HPV AND HEAD AND NECK DISEASES

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INTRODUCTION

The ubiquitous Human papillomavirus, HPV, is responsible of an impressively frequent infection in humans. Actually, it is estimated that nearly 440 million individuals are HPV-infected worldwide. HPV is a very complex group of pathogenic viruses as more than 120 different genotypes have been identified so far. All are epitheliotropic viruses, specifically for squamous epithelia. These genotypes have different transmission modalities (sexual or non-sexual) and induce totally different diseases (from trivial plantar warts to invasive cancers for example of the cervix). HPVs responsible for benign epithelial hyperproliferation are named "low-risk" types while HPVs associated with premalignant lesions and invasive squamous cell carcinoma are named "high-risk" types. In the head and neck region, HPV infections may result

in benign lesions (HPV-6, -11, -13 and -32) of the oral cavity and larynx or in squamous cell carcinoma (HPV-16 and -18) in particular in the oropharynx.

SINO-NASAL DISEASES

Benign sino-nasal papilloma (either exophytic, inverted or cyclindric cell papillomas) and sino-nasal SCC have substantial clinical similarities to HPV-related diseases at other anatomical sites (morphologic aspect, multi-centricity and recurrence rate). Actually HPV DNA has been identified in some cases.

BENIGN LESIONS OF THE ORAL CAVITIES

Various lesions have been described: benign squamous cell papillomata, condyloma accuminatum, verruca vulgaris, focal epithelial hyperplasia and koilocytic dysplasia. As many of these oral infections are sexually transmitted, it is not rare that HIV infections may coexist in some cases (in particular for condyloma accuminatum, focal epithelial hyperplasia and koilocytic dysplasia).

BENIGN LESIONS OF THE LARYNX

Laryngeal papillomatosis despite its histological benign character remains a real therapeutic concern as recurrence is very frequent justifying the name of recurrent respiratory papillomatosis (RRP). It may occur during the first years of the life (juvenile-onset RRP) or in young adults (adult-onset RRP). HPV-6 and -11 are implicated in causing RRP. HPV-11 has been reported as causing more rapid growth and higher risk of recurrence. Some cases of malignant evolution have been attributed to the "high-risk" HPV-16. As HPV-6 and -11 genotypes are also frequently found in genital warts, a mother to child transmission during vaginal delivery has been often suggested in juvenile RRP. However as HPV-induced genital warts are very frequent while juvenile RRP is a rare disease (even if the most frequent benign tumor of the larynx during childhood), an associated host immune deficit has also been suggested. For adult RRP a sexual transmission is often suggested. The evolution is unpredictable with reported spontaneous regression, frequently observed recurrences and sometimes malignant transformation. The treatment consists mainly in endoscopic resection or destruction (microsurgical resection, laser resection, photodynamic therapy). Adjuvant therapies have been advocated (α-interferon for example). Vaccines are under consideration and evaluation.

SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

Over the past decade an impressively growing literature has paid attention to HPV-related head and neck squamous cell carcinomas (SCC). Predominantly HPV-16 but also HPV-18 are the most frequently involved genotypes. Their oncoproteins E6 and E7 play a key role in carcinogenesis by inhibiting the tumor suppressor proteins p53 and pRb. E6 binds to p53 and subsequently generates its degradation resulting in its inability to arrest cell growth or to promote apoptosis. E7 binds to pRb resulting in E_2F protein freeing that favors the cell progression into S phase. Causal relationship between "high-risk" HPVs and different head and neck primary sites has been studied. If evidence of linking "high-risk" HPVs and laryngeal SCC remains debatable (direct relationship and/or association with other risk factors such as tobacco exposure) on the contrary there is a clear evidence on HPV as an etiological factor in oral and moreover in oropharyngeal SCC in particular in tonsillar SCC. A sexual transmission is definitely suggested. These HPV-related SCC carry a better outcome in terms of response to treatment (radiotherapy and/or chemotherapy) and survival. The viral load seems of prognostic importance (the higher load, the better prognosis). Preventive and/or therapeutic vaccines are also under evaluation.

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