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Case Report Open Access

Oral Carcinoma Associated with Chronic Use of Electronic Cigarettes

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Abstract

The electronic cigarette (E-cigarette) is a handheld electronic device that vaporizes a nicotine-containing fluid for inhalation. Invented in 2003 by Chinese pharmacist Hon Lik, the E-cigarette was developed as a substitute for tobacco cigarettes. The use of E-cigarettes continues to grow in popularity in most parts of the world, and many consider their use and the use of other electronic nicotine delivery systems (ENDS) to be healthier than smoking tobacco cigarettes. There is a paucity of medical research, however, to support that notion. In particular, the impact of chronic use of E-cigarettes and ENDS has not been studied adequately. Herein, we report two cases of oral carcinoma associated with chronic use of E-cigarettes. These highlight the need for increased awareness of this important, and potentially fatal, risk. Physicians, dentists and other health care providers must be made aware and should consider regularly-scheduled, comprehensive oral examinations of their patients that regularly use E-cigarettes or ENDS. In the United States, the Food and Drug Administration (FDA) collects adverse effect and safety data at their Safety Reporting Portal for Tobacco Products (https://www.fda.gov/TobaccoProducts/PublicHealthScienceResearch). Adverse effects suspected to be related to the use of E-cigarettes or ENDS should be reported to the FDA or to analogous regulatory governances in other countries.

Keywords: E-cigarette; Electronic cigarette; Electronic nicotine delivery systems; ENDS; Oral carcinoma; Oral cancer; Squamous cell carcinoma

Introduction

Hookah pens, vaporizers, vape pens, E-cigarettes and E-pipes are some of the many type of Electronic Nicotine Delivery Systems (ENDS). In addition to liquid containing nicotine, propylene glycol, glycerin, flavorings and water are vaporized into an aerosol that the user inhales [1-4]. Many ENDS are commercial manufactured to look like conventional cigarettes or cigars, but some are manufactured to resemble everyday items (e.g. pens), and other types of ENDS (e.g. hookah devices) bear no resemblance to cigarettes or cigars. Claims that ENDS contain "only water vapour and nicotine" are false: the vapour has been found to contain varying amounts of heavy metals (Nickel, Tin, Silver, Aluminum, Mercury and Chromium) as well as carbonyls and other organic volatile compounds [4].

Herein we describe two cases of oral carcinoma associated with chronic E-cigarette use in otherwise healthy individuals. In both cases, their use of E-cigarettes began in 2003 and continued for more than 10 years. Neither patient had a family history of oral carcinoma nor did either have a history of known risk factors for oral carcinoma (e.g. hematopoietic stem-cell transplant, chronic heavy alcohol consumption, smoking or Human Papilloma Virus infection) [5,6]. Neither patient had diagnoses of acute or chronic oral infections caused by other microorganisms (e.g. fungi, bacteria, virus). Neither patient had a history of consumption/chewing of tobacco, paan (betel leaf mixed with areca nut) or other leaf types. Importantly, both presented with the same triad of symptoms - unintended weight loss, dry mouth, and difficulty swallowing. As the popularity of E-cigarettes and ENDS continues to increase across the world, health care providers need to be aware of the possible increased risk of oral carcinoma [6].

Case Reports

Case 1

A 66-year-old male presented to the out-patient office (otolaryngology) with chief complaints of unintended weight loss, dysphagia and xerostomia. His immunization records were up to date for Human Papilloma Virus, Varicella Zoster Virus and Hepatitis B Virus. His past medical history was unremarkable other than a social history positive for use of E-cigarettes (20 times per day for past 13 years). Examination of the oral cavity was consistent with xerostomia, and there were several areas of induration and paresthesia of the tongue. Several exophytic masses were present with surrounding hyperkeratotic areas with histological features of lichen planus. As infection or carcinoma were the chief suspects, the following clinical laboratory tests were ordered: complete blood count; complete blood chemistry panel; and blood calcium, liver enzymes, ferritin, urea, alpha-antitrypsin and alpha-anti-glycoprotein levels. Importantly, increased levels of serum ferritin, alpha-antitrypsin, and alpha-anti-glycoprotein are often associated with later stages of oral cancer. A tissue biopsy was performed and reported as follows: A small piece of tissue was cut from an abnormal paraesthesia, keratotic region at the anterior aspect of the tongue. This incisional biopsy was taken at the office, and neither general anesthesia nor localized anesthesia were needed. The removed tissue was cut into thin sections, placed on slides and stained before further processing to "frozen section" and "permanent section". Histopathology revealed a moderately

collagenous connective tissue stroma infiltrated with nests and islands of tumor epithelial cells. The tumor cells exhibited a basaloid appearance with hyperchromatic nuclei and scanty cytoplasm and were arranged in a lobular configuration. Occasional squamous differentiation was also noted and a large number of mitotic figures with nuclear atypia were observed. A diagnosis of basaloid squamous cell carcinoma was given. Oncologist was notified to follow-up.

Case 2

A 59-year-old male presented to an out-patient otolaryngology office with a chief complaint of a 9-month history of a non-healing ulceration of the lower lip. No pain or discomfort was reported by the patient, but the patient reported having some difficulty swallowing and severe dry mouth. No history of trauma to the area was reported and the patient denied a history of alcohol use. The patient reported consistent, routine dental care throughout his life but reported that he had smoked 30 E-cigarettes per day for the past 13 years. The patient's health history was otherwise unremarkable. Other than an ulcerative lesion (1-cm in diameter) on the vermilion of the lower lip, examination of the head and neck region was without abnormalities. Vitals signs were within normal limits, and no palpable lymph nodes were detected. No other abnormal extra oral findings were noted, and palpation of the lesion revealed induration at the periphery of the lesion. Basal squamous cell carcinoma was suspected, and the following clinical laboratory tests were ordered: complete blood count; complete blood chemistry panel; and blood calcium, liver enzymes, ferritin, urea, alpha-antitrypsin and alpha-anti-glycoprotein levels. Again, it is important to note that increased levels of serum ferritin, alpha-antitrypsin and alpha-anti-glycoprotein are often associated with later stages of oral cancer. An incisional tissue biopsy was examined for histologic analysis, and histopathological examination revealed a dysplastic stratified squamous epithelium infiltrating into underlying moderately collagenous connective tissue. The infiltrating tumor cells had a basaloid appearance. Nuclear atypia was observed and pleomorphisms with large numbers of mitotic figures were noted. A diagnosis of basaloid squamous cell carcinoma was made, and an Oncologist was scheduled for follow-up.

Summary

Clinical findings

Oral cancer may occur on the floor of the mouth, the lining of the cheek, the gingiva (gums), the lips or the palate (roof of the mouth) [7]. Early-stage symptoms can include persistent red or white patches, a non-healing ulcer, progressive swelling or enlargement, unusual surface changes, sudden tooth mobility without apparent cause, unusual oral bleeding or epitaxis and prolonged hoarseness. Late-state symptoms can include induration of affected areas(s), paresthesia/dysesthesia of the tongue or lips, airway obstruction, chronic serous otitis media, dysphagia, cervical lymphadenopathy, ánd persistent pain. Oral cavity cancers can manifest as a red lesion (erythroplakia), a granular ulcer with fissuring or raised exophytic margins, a non-healing extraction socket or as a lesion fixed to deeper tissues [8].

Laboratory findings

A diagnosis of oral cancer is confirmed by tissue-biopsy microscopy. As more than 90% of oral cancers are squamous cell carcinoma, a FOXM1-based diagnostic test, quantitative malignancy diagnostic system (qMIDS), is used to confirm diagnosis and quantify the aggressiveness of squamous cell carcinomas [9,10]. Bacterial identification testing also has some predictive value: *C. gingivalis*, *P. melaninogenica* and *S. mitis* have a predictive value of about 80% for oral squamous cell carcinoma. About 5% of oral cancer are verrucous carcinoma, a very slow-growing cancer also comprised of squamous cells and the remainder (<5%) of oral carcinomas are either minor salivary gland carcinoma or lymphoma [9,10].

Treatment

Surgical excision can be curative for oral cancers limited in size. Inoperable tumors are treated with radiation +/- chemotherapy, and more definitive treatment often combines these with surgery (e.g. maxillectomy, mandibulectomy, glossectomy and radical neck dissection) [8].

Pathophysiology

Tobacco is a known risk factor for oral cancer, and about 80% of patients with oral cancers have a history of smoking or chewing tobacco. An interaction between redox-active metals in saliva and the low reactive free radicals in tobacco smoke that results in saliva losing much of its antioxidant capacity [8]. Other known risk factors include gender (males are twice as likely as females to develop oral cancer), routine alcohol consumption (70% of patients with oral cancer regularly consume alcohol), chewing betal quid (a leaf from the betel plant wrapped around areca nut and lime) combined or without tobacco, human papilloma viruses (HPV) infection (about 25% of patients with oral cancer have HPV, particularly HPV-16), immune-system suppression, lichen planus infection (itchy rash +/- white lines or spots in oral cavity) and graft-verse-host disease (secondary to stem-cell transplant) [3,6,9].

Discussion

Nicotine solutions commercially available for use with ENDS and E-cigarettes can contain up to 100mg/mL of nicotine (as little as 1mg of nicotine can cause symptoms in a toddler and 6 to 13 mg/kg can be lethal in toddlers) [4]. In addition to nicotine, diethylene glycol, ethylene glycol, ethanol, formaldehyde, acrolein and various amounts of heavy metals (nickel, tin, silver, aluminum, mercury and chromium) comprise the inhaled vapour [4]. The effects of chronic exposure to these chemicals are unknown but should not be considered benign (several have known toxicity). Patients seeking smoking cessation should consider approved nicotine replacement delivers products (gums, patches, lozenges) instead of the use of E-cigarettes or ENDS.

Conclusion

Tobacco cigarette smoking is a known risk for cancers, including oral cancer. Patients and clinicians (physicians, dentist and nurses) need to be aware that the use of electronic-cigarettes (E-cigarettes) or other electronic nicotine delivery systems (ENDS) may also be associated with an increased risk of oral cancer. Here we describe two patients, with positive history for chronic E-cigarette use, that developed oral cancer without any identifiable risk factors other than E-cigarette use. Further investigation is warranted.

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Conflict of Interest

None

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