

CASE REPORT

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Management of large multiple oral papillary lesions suspected Acanthosis Nigricans: a case report

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Abstract

Background: Papillary oral pathologies are a heterogeneous group. Both virus-associated and non-virus-associated, malignant and benign entities may enter the differential diagnosis. In some cases, oral papillary lesions are part of a variety of skin or systemic disorders and syndromes. It is a challenge for clinicians to identify and treat the various etiology of oral papillary lesions.

Case presentation: This case report describes the successful management of large multiple oral papillary lesions in a 65-year-old female. Combined the clinical features, pathological findings and medical history, the patient was tended to be the diagnosis of Acanthosis Nigricans and was successfully managed. The neuro-endocrine-immune network and mechanical factors in the pathogenesis of oral papillary lesions of Acanthosis Nigricans were discussed. Common questions regarding differential diagnosis, the management of oral papillary lesions of Acanthosis Nigricans patients and follow-up visits are addressed.

Conclusions: The neuro-endocrine-immune network and mechanical factors play important roles in the pathogenesis of oral papillary lesions with Acanthosis Nigricans. Removing traumatic factors of oral mucosa and the treatment of underlying systemic diseases is necessary for Acanthosis Nigricans patients with oral papillary lesions. The clinical management plan should comprise both the local treatments of oral papillary lesions and the systemic treatment of underlying diseases. Multidisciplinary correlation is helpful and the patient's collaboration is necessary to arrive at the correct diagnosis and successful long-term treatment effect. From the clinician's perspective, recognizing various causes and clinical presentations of oral papillary lesions will help guide management.

Keywords: Acanthosis Nigricans, Oral papillomatosis, Human papillomavirus, Clinical management, Case report

Background

The oral cavity is site to normal anatomic papillary structures such as lingual papillae, while a site to abnormal papillary lesions as well. These papillary lesions are commonly associated with virus infections or complex systemic diseases. Human papillomavirus (HPV) could induce papillary lesions of oral mucosa. Aside from HPV-induced lesions, oral papillary lesions also consist of a variety of reactive and neoplastic conditions (Mainville

2019). Acanthosis Nigricans is a systemic disorder that could associated with oral papillary lesions. In some cases of Acanthosis Nigricans, especially when associated with malignancies, Acanthosis Nigricans may greatly affect the mucosa of lips and the oral cavity, resulting in hyperkeratosis and increasing papillary hyperplasia (Mainville 2019; Lause and Kamboj 2017; Phiske 2014; Popa et al. 2019).

This case report describes the successful management of large multiple oral papillary lesions in a 65-year-old female. Combined the clinical features, pathological findings and medical history, the patient was tended to be the diagnosis of Acanthosis Nigricans. The differential

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diagnosis, pathogenesis and the essential management of oral papillary lesions with Acanthosis Nigricans were discussed.

Case presentation

A 65-year-old woman presented the stomatology department with a more than 1-year history of multiple oral mucosal tumors. The patient described a small tumor of buccal oral mucosa about 1 year ago, which was the size of about 3 mm in diameter at that time, and then the development of multiple tumors of left buccal and palatal mucosa. The patient did not see a doctor in time because of some individual reasons and the multiple tumors in her oral cavity gradually grew up. Recently due to eating and speaking the patient often bit the tumors incidentally and she could not use her removable partial denture because of the tumors. She felt pain of oral mucosa and uncomfortable. The patient had medical history of hyperthyroidism, thyroidectomy, Hepatitis C infection and familial hypotension. The patient denied history of diabetes, drug allergy history and family cancer.

Physical examination showed the face was symmetrical, the mouth opening degree and the opening type was normal. Oral examination showed that 16, 17, 26, 27, 46 and 47 were missing. The left buccal mucosa and palatal mucosa presented with multiple oral papillomatosis. The papillary lesions of left buccal mucosa were about 4.2 cm * 7.1 cm, irregular, no movability, mild hardness and some lesions were prone to bleeding by palpation. The lesions of palatal mucosa were about 3.2 cm * 4.1 cm, irregular, no movability, mild hardness and some lesions were prone to bleeding by palpation. There was no papillary lesions and obvious abnormal pigmentation on the skin. Figure 1 shows the manifestations of oral cavity.

Laboratory examination revealed complete blood count (CBC), liver and kidney function, blood lipid and blood glucose were normal. Hepatitis B, Hepatitis C, syphilis, tuberculosis bacilli, HIV testing were negative. Carcinoembryonic antigen CEA testing was normal, immunoglobulins IgG4, IgG, IgA and IgM testing were normal, but immunoglobulin E was elevated to 264 IU / ml (normal 0–100 IU / ml).

The fungal smear of the oral mucosa and the lesions tested negative. The high-risk and low-risk HPV tested negative for mucosal exfoliated cells of the lesions. Computed Tomography of chest was normal and Occlusal X-ray showed that there was no significant bone resorption of the palate plate. Gastrointestinal endoscopy findings were normal.

Histological findings: squamous epithelial papillary hyperplasia. Figure 2 shows the histological manifestations.



Fig. 1 The manifestations of oral cavity

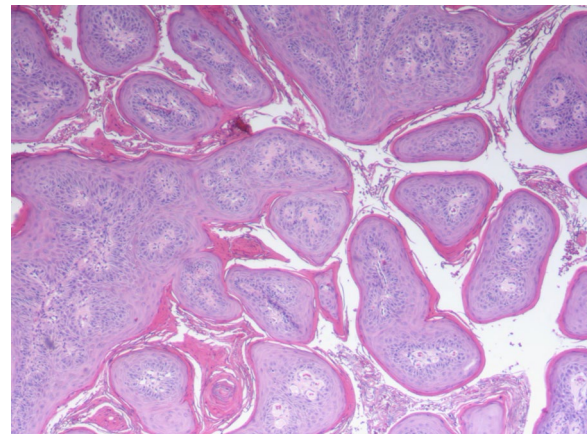


Fig. 2 Histological findings: squamous epithelial papillary hyperplasia

Immunopathological findings: Ki67 positive cells restricted to the basal layer. Figure 3 shows the immunopathological manifestations of Ki67.

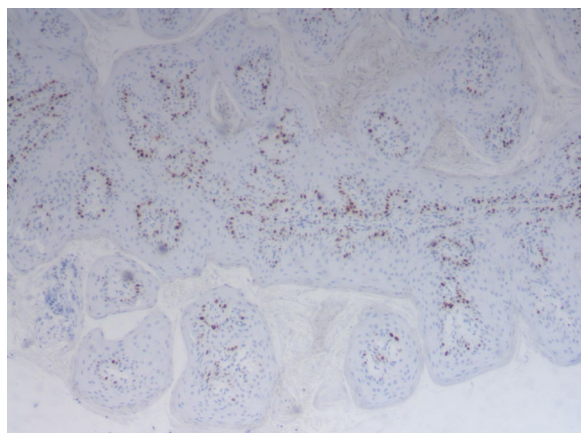


Fig. 3 Ki67 positive cells restricted to the basal layer

Diagnosis

The patient had a history of increasing oral papillomatosis for more than 1 years and during this period, she experienced fatigue, poor sleep, irregular eating, depression, weight loss because of personal reasons. The patient had medical history of hyperthyroidism, thyroidectomy, Hepatitis C infection and familial hypotension. Histological findings showed squamous epithelial papillary hyperplasia and Ki67 positive cells restricted to the basal layer. Combined the clinical features, pathological findings and medical history, the patient was tended to be the diagnosis of Acanthosis Nigricans.

Treatment

Both local oral mucosa and underlying systemic diseases management were included the treatment plan.

The management of local oral mucosa included:

1. Adjustment and polishing the sharp tooth tips to remove traumatic factors of oral mucosa.
2. Surgical resection of the multiple papillomatosis of oral mucosa. Interferon gel topical application was given for 2 weeks postoperatively, four times daily.
3. To get successful curative effect in long-term and to prevent recurrence of oral papillomatosis after surgical resection, the patient was advised to avoid dry and rough foods, spicy foods, alcoholic beverages, carbonated beverages and tobacco.

The management of underlying systemic diseases included:

1. The treatment of thyroid disorder and other systemic disorders.



Fig. 4 The manifestations of oral cavity after the treatment for 18 months

2. Pay attention to eating regularly, enough water drinking, adequate sleep, positive attitude and so on.

Follow-up and outcomes

The patient was given advice to keep regular follow-up visits for every month and the patient did it well.

Figure 4 shows the manifestations of oral cavity after the treatment for 18 months.

Differential diagnosis

Human papillomavirus (HPV) could induce papillary lesions of oral mucosa. The World Health Organization recognizes four HPV related oral lesions: squamous cell papilloma, condyloma acuminata, verruca vulgaris and multifocal epithelial hyperplasia. Squamous cell papilloma tends to be solitary. Verruca vulgaris is common in skin and relatively uncommon intraorally. The verruca vulgaris lesion involving oral mucosa is usually less than one centimeter. Oral condyloma acuminata commonly corresponds to the counterpart of genital condyloma (Piña et al. 2019). Multifocal epithelial hyperplasia usually affects specific groups of individuals such as Eskimos,

Amerindians of North, South and Central America (Piña et al. 2019; Patil et al. 2019).

Regarding to squamous papilloma, positivity for HPV is extremely variable in the literature. In some articles the squamous papilloma was mostly HPV negative (Piña et al. 2019; Beta 2019). It was reported that abnormal expression of Ki67 was associated with the HPV related lesions (Piña et al. 2019; Beta 2019). Ki67 usually showed a non-restricted basal layer positivity in HPV positive lesions, while HPV negative lesions showed Ki67 positive cells restricted to the basal layer (Piña et al. 2019; Beta 2019). It is reported that most oral papillary lesions of condyloma acuminata, verruca vulgaris and Multifocal epithelial hyperplasia share low-risk HPV subtypes. But the reasons of why these lesions belong to the same spectrum with different clinical presentation is still unknown (Piña et al. 2019).

Papillary lesions also include a variety of developmental, reactive and neoplastic conditions not driven by HPV infection (Mainville 2019; Lause and Kamboj 2017; Phiske 2014; Popa et al. 2019). Acanthosis Nigricans (AN) is clinically manifested as dark, velvety, and thickened skin and histopathologically characterized by papillomatosis and hyperkeratosis. In some cases, especially when associated with malignancies, Acanthosis Nigricans may interest the mucosa of lips and the oral cavity, resulting in papillary hyperplasia (Mainville 2019; Lause and Kamboj 2017; Phiske 2014; Popa et al. 2019; Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021). A high prevalence of AN has been observed recently. Different varieties of AN include benign, obesity associated, syndromic, malignant, acral, unilateral, medication-induced, mixed AN and so on. Diagnosis is largely according to clinical manifestation and histopathology features needed only for confirmation (Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021).

The pathogenesis and treatment of oral papillary lesions with Acanthosis Nigricans

AN is in fact an echo of a systemic problem or disease: metabolic disorder (most frequently), endocrine syndrome, medication side effects, malignancy, genetic factors and so on (Brady et al. 2021). How could these different systemic problems eventually induce skin and mucosa papillary lesions? The skin as well as mucosa conditions are under the regulation of psychology-endocrine-neuro-immune network through signaling molecules including neurotransmitters, hormones, cytokines, and other types of secreted proteins. Psychological factors such as stress, anxiety and depression, nervous system, endocrine system and immune system act as an integrated psychology-endocrine-neuro-immune network unit to optimize health and

develop defense against various complex pathological processes. The pathophysiology of AN seems to relate to a multitude of factors that are not fully understood (Mainville 2019; Lause and Kamboj 2017; Phiske 2014; Popa et al. 2019; Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021).

Sometimes, AN is the first observed sign of a malignancy or chronic metabolic disorder. Therefore, it is not to be taken lightly. The patients suspected to be AN should be subjected to thorough history taking and clinical examination. Age, sex, occupation, history of smoking, alcohol intake, history of drug intake, family history of AN, blood pressure, other skin diseases, diabetes and other systemic diseases, duration of disease, and so on should be recorded. Since some cases of AN precede or are discovered simultaneously with malignant pathology, the clinician must thoroughly investigate the patient to be able to exclude the paraneoplastic AN (Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021). Trying to discover and treat the underlying disease is important part of the management to achieve successful curative effect in long term. AN is a sign of various systemic causes. The evolution of the skin and oral mucosa condition associated with the evolution of underlying disease, so the treatment of the AN should aim the causing disorder either. It was reported that hyperkeratosis diminishing in some patients, following metabolic disorders correction by maintaining a low-calorie diet and sustained physical activity, or obesity control by weight loss (Mainville 2019; Lause and Kamboj 2017; Phiske 2014; Popa et al. 2019; Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021).

The distribution pattern of AN with high frequency on the neck, axillae, lips can be caused by potentiator cofactors such as friction (Popa et al. 2019). Mechanical factors have an important role in proliferation of skin and oral mucosal keratinocytes, their influence being integrated by complex cellular signaling (Popa et al. 2019; Higgins et al. 2008; Panda et al. 2017; Brady et al. 2021). The oral lesions are vulnerable to mechanical and traumatic factors because of chewing and speaking. In the cases of AN interested in lips and oral mucosa, clinicians are reminded that it is necessary to discover and remove traumatic factors of oral mucosa such as removal the inappropriate prosthesis, adjustment and polishing the sharp tooth tips.

Regarding to the psychology-neuro-endocrine-immune network, which could promote the positive of psychology-neuro-endocrine-immune loop such as positive attitude, regular exercise, proper diet and so on could be beneficial to the patients for successful curative effect and prevention of recurrence.

The local treatments also usually applied for esthetic and functional reasons comprise several methods such as

surgical resection, laser procedures, prescribing topical keratolytics: retinoids and podophyllin and so on.

Conclusions

Papillary oral pathologies are a complex heterogeneous group. Recognizing various causes and clinical presentations of oral papillary lesions will help guide clinical management. The neuro-endocrine-immune network and mechanical factors play important roles in the pathogenesis of oral papillary lesions with Acanthosis Nigricans. Removing traumatic factors of oral mucosa and the treatment of underlying systemic diseases is necessary for Acanthosis Nigricans patients with oral papillary lesions. The local treatments of oral papillary lesions also usually applied for esthetic and functional reasons comprise several methods such as surgical resection, laser procedures and so on.

Abbreviation

AN: Acanthosis Nigricans.

Acknowledgements

The author would like to thank Dr. Ma Li for his contribution in excision biopsy and Dr. Cheng Xian-kui for his contribution in histological examination.

Authors' contributions

Min Zhao performed the physical examination, oral cavity examination and removing traumatic factors of oral mucosa, follow-up visits and multidisciplinary consultation. Min Zhao was a major contributor in excision biopsy and the contributor in writing the manuscript. The author read and approved the final manuscript.

Funding

No funding was received in association with this article.

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The author has declared that no competing interest exists.

Received: 12 October 2021 Accepted: 5 January 2022

Published online: 15 January 2022

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