Human papillomavirus in recurrent respiratory papillomatosis, tonsillar and mobile tongue cancer

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt förvar i Föreläsningssalen ÖNH, by 1B plan 3 fredagen den 21:a oktober, kl. 09:00.

Avhandlingen kommer att förvaras på engelska.

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Abstract
The aims of this doctoral thesis were to characterize patients with recurrent respiratory papillomatosis (RRP) in northern Sweden, including voice quality and quality of life, evaluate the incidence of tonsil cancer longitudinally in northern Sweden and to study the correlation between human papillomavirus (HPV), its surrogate marker p16 and HPV receptor syndecan-1 in tonsillar cancer and mobile tongue cancer.

A total of 27 consecutive patients with RRP, preferentially HPV6 males, were evaluated using the voice handicap index (VHI) and SF-36 questionnaires to assess the impact on life and voice in a RRP population. The values were compared to normative data. HPV DNA was extracted from paraffin-embedded biopsies and detected by polymerase chain reaction (PCR), to study tonsillar (n= 65) and mobile tongue cancer (n=109). Expression of HPV surrogate marker p16 and the HPV receptor syndecan-1 was analyzed by immunohistochemistry. RRP patients with more than one surgery per year were younger than those treated less frequently and had significantly impaired voice quality as compared to normative data. Females, patients with frequent surgical treatment sessions and high-risk HPV-infected patients were particularly vulnerable and rated their quality of life as significantly low in several domains compared to normal subjects. Patients with high surgical treatment frequency were significantly younger and had more widespread RRP lesions, compared to patients treated less frequently. A total of 65 tonsillar cancer biopsies were analysed for HPV status and p16, 74% were males with a median age of 58 years. The incidence of tonsillar cancer revealed a 2.7-fold incidence increase in men between the years 2000 and 2012. We demonstrated a strong association between p16 and HPV infection in tonsillar malignancies. These findings are in contrast to the mobile tongue cancer cases where no evidence of HPV DNA could be detected. There was no difference in the expression of the primary HPV receptor, syndecan-1, between tonsillar and mobile tongue cancer.

This thesis confirms the existence of a more care-intensive RRP population. The frequency of RRP operations, age at onset, gender and genotype of HPV may be used as factors to predict voice disability. It identifies a 2.7-fold increase in the incidence of tonsillar cancer, HPV and p16 in men between 2000-2012. We can use p16 to detect HPV in tonsillar cancer but not in mobile tongue cancer. This thesis provides scientific data to support a gender-neutral vaccination since both RRP and tonsillar cancer mainly affect men.

Keywords