivitis, periodontitis, and signs of gastro-esophageal reflux [1].

It is now proven that prolonged use of β2-mimetic agents is associated with an increased rate of dental cavities [2], which can be explained by the various actions of these agents: reduced salivary production and secretion, along with increased Lactobacillus sp. and Streptococcus mutans populations in the oral cavity [2]. Also, β2-agonists favor relaxation of the smooth muscle of the lower esophageal sphincter, followed by gastro-esophageal reflux [3] and a lower pH in the mouth, a pH < 5.5 being correlated with enamel demineralization. Inhaled drugs, especially dry-powders, contain fermentable carbohydrates and sugar as carriers, further increasing the rate of tooth decay [4].

Inhaled corticosteroids (ICS) are widely used in asthma and COPD treatments, a significant percent of the administered dose remaining in the oro-pharyngeal region and being associated with several topical effects: oral candidiasis, dysphonia, perioral dermatitis, pharyngitis, reflex cough, sensation of thirst, tongue hypertrophy [5].

These local side effects are not as important as the systemic secondary effects, yet they can affect...
patient’s compliance to treatment. Among ICS, beclomethasone dipropionate has a more favorably profile, being inhaled as an inactive form, activated in the lung by esterases, with little activation in the oropharynx, in contrast to fluticasone propionate and budesonide, which are inhaled in the pharmacologically-active form and have an increased incidence of oral side effects. The “paradoxical” local inflammatory effect associated with the use of an anti-inflammatory drug is caused by the various components of the inhaled substances: the propellant, lubrication components, and lactose, which can all be the cause of the direct inflammatory reaction [5,6].

Corticosteroids are weak acids with little effect on oral pH, however patients undergoing treatment with ICS experience overgrowth of Candida species at oropharyngeal level, often self-limiting, as due to the inhibition of the immune system. Clinical aspects of such lesions include whitish papules and plaques, inflamed or bleeding tissue under the lesions. Also, an increased prevalence of gingivitis has been noticed [7,8].

For pneumologists and dentists, monitoring, early recognition, and appropriate management of these oral lesions are requested, in order to improve the life quality of chronic respiratory patients, while the task of dentists is to carefully ask patients about their pulmonary conditions and treatment, paying increased attention to the characteristic lesions in the mouth. Using a spacer, decreasing frequency of administration, and properly rinsing the mouth are simple and effective measures to prevent oral corticosteroid-related pathology.

3. PULMONARY OBSTRUCTIVE DISEASES

Pulmonary obstructive diseases represent the main spectrum of chronic respiratory maladies in the modern world, due to increased exposure to risk factors, such as smoking, obesity, diabetes, air pollutants, and other noxious environmental factors. Such diseases share an obstructive syndrome located in the inferior or upper airways, also impacting oral cavity health. Chronic obstructive pulmonary disease (COPD). Smoking is one of the major risk factors for both COPD and oral pathology as a periodontal disease. Epidemiological studies are suggesting an association between COPD and periodontal disease [9] but, most probably, the common link between these two conditions is exposure to tobacco smoke. Some studies are indicating that COPD is associated with marginal bone loss [10]. Other common issues are thrush - the most frequent mucosa ailment, and worsening of the dental status: gingival bleeding and pocket depth, reduced teeth number or even toothlessness, increased incidence of dental plaque [10-12]. Data are controversial due to the different periodontal disease variables involved: pocket depth or attachment loss, while the endpoint used in the trials - tooth loss - is not due only to periodontal diseases, but can be the result of dental cavities. Some authors suggest that chronic airways obstruction is not associated with significant increase in pocket depth or a decreasing number of the remaining teeth, comparatively with smokers with normal spirometry, when adjusted to age [13]; on the opposite side, Wang et al. [12] found out in COPD patients fewer remaining teeth compared to the control group, even if one third of it was represented by current or former smokers. In addition, these patients have a denture plaque biofilm that acts like a reservoir of pathogens in the upper and lower airways, the lower respiratory tract being colonized with aspirated pathogenic bacteria [14].

As to malignancy, a cohort study evaluating the risk of cancer in first-time hospital-diagnosed COPD patients concluded that these patients are exposed to a considerably increased risk of developing tobacco-related cancers, including cancers of the oral cavity, larynx, and tongue, alongside lung cancer [15].

Asthma. The most frequent oral health conditions associated with asthma are dental cavities and erosions, periodontal disease and oral candidiasis [16]. The salivary secretion is the main protective factor involved in oral health. In asthmatic patients, the use of β2-agonists reduces the salivary secretion rates by 26 to 36%, compared to non-asthmatics, affecting composition, and altering this important
defensive barrier [2,17]. Furthermore, such patients, particularly those of pediatric age, have a prominent oral breathing pattern, contributing to gingivitis, due to dehydration of alveolar mucosa, alongwith various immunological factors which increase gingival inflammation. Several elements - e.g., excessive thirst, the attempt to wash away the taste of inhaled medication, to counterbalance the desiccating effect of mouth breathing, and the reduced salivary flow induced by β₂-agonists - are related with an excessive consumption of cariogenic drinks [18].

An interesting issue is the influence of oral pathogens over allergy, a prominent feature in asthma. Several recent studies speculated that exposure to oral pathogens associated with periodontal diseases, such as gingivitis or periodontitis, might play a protective role against development of asthma and allergy, although large prospective birth cohort studies are still missing [19]. Previous results of the Third National Health Nutrition Examination Survey (NHANES) [20] highlighted the importance of oral colonization with Porphyromonas gingivalis, reflected by the higher titers of Ig G antibodies against P. gingivalis, associated with a lower prevalence of asthma. Card et al. [21] confirmed that allergen-induced hyperresponsiveness of the airways is significantly decreased when infection with P. gingivalis is established after sensitization to allergen.

**Obstructive sleep apnea syndrome (OSAS).** In patients with OSAS, oral inflammation could play an important pathogenic role, the inflammatory process of the pharynx, uvula, soft palate, and oral cavity being associated with increased production of nitric oxide (NO); measurement of oral exhaled NO, as a marker of airway inflammation, appears increased in OSAS, being related to hypoxemia severity and obstructive episodes [22]. However, the highest levels of nitric oxide are found in asthma, even if, in these patients, the NO sources are the bronchi and alveoli [23].

Dental services are also very helpful in the therapeutic management of these patients, preparing and fitting oral devices for mandible advancement (ODMA), aimed at relieving upper airway obstruction by forward displacement of the mandible, tongue and other oro-pharyngeal structures, indirectly moving the suprahoid and genioglossus muscles in anterior direction [24-26]. This therapy is frequently associated with several oro-facial side effects, usually acceptable: teeth and jaw tenderness, myofascial pain, gum irritation, increased salivation or xerostomia. Nevertheless, there are some reports of exaggerated gag reflex, periodontal lesions or fractures of teeth or dental fillings, while long term use of these devices is associated with temporo-mandibular joint disease and temporary bite change in the morning after the removal of the device in almost all patients [27]. Moreover, some authors report permanent occlusal alteration after long-term treatments [28], evidencing the importance of regular follow-up and dental examination of the patients using this type of devices.

### 4. SYSTEMIC DISEASES WITH ORAL AND PULMONARY INVOLVEMENT

**Sarcoidosis** is a systemic disease with granulomas in the lungs and adenopathies, affecting almost all organs. The oral cavity lesions in sarcoidosis are localized swelling or nodules, painless ulcerations of the gingiva, buccal and labial mucosa, palate, and gingival inflammation, hyperplasia or recession, diagnosis being made through biopsy, that reveals non-caseating granulomas. Involvement of the tongue is very rare, including swelling, enlargement and ulcerations, as well as of the salivary gland, which leads to a tumor-like appearance [29]. Parotid gland impairment appears in 6% of patients, especially in women, the clinical picture including a painless tumor-like appearance, sometimes with xerostomia. A rare but very suggestive clinical presentation associated with glandular involvement is the Heerfordt-Waldenström syndrome, which includes systemic sarcoidosis, xerostomia, parotid gland swelling – usually bilateral - uveitis, and facial nerve palsy [30,31]. The jaw bone involvement affects equally the maxilla and mandible, the symptoms being due to the lytic character of the lesion: teeth loosening,
radiating pain, nasal obstruction, mandible tumefaction or maxillary bone loss [29].

Wegener granulomatosis, a necrotizing granulomatous vasculitis of the small-to-medium vessels, has a common oral involvement, expressed as ulcerations on oral mucosa or palate, tooth mobility and loss. The pathognomonic finding is granular hyperplastic gingivitis or the so-called “strawberry gingivitis”, with red interdental papillae covered with hyperplastic purple petechiae. This clinical sign is essential for an early suspicion of diagnosis, and oral biopsy is mandatory for preventing a serious multiorgan involvement of the respiratory airways and kidneys [7, 32-33].

5. OTHER PULMONARY DISEASES

Lung cancer causes more than 25% of the oral metastases, the jawbones being more frequently affected, compared to the soft tissue of the oral cavity. The mandible is the most exposed bone, more than 55% of the metastases being located here, while some studies report that oral metastases could be the first manifestation of this type of cancer, announcing unfortunately an advanced stage of neoplastic pulmonary disease [34]. When located in the soft tissue, the metastases appear as a submucosal mass, highly vascularized, frequently hemorrhagic, rarely ulcerated, or, more frequently, as a hyperplastic reactive lesion [35]. When the mandible is interested, insidious paresthesia of the lower lip on the affected side, rapidly progressing local swelling and pain appear, as tumor invades the inferior alveolar nerve, bone, and soft tissue [36]. Clinical profile of the patient with oral metastases also includes male sex, and age > 50 years [34].

Pulmonary tuberculosis can lead to oral lesions in both primary and secondary stages. Mouth involvement in secondary tuberculosis is usually a result of reactivation and hematogenous spread from the primary infection of the lung, the lesions being very similar to those of a squamous cell carcinoma: irregular ulcerations with peripheral thickening and dirty-appearing base, biopsy and culture being necessary to confirm the granulomatous inflammation. Secondary oral tuberculosis usually leads to the diagnosis of asymptomatic pulmonary tuberculosis. Therefore, all cases of incidentally discovered oral tuberculosis, even in asymptomatic patients, should be submitted to investigations for identifying its primary site [37-39].

Cystic fibrosis is a genetic disorder caused by mutations in the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein, affecting mostly the respiratory tract, with chronic cough and sputum, dyspnea, recurrent infections, and associated pancreatic insufficiency and malnutrition [40]. Oral manifestations of the disease are generated by the effects on the salivary glands, the sublingual ones being the most affected, followed by submandibular glands, due to the presence - at that level - of mucous acinar cells; parotid glands are less affected because of their serous structure. The affected glands are enlarged and can be easily palpated; disturbances in the composition of saliva could lead to xerostomia and require artificial saliva to keep oral mucosa moist. The calcium content, mean pH, and buffering capacity of the saliva are elevated. Patients with cystic fibrosis can also present cheilosis from vitamin deficiency, tooth discoloration, and hypoplastic defects of permanent dentition, the latter associated with tetracycline use during the period of tooth formation; replacing tetracycline with other antibiotics was followed by a reduction of this type of dental defects [41]. Data provided by various studies are conflicting, however, it seems that the incidence of dental cavities in pediatric patients with cystic fibrosis is lower than in age-matched healthy control population, although these patients display a higher incidence of enamel defects. This could be related to an increased calcium content, buffering capacity of saliva, and prolonged treatment with antibiotics. Some of these patients may also suffer from chronic nose and sinuses obstruction, associated with oral breathing pattern and anterior open bite [40-42].

The main findings in clinical exam of the oral cavity and the different therapeutic options of various pulmonary diseases involving the mouth are summarized in Table 1.
Table 1. Pulmonary conditions and the corresponding oral cavity involvement

<table>
<thead>
<tr>
<th>Pulmonary conditions</th>
<th>Oral cavity involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled medication</td>
<td>Deleterious effects on the quantity and quality of saliva, decreased oral pH (β₂-agonists), candidiasis, dysphonia, tongue hypertrophy (ICS), xerostomia</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Periodontitis, thrush, worsening dental status, loss of alveolar bone, colonization of airways from denture plaque biofilm</td>
</tr>
<tr>
<td>Asthma</td>
<td>Dental cavities and erosions, periodontal disease, candidiasis, colonization with P. gingivalis (lowers prevalence of asthma)</td>
</tr>
<tr>
<td>Obstructive sleep apnea syndrome</td>
<td>Inflammation (pharynx, uvula, soft palate, oral cavity), increased oral exhaled NO, therapy (ODMA)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Jaw metastases (mandible), submucosal mass or hyperplastic reactive lesion (soft tissue metastases)</td>
</tr>
<tr>
<td>Wegener granulomatosis</td>
<td>“Strawberry gingivitis”, ulcerations (oral mucosa, palate), tooth mobility and loss</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Painless ulcerations, gingivitis, localized swelling or nodules</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>Irregular ulcerations (secondary oral tuberculosis, hematogenous spread)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Xerostomia, tooth discoloration and hypoplastic defects (tetracycline), elevated calcium content, pH and buffering capacity of saliva</td>
</tr>
</tbody>
</table>

6. CONCLUSIONS

Considering the comprehensive approach to chronic pulmonary patients, regular dental services and careful oral cavity exams are more than necessary for the management of these diseases, from diagnosis to therapeutic resources, favoring an early recognition, lowering the rate of infectious exacerbations, and increasing life quality. An active collaboration among dentists and pulmonologists or somnologists, for patient’s ultimate benefit, is absolutely necessary.

References


