Human Papillomavirus (HPV) oral lesions surgical management with Nd:YAG laser versus blade and QMR scalpel: a single center experience in 251 cases

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HPVs are a large and varied group of viruses capable of infecting both animals and humans. They have evolved together with their respective hosts and are isolable in different and numerous species of birds, reptiles, marsupials and mammals. The present study aims to analyze and compare the epidemiological aspects of 251 HPV-associated benign lesions treated with three different surgical approaches. Between January 2004 and December 2019, 251 HPV-associated benign lesions (papillomas and / or condylomas) were treated at the Center of Medicina e Patologia Orale Laser Assistita of the University of Parma. After loco-regional anesthesia, the excisional biopsy was performed with A): 15C scalpel blade; B): molecular quantum resonance scalpel (RQM); C): Nd: YAG laser (1064 mn, 3.5W, 70Hz). The epidemiological analysis considered: gender, age, site of the lesion, surgical technique and recurrence. Our study did not show substantial differences in gender prevalence and the mean age of 50 years (minimum 8 years, maximum 85 years). Our study showed that HPV-associated lesions are localized in almost half of patients (47.9%) on the tongue or hard palate, less frequently on the cheeks (16.3%) and on the upper or lower lip (14,4) and in less than 10% of patients in the soft palate. Our study showed a low relapse rate (3%) for all three therapeutic approaches used, meaning that the cold blade, ROM scalpel and Nd: YAG laser can be successfully used to treat lesions associated with HPV, the laser approach has proved to be slightly more effective: probably thanks to the radicalization obtained through carbonization of the biopsy surrounding tissues. Since a small group of these viruses are the responsible agent of several types of human cancers (including squamous cell carcinoma of the oral cavity), early screening and treatment of HPV-associated lesions is essential to prevent the development of oncological diseases.

Human papilloma viruses (HPVs) are small DNA-viruses without pericapsid. They show a peculiar tropism for squamous epithelial tissue; their capsid has an icosahedral shape of about 60 nm in diameter and contains both the single circular DNA molecule and the double strand (1). HPVs are among the oldest known viruses; it is estimated that they first developed 330 million years ago and originated in the late Paleozoic era (2). HPVs are a large and varied group of viruses capable of infecting both animals and humans: they have evolved together with their respective hosts and are isolable in

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different and numerous species of birds, reptiles, marsupials and mammals (3). HPVs are members of the Papillomaviridae family which is divided into 39 genera (4, 5).

To date, more than 250 different types of HPV have been identified and classified into five different genera: Alpha-; Beta-; Range-; Nu- and Mu-papillomavirus (6). HPVs with tropism for the epithelia of the oro-genital mucosa belong mainly to the Alphapapilloma virus genotype: the alpha genus is therefore of primary clinical importance as it contains both the so-called "low risk" and "high risk" HPV, responsible for wide variety of HPV-associated clinical manifestations (7).

Following exposure by injury or microtrauma of the basal epithelium, HPV viruses are able to infect the basal cells of multilayered squamous epithelium asymptomatically (8). In basal cell nuclei, the viral



Fig. 1. Clinical aspect of the lesion before surgical treatment.



Fig. 2. Surgical intraoperatory detail.



Fig. 3. Surgical margins of the excisional biopsy.



Fig. 4. Bioptic specimen.

genome remains as a low-replicating plasmid and the expression of viral proteins is regulated by the degree of differentiation of infected cells during their migration movement towards the epithelial surface (9). Virus particles are produced only in the most superficial layer of the epithelium and from there they are diffused into the surrounding environment and are able to infect new target cells (9).

In the oral cavity, possible reservoirs of latent HPV infection include: gingival pockets associated with periodontal disease, ductal epithelium of the salivary glands, cryptic tonsillar epithelium and oropharynx (10, 11). Previously, transmission of HPV was considered to be an exclusively sexually transmitted disease (12) but horizontal transmission was proven be only one side of possible transmission, in fact HPV has also been found in non-sexually active patients, infants and newborns, both in oral and genital mucosa (13).



Fig. 5. Surgical site right after laser surgery with Nd:YAG laser (1064 mn, 3.5W, 70Hz).



Fig. 6. Clinical aspect at 10 days follow-up visit.



Fig. 7. *Histocitopathological analysis. H&E 100x. Thermal modification of 100 micron in the cutting area.*

These results imply a vertical mode of transmission: perinatal transmission would explain the presence of HPV in non-sexually active patients; studies have been published that have shown that children born to HPV positive mothers have a higher risk of becoming virus positive themselves (15, 16).

Oral HPV infection is often associated with benign lesions such as papillomas and acuminate squamous cell warts (17, 18). More rarely, HPV infection manifests as focal epithelial hyperplasia: a benign familial disorder with autosomal-recessive inheritance characterized by multiple associated lesions (19). Less frequently, HPV is associated with precancerous and malignant lesions: specific types such as HPV-16 and HPV-18 are strongly involved in the multifactorial process of development of oropharyngeal squamous cell carcinoma (20, 21).

The present study aims to analyze and compare the epidemiological aspects of 251 HPV-associated benign lesions treated with three different surgical approaches.

MATERIALS AND METHODS

Between January 2004 and December 2019, 251 HPVassociated benign lesions (papillomas and / or condylomas) were treated at the Center of Medicina e Patologia Orale Laser Assistita of the University of Parma. After locoregional anesthesia, the excisional biopsy was performed with: A) 15C scalpel blade; B) molecular quantum resonance scalpel (RQM); and C) Nd: YAG laser (1064 mn, 3.5W, 70Hz). When necessary, 3.0 silk stitch suture was applied and removed during the one-week follow-up visit. Histocytopathological analysis was performed for each biopsy sample to confirm the diagnostic hypothesis. An excisional biopsy was performed with laser surgery (Fig. 1-7). The minimum follow-up time for inclusion in the study was 6 months.

RESULTS

The total of 251 HPV-associated lesions were surgically removed in patients with a mean age of 50 years (minimum 8 years, maximum 85 years). The epidemiological analysis considered: gender, age, site of the lesion, surgical technique and recurrence. Figure 8 shows the number of HPV-associated lesions and their distribution by decade of age. One

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hundred and forty-three lesions (56.9%) were found in female patients while 108 (43.1%) in men (Fig. 9).

Table 1 shows the number of lesions per oral site and their prevalence rate (Fig. 10). displays sites' ratio. 49 lesions (19.5%) were treated with the Nd: YAG laser, 32 with RQM scalpels (12.7%) and 170 (67.8%) with 15C blade scalpels. Recurrence (3%) was observed in 8 patients, after a mean time of 14 months. Recurrence occurred in 6 patients treated with 15C blade scalpel (3,5%), in one patient treated with RQM scalpel (3,1%) and in one patient treated with laser (2%) (Fig. 11). compares all 3 surgical technique with recurrence.

DISCUSSION

HPV-associated lesions are commonly diagnosed in both young and elderly patients, but most commonly during the third, fourth and fifth decade of age (22). In agreement with the published



Fig 8. Age distribution in 251 treated patients.



Fig. 9. Gender ratio in 251 treated patients.



Fig. 10. Site's ratio in 251 treated patients.



Fig 11. *Comparison of all 3 surgical technique between recurrence and no recurrence.*

literature, our study did not show substantial differences in gender prevalence: the values of the overall prevalence rate of oral HPV infections were similar in men and women (23) and the mean age shown is 50 years old (23). Our study showed that HPV-associated lesions are localized in almost half of patients (47.9%) on the tongue or hard palate, less frequently on the cheeks (16.3%) and on the upper or lower lip (4, 14) and in less than 10% of patients in the soft palate: these data show that a thorough physical examination of the oral cavity is of key importance for the early diagnosis of small or hidden lesions in inaccessible areas of the oral cavity.

Treatment of oral papillomas and condilomas can sometimes be complex as HPVs tend to spread and disseminate, causing multifocal and disseminated lesions in the oral cavity. Furthermore, HPV-related lesions tend to recur if incompletely removed. Our study showed a low relapse rate (3%) for all three therapeutic approaches used, meaning that the cold blade, RQM scalpel and Nd: YAG laser can be successfully used to treat lesions associated with HPV, the laser approach has proved to be slightly

Sites	Nr. of <u>lesions</u>	Percentage (%)
Gengiva	30	11,9
Lip	36	14,4
Cheek	41	16,3
Hard Palate	48	19,1
Soft Palate	24	9,5
Tongue (body)	36	14,4
Tongue (margins) + oral paviment	36	14,4
Total	251	100

 Table I. Prevalence of treated sites.

more effective: probably thanks to the radicalization obtained through carbonization of the biopsy surrounding tissues.

HPVs are DNA viruses linked to cervical and anogenital cancer. The literature has also established their role in the development of oral and oropharyngeal cancer in both male and female patients. Since a small group of these viruses are the responsible agent of several types of human cancers (including squamous cell carcinoma of the oral cavity), early screening and treatment of HPV-associated lesions is essential to prevent the development of oncological diseases. Histocytopathological examination, possibly with viral genotyping, is crucial for definitive diagnosis and predicting the patient's level of risk.

The hard palate and tongue were found to be the most commonly involved sites while complete surgical excision was confirmed to be the goldstandard treatment, with low lesion recurrence rates.

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