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RISK OF CERVICAL CANCER AMONG WIVES OF MEN WITH CARCINOMA OF THE PENIS

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Abstract

The relationship between carcinomas of the penis and cervix uteri was analyzed in married couples. The final series comprised 239 patients with squamous cell carcinoma of the penis and their 224 wives. Two wives were found to have squamous cell carcinoma of the cervix uteri. The expected number of cervical cancers within the group of wives was 1.88, the relative risk thus being 1.05 (95% confidence interval 0.13–3.8). The incidence of condylomas has increased during the recent decades, while that of carcinomas of the penis and uterine cervix has decreased. The results of this study did not support the hypothesis that wives of men with penile cancer incur an increased risk of carcinoma of the cervix uteri. Although there is much evidence from a large number of studies that human papilloma virus (HPV) has a role in the aetiology of cervical cancer, our study suggests that HPV associated with genital malignancies has a low infectivity or that these cancers have multifactorial aetiology.

Key words: Penis, cervix uteri, squamous cell carcinoma.

A relationship between carcinomas of the penis and cervix uteri in married couples has been reported in case reports (1–5) and in larger series (6–9). The risk of cervical carcinoma has been found to be higher among wives of men with penile carcinoma than among controls or in the general population.

An infectious aetiology for cancer of the cervix uteri has been suggested in many reports (10–12). Herpes viruses (13, 14) and particularly human papilloma virus (HPV) (15–18) have been proposed as aetiological factors.

The human papilloma virus has been found in warts, papillomas, condylomas and other benign lesions of the cervix. The entire spectrum of female anogenital tumours, from benign to malignant, can carry unintegrated HPV DNA genomes (18), with malignant change being mainly dependent on the type of the virus. More than 50 HPV types have been detected and types 16 and 18 have been found to be closely associated with female genital cancer (cf. 17). Recently HPV-16 and HPV-18 have also been detected in penile carcinoma by hybridisation methods (19).

With background of the suspected infectious aetiology of penile and cervical carcinomas, the relationship between these two cancers in married couples was analyzed in Finland where the risks of both these cancers are relatively low.

Material and Methods

The basic series consisted of 275 cases with cancer of the penis (excluding cancers of the urethra), diagnosed in Finland during the 23-year period of 1955–1977, and reported to the Finnish Cancer Registry. After histological re-examination, five patients with benign penile lesions and one patient with a metastasis to the penis from a prostate carcinoma were excluded. In 24 cases, the histological samples were not available and these patients were excluded. In 239 of the remaining 245 cases, the tumour proved to be squamous cell carcinoma.

Aetiological factors, age-adjusted and age-specific incidences of these patients with penile cancer have been earlier thoroughly analyzed (Maiche, 1988).

Of these 239 patients with squamous cell carcinoma of the penis, 224 were married at least once in their life, 10 were never married, and in 5 cases the information was not available (Table 1). For the 224 married men, 256 wives were recorded. The names, personal identification numbers (for those alive on January 1, 1967), length of marriage

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Table 1

Marital status and number of wives of 239 patients with squamous cell carcinoma of the penis

Status	No. of carcinoma patients	No. of wives
All cases	239	256
Ever married	224	256
Never married	10	—
Marital status unknown	5	—
Died before 1953	—	16

and the dates of death of the wives were obtained from the parish registers or from the civil registers.

Sixteen wives had died before 1953 and were excluded from the analysis (the Finnish Cancer Registry initiated data collection in 1953). Following this exclusion there were 240 wives, who constituted the final study series. They were followed up for cancer through the files of the Finnish Cancer Registry and for death through the Central Statistical Office. All the cases of cervical cancer and other cancers detected during 1953–1980 were recorded. The observed number of cervical cancers was compared with that expected, calculated on the basis of the age and calendar period-specific person-years at risk lived by the wives, and the national age and calendar period-specific incidence rates produced by the Finnish Cancer Registry.

Results

The marital status of the patients is described in Table 1. From the files of the Finnish Cancer Registry, 22 wives of men with squamous cell carcinoma of the penis were found to have had cancer during the 28-year follow-up period of 1953–1980 (Table 2). Two of these were squamous cell carcinomas of the cervix uteri. In both instances, penile cancer of the husband had been detected earlier than the cervical cancer of the wife (intervals of 1 and 5 years). The marriages had lasted for 21 and 31 years respectively, before the diagnosis of penile cancer of the husband. Both of them had had phimosis, but neither condylomata nor other infectious diseases of the urogenitals had been recorded.

Table 2

Cancers among 240 wives of 224 men with squamous cell carcinoma of the penis in 1953–1980

Cancer	No. of cases
Adenocarcinoma of the breast	6
Basal cell carcinoma of the skin	4
Adenocarcinoma of the stomach	2
Squamous cell carcinoma of the cervix uteri	*2*
Adenocarcinoma of the rectum	1
Squamous cell carcinoma of the lung	1
Anaplastic carcinoma of the ovary	1
Transitiocellular carcinoma of the ureter	1
Medullary carcinoma of the thyroid	1
Reticulosarcoma of the sacrum	1
Acute promyelocytic leukaemia	1
Metastatic carcinoma NUD	1
Total	22

The expected number of cervical cancers within the group of wives was 1.88, the relative risk thus being 1.05 (95% confidence interval 0.13–3.8) (Table 3).

The age-adjusted incidence of cancer of the penis in Finland has decreased slightly during the period 1958–1982 (20). The age-specific incidence rates increased with age (20). The incidence of cancer of the uterine cervix has decreased significantly during the period 1955–1980, especially in the younger age-groups (21) and higher incidence rates were found in the older age-groups (21).

Discussion

In recent years there has been a large number of studies suggesting that cervical cancer is caused by or associated with human papilloma virus, particularly types 16 and 18. Penile cancer is a similar disease but with less evidence of the association with HPV. The main purpose of this study was to examine whether penile and uterine cervix carcinomas might be sexually or venereally transmitted diseases with a common aetiology.

Benign genital tumours like condyloma were observed to be common in the present series of 239 patients with squamous cell carcinoma of the penis. At least 20% of the cases had had clinical condylomas (20), while the number

Table 3

Reports of the occurrence of cervical carcinoma among wives of men with penile cancer

Authors (ref.)	No. of patients	No. of wives	No. of cervical cancers		Relative risk
			Observed	Expected	
Martinez (7)	889	?	8	1.2	6.7
Graham et al. (6)	227	?	6	1.84	3.3
Smith et al. (9)	?	711	11	3.9	2.8
Present study	224	240	2	1.88	1.1

of subclinical HPV infections might have been markedly higher, as has been detected in females (17). However, it must be noted that HPV infections have not been studied as intensively in males as in females.

In recent years the incidence of benign HPV induced diseases, like condylomas and premalignant cervical lesions, have generally markedly increased (16) while the incidence of penile and uterine cervix cancers have decreased in the population examined (20, 21). The decrease in the incidence of carcinoma of the uterine cervix is more marked in the youngest age-groups, evidently due to the screening program performed systematically in Finland since the early sixties.

The results of this study do not support previous reports in the literature (Table 3) that wives of men with penile cancer have an increased risk of developing cancer of the uterine cervix. However, the results of our study could be explained statistically as due to the fairly limited number of patients, resulting in a wide confidence interval so that a possible small excess of spouses with cervical cancer cannot be excluded. The low incidence rates of both cancers might mean that the transmission of the disease is an unusual event in this population. IF HPVs are aetiological agents in both of these cancers, their infective rate might be low and/or the incubation period from primary infection to malignant transformation might be exceptionally long, even many decades. Furthermore, some HPV types infecting the genital tract are known to have very low or no malignant potential.

However, the relative risk (1.1) in this study is not significantly lower than the relative risk in the three other studies calculated together (25/6.94 = 3.60) (Table 3). The 95% confidence interval (CI) in the three earlier studies together is 2.3–5.3 and if the CI in the present study is pooled with the other three, the 95% CI is 2.0–4.5. Obviously our study cannot reject the hypothesis that wives of men with penile cancer incur an increased risk of carcinoma of the cervix uteri.

Finally, it is evident that the aetiology of squamous cell carcinoma of the penis is multifactorial with factors like phimosis and lack of hygiene and probably also HPV infection (20). A similar situation may prevail in cervical cancer.

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