Anogenital warts: epidemiology, treatment and association with cervical atypia

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SUMMARY

In Northern Ireland in 1984 anogenital warts were diagnosed in 592 (352 male, 240 female) genitourinary medicine clinic attenders. Of these patients, 561 were heterosexual, 28 homosexual and three male bisexual. In the male patients 290 had penile warts, 67 meatal warts, 59 perianal warts, 25 anal canal warts and five rectal warts. In the female patients, 193 had vulval warts, 27 vaginal warts, 25 cervical warts, 107 perianal warts, 30 anal canal warts and one a rectal wart. Sexual partners were brought to the clinic by 345 patients and of these 93 male and 100 female partners had genital warts.

The mean time from exposure to development of warts was 17 weeks SE ± 1.5 (range 1 week - 12 months). As treatment, podophyllin 25% was used alone in 218 patients, and 132 were known to have had clearance of warts. At least one other sexually transmissible infection was found in 407 (69%) of patients. Cervical smears were taken in 164 women and were abnormal in 40 (24%). Cervical cytology was recorded in 89 regular sexual partners of male patients and was abnormal in 23 (26%).

INTRODUCTION

The study of human papilloma viruses (HPV) has been constrained by a number of problems, the principal one being the lack of an in vitro technique for propagating the virus. The virus is easily seen by electron microscopy in common skin warts and was first identified in 1949 but it was not until 1968 that similar particles were seen in extracts from anogenital warts. The use of molecular biological techniques has, in recent years, led to the identification of 46 types of HPV DNA, these being enumerated in the order in which they have been identified. The common anogenital wart contains HPV types 6 and 11 but the main interest is the presence of DNA from HPV types 16, 18, 31, 33 and 35 in 80 - 90% of cervical carcinoma with integration of the cellular genome in the cervical-carcinoma tissue. No method exists by which these DNA types can be identified on a routine basis, and until this becomes available all persons with genital warts and their contacts need adequate investigation and follow-up for identification of potentially malignant lesions. In addition, such patients require

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investigation for other sexually transmitted diseases (STD) with which there is a high association. Traditional treatment methods for anogenital warts are generally considered unsatisfactory but there is scant data available.

The aim of the present study was to review in retrospect all of the patients attending our clinic in 1984 with a diagnosis of anogenital warts, to analyse the clinical characteristics, rates of HPV infection, efficacy of treatments, occurrence of other sexually transmitted diseases, frequency of anogenital warts in sexual contacts and the result of cervical cytology in female patients.

METHODS

All patients who had the diagnosis of anogenital warts in 1984 confirmed at any of the three genitourinary medicine clinics in Northern Ireland (Belfast, Coleraine and Londonderry) had their medical records examined retrospectively. Age, sex, sexual orientation, month of diagnosis, duration of infection, site of warts, treatment given and duration of treatment were noted. Other sexually transmitted diseases found in these patients were recorded. Sexual contacts were traced from hospital records. Cervical cytology was recorded both in female patients with warts and female sexual partners of males with warts. The treatment in use during the study period was podophyllin 25% initially, except in pregnancy, or for flat keratinised and intrameatal warts. Concentrated trichloroacetic acid and cryotherapy (Spembly cryoprobe No. SRIR) were used in the latter and in all patients unresponsive to podophyllin.

RESULTS

In 1984 in Northern Ireland anogenital warts were diagnosed in 592 clinic attenders (352 male, 240 female). Of these patients, 561 (95%) were heterosexual, 28 (5%) were male homosexual and three (0.5%) were male bisexual. There was no clear pattern in the monthly rate of diagnosis of anogenital warts (the range was 36–63 cases per month). Ages ranged from two to 68 years, mean 25 years ± SE 0.3 (0–15 years — four patients; 16–19 years — 90 patients; 20–24 years — 240 patients; 25–29 years — 136 patients; 30–34 years — 66 patients; 35–39 years — 29 patients, and over 40 years — 27 patients).

Of the whole group 401 were new patients with a first infection of anogenital warts, 13 were new patients with a known history of anogenital warts treated in another hospital, 119 were previous clinic attenders with a first presentation of anogenital warts and 59 had a relapse or new infection of anogenital warts.

Sites of infection. In the 352 male patients, 290 (82%) had penile warts, 67 (19%) had meatal warts, 59 (17%) had perianal warts, 25 (7%) had anal canal warts and five (1%) had rectal warts. In the 240 female patients, 193 (80%) had vulval warts, 27 (11%) had vaginal barrel warts, 25 (10%) had cervical warts, 107 (45%) had perianal warts, 30 (12%) had anal canal warts and one (0.4%) had a rectal wart.

Sexual partners. Of the 592 patients, 345 (58%) brought a total of 392 sexual partners to the clinic. One partner was brought by 311 patients, two partners by 26 patients, three partners by six patients, five partners by one patient and six partners by one patient. Proportionately more female patients, 163 (68%) than male patients, 182 (52%) brought partners to the clinic (p < 0.0005). Of the 392 contacts who attended the clinic, 193 (49%) had anogenital warts — 93 (52%) male and 100 (48%) female.

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Incubation. The time between first exposure to infection from a partner known to have anogenital warts and the development of anogenital warts was clearly inferred in only 67 patients. This was less than one month in six patients (9%), less than two months in 20 patients (30%), less than three months in 35 patients (52%) and less than six months in 55 patients (82%). All patients had developed warts by 12 months. The mean time to development of warts was 17 weeks ± SE 1.5 and the median time was 12 weeks.

The period of time the patient had noted warts before diagnosis was given by 326 patients: 156 patients (48%) had warts for 0 – 4 weeks, 72 (22%) for five to eight weeks, 32 (10%) for nine to 13 weeks, 34 (10%) for 14 – 26 weeks and 32 (10%) for more than 26 weeks.

Treatment. Podophyllin 25% was used in 493 patients and was the only treatment in 218 patients. In this latter group, 119 (55%) had one application only, 44 (20%) had two applications, 29 (13%) had three applications, nine (4%) had four applications, nine (4%) had five applications and eight (4%) had six or more applications. In this group of 218 patients, after treatment 132 were known to have had clearance of their warts (had had one visit to the clinic after their last treatment when they were observed to have no warts present) and the other 86 were clinic defaulters. Trichloroacetic acid was used in 245 patients, 160 (65%) had two applications, 51 (21%) had four applications, 10 (4%) had six applications and 24 (10%) had more than six applications. It was the sole treatment in only 16 patients. Cryotherapy was used to treat warts of the urethral meatus in 60 patients with 32 (53%) having one treatment only, 15 (25%) having two treatments, eight (13%) having three treatments and five (8%) having four or more treatments. Cryotherapy was used in sites other than the urethral meatus in 159 patients: 92 (58%) having one application, 33 (21%) having two applications, 22 (14%) having three or four applications, six (4%) having five or six applications and six (4%) having seven or more applications.

Clinic attendances. Attendances before cure or default were one or two visits — 287 (48%); three or four visits — 110 (19%); five or six visits — 65 (11%); seven or eight visits — 38 (6%) and nine or more visits — 92 (16%) patients. The duration of treatment was up to two weeks in 257 (43%) patients, and over 26 weeks in 51 (9%) patients. The overall known cure rate was 53% (314 patients). Relapses occurred in 63 patients (11%) after eight weeks clear of warts and, of these patients, 14 (2%) had a relapse after six months clear of warts.

Other infections. A total of 407 patients (69%) had other sexually transmissible diseases present. These diseases were: non-specific genital infection — 308 patients (52%); Gardnerella vaginalis — 119 patients (20%); candidiasis — 102 patients (17%); gonorrhoea — 45 patients (8%); pediculosis pubis — 15 patients (2.5%); trichomonas — 12 patients (2%); herpes — 10 patients (2%), and scabies in two patients (0.3%).

Cervical cytology. Cervical smears were taken from 164 women with anogenital warts and, of these, 40 (24.4%) were reported as abnormal. The abnormalities reported were koilocytosis in one case, dysplasia in 31, cervical intraepithelial neoplasia III in seven and carcinoma-in-situ in one. In the group with cervical warts (25 patients), 20 had cervical cytology, with 12 (60%) having abnormality, and eight (40%) normal smears. Cervical cytology was recorded in 89 regular sexual partners of male patients with genital warts, and was abnormal in 23 patients (26%). Of this latter group, anogenital warts were recorded in only 12
patients (52%), including one patient with cervical warts. The cervical cytology abnormalities noted were dysplasia in 19 cases and CIN III in four.

DISCUSSION
The epidemiology of anogenital warts behaving as a sexually transmitted disease has already been established in studies by Oriel.\textsuperscript{16, 17} In this study the findings are as would be expected from a sexually transmitted infection, with the male-to-female ratio reflecting that of our overall clinic attenders, the predominant age group affected being the 16–30-year-old group and sexual contacts being affected in 49% of cases. In Oriel's first study,\textsuperscript{16} 64% of contacts were seen to have warts; our study, however, included both casual and regular partners, whereas his looked at regular partners only and consequently his subjects would have had an increased exposure to infection. The association with other sexually transmitted diseases in 69% of cases is characteristic and underlines the importance of adequate screening.

The retrospective nature of this study makes it difficult to obtain accurate information regarding the incubation period of warts. Our finding of a mean incubation period of 17 weeks in the 67 patients whom we thought could be accurately assessed was longer than the 2.8 months noted by Oriel.\textsuperscript{16} A presumed incubation period of up to one year was noted in some of our cases, whereas Oriel gave a maximum of nine months. This variable latency period in wart virus infection suggests that contact tracing should in some cases be extended up to one year if there is no definite history of contact within this period.

Previous reports suggest that males are less likely than females to bring contacts to the clinic;\textsuperscript{18} this is reflected in the present study, and is particularly worrying in view of the association between HPV infection and cervical dysplasia and malignancy.\textsuperscript{3–14} The response rate to contact tracing in this study of 58% of patients bringing partners for examination left many people untraced. While there is some doubt about the carcinogenic role of HPV,\textsuperscript{13, 14} there is strong evidence in support of a link between HPV and cervical dysplasia and therefore it was not surprising that, of women with anogenital warts who had cervical smears, 24% were abnormal and, in the subgroup of women with cervical warts, 60% had cytological abnormality on smear testing. It was also worrying that in the female partners of men with anogenital warts, cervical abnormality was reported in 26% of contacts while less than half of these patients actually had clinical warts. Seventy-six women did not have smear testing during this study period because it was routine to check cytology after treatment and they defaulted. All female patients now have cytology at their first visit. While only one patient in our cohort had carcinoma-in-situ, it appears likely from the known tendency of cervical dysplasia to progress to more serious lesions that a similar progression may occur in this group.\textsuperscript{15} In the present state of knowledge, it would appear that both women with anogenital warts and the female partners of men with anogenital warts should have at least annual cervical cytological screening as part of regular health care with further investigation of cytological abnormality.

The treatment of warts continues to be problematical. In this series 218 patients had 25% podophyllin applied as the sole treatment; of these 75% either responded completely or defaulted after one or two treatments, and a further 17% did so after three treatments. Because trichloracetic acid was used as an adjunct to podophyllin at our clinic, it was impossible to assess its use as an individual agent, but, when used in combination with podophyllin or cryotherapy,
86% of patients had four or less treatments. Cryotherapy similarly was an adjunct to therapy but was used four or less times in 93% of patients. It appears that successful treatment of warts is achieved in the great majority of patients with four treatments with these conventional agents and that further treatment beyond this point is often frustrating for the physician and futile for the patient. It was disappointing that cryotherapy of the urethral meatus was unsuccessful in 47% of patients after one treatment. This is in contrast with the high success rates of Ghosh who reports 20 of 28 patients (71%) with genital warts cured by one application of cryotherapy alone. This difference is unexplained, since a similar cryotherapy technique is used in both centres.

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