

Proctoscopy should be mandatory in men that have sex with men with external anogenital warts

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ABSTRACT

Introduction: The aim of this study was to evaluate anal pathology in men having sex with men (MSM) seen at our proctology outpatient clinics.

Methods: The charts of 74 MSM treated by the author between January 2002 and April 2006 were reviewed.

Results: Three of 74 patients (4%) had proctitis and 96% had anogenital condylomata acuminata (warts). 49 out of 71 (69%) had external anogenital as well as intra-anal warts and 13 (18%) had only intra-anal warts. In 14 an intra-anal dysplasia and in 2 patients intra-anal verrucous carcinomas were detected. The average duration of disease before referral to our institutions was more than 9 months. Half of the patients were previously treated for anogenital warts with ointments and suppositories at other institutions, including 17 that were "treated" with ointments and/or suppositories for hemorrhoids prescribed by family physicians. The patients mostly had widespread disease and sixty-nine of them required surgery. In the follow-up period there was no recurrence of warts and only itching was observed in 31 (44%) patients. Therapy with imiquimod was introduced for 3 months in twenty-two cases with intra-anal dysplasia. No major side effects were noticed despite intra-anal use.

Conclusion: Proctoscopy and histological examination of intra-anal lesions in cases of external anogenital warts should be mandatory in MSM patients. I would like to encourage other physicians to use this approach, which enables detection of intra-anal warts, dysplasia, and even carcinoma in the asymptomatic stage.

Introduction

In men that have sex with men (MSM), the anal region can be used for obtaining sexual satisfaction. The prevalence of homosexual intercourse has increased (1, 2), as has the practice of receptive anal intercourse (1,

Recent studies (3–7) report an alarming incidence of dysplasia in MSM with anal condyloma that is caused by some types of the human papilloma virus (HPV). The incidence of anal cancer among homosexual men exceeds that of

KEY WORDS

sexually transmitted diseases, condylomata acuminata, intra-anal dysplasia, verrucous carcinoma, recurrence, proctoscopy, therapy with imiquimod

Table 1. Location of condylomata acuminata.

Location of condylomata acuminata	%	n
Intra-anal and perianal	35	25/71
Perianal	25	18/71
Intra-anal	18	13/71
Penile, perianal, intra-anal	13	9/71
Penile and intra-anal	3	2/71
Penile and perianal	3	2/71
Penile	3	2/71

cervical cancer in women, and HIV-positive homosexual men are at even higher risk than HIV-negative men (3). Goldie et al. (6, 7) demonstrated that cytological screening every 2 or 3 years for anal squamous intraepithelial lesions in HIV-negative MSM, and every year in HIV-positive MSM, would provide cost-effective life-expectancy benefits.

The aim of this study was to evaluate the anal pathology in MSM seen at our proctology outpatient clinics and to use these data to convince other physicians of the importance of proctological examinations in MSM in the absence of any proctological or dermatovenereal symptoms in the anogenital region.

Methods

The charts of all male patients treated by the author with a diagnosis of condylomata acuminata, proctitis of unclear origin, or STD proctitis between January 2002 and April 2006 were reviewed. In condylomata acuminata patients, attention was paid to the location, pathologic evaluation of biopsy specimens, recurrence rate, sexual orientation, coexistence of other sexually transmitted diseases including HIV status, and previous treatments by other specialists. In cases of proctitis, I considered the results of biopsy, the rectal culture, and the response to antibiotic therapy.

Digital examination and proctoscopy were performed 2, 4, and 12 weeks after surgical excision of anogenital warts. The minimal follow-up for patients included in the study was 3 months. Patients with a history of intra-anal warts require proctoscopy every year. Patients with a history of dysplasia and/or carcinoma

were contacted by phone to remind them if they had failed to report for a check-up. Testing for the most common sexually transmitted diseases was strongly recommended, but patients that refused testing for HIV and other STDs were also treated.

During the last 2 years adjuvant therapy with imiquimod (Aldara 5% cream) was introduced for 3 months in patients with more than two intra-anal and perianal recurrences and/or intra-anal dysplasia in the follow-up period. Patients apply the imiquimod cream with a finger inserted in the anus.

Histopathology was performed at the diagnostic center Bled and at the Institute of Pathology, Medical faculty, University of Ljubljana.

Results

The incidence of patients with proctological STDs frequenting our clinics has increased dramatically in the last 12 months. Half of the patients included in the study were treated during this period.

The average age of patients was 33 years (18 to 51 years). The majority of patients (47/74) described their sexual orientation as homosexual/gay or bisexual (19/74), whereas for the remaining ones the sexual orientation was not known. Nine patients were HIV seropositive, 47 were HIV negative, and in the remaining ones the HIV status was not known. Six patients were HBV positive and one had second-stage syphilis. Symptomatic urethral gonorrhea was detected in one patient, who also had asymptomatic intra-anal warts with minor dysplasia.

Sixty-nine patients with anogenital warts were operated. The warts' location and the evaluation of the specimens removed are presented in Tables 1 and 2. Three HIV-positive men had moderate intra-anal dysplasia, minor dysplasia, and intra-anal verrucous carcinoma in situ, respectively. There was no dysplasia in perianal or penile warts. All patients with warts around the urethral meatus were directed to the urologist with a request for urethroscopy. In one of fifteen patients with penile warts, intraurethral condyloma was found.

The average duration of disease before referral to our institutions was more than 9 months. As far as is known, only 7 patients came for preventive proctoscopy because their partners or friends had been previ-

Table 2. Incidence of dysplasia/carcinoma.

Incidence of dysplasia/carcinoma	%	n
Verrucous intra-anal carcinoma in situ	3	2/71
High-grade dysplasia	1	1/71
Moderate-grade dysplasia	6	4/71
Minor-grade dysplasia	13	9/71
No dysplasia	77	55/71

Table 3. Recurrence rate.

Recurrence rate	%	n
No recurrence	44	31/71
One recurrence	20	14/71
Two recurrences	15	11/71
Three recurrences	8	6/71
More than three recurrences	13	9/71



Fig. 1. Flat intra-anal warts undetectable through palpation above the dentate line with moderate grade dysplasia in HIV-positive MSM.

ously treated for anogenital warts at our clinics. Patients with intra-anal carcinoma in situ were 19 and 29 years old with a duration of anal symptoms for 6 months and 2 years respectively. A 29-year-old HIV-positive man with a long history of skin tags and atypical perianal warts was previously refused by two surgeons with the explanation that he only had an esthetic problem. Another man was a 19-year-old HIV-negative man that periodically noticed blood after anal intercourse or defecation, but his family physician treated him with suppositories for hemorrhoids until the patient himself performed a digital rectal examination and noticed an unusual process. Both patients had carcinoma in situ lesions smaller than 1 cm in diameter, and were treated by local excisions only. After follow-ups of 36 and 24 months respectively there was no recurrence. Macroscopically the intra-anal lesions did not differ from non-



Fig. 2. Widespread perianal and intra-anal warts with no dysplasia in HIV-negative MSM.

malignant warts, and the carcinoma in situ was detected by biopsy.

Seventeen patients with perianal and intra-anal warts were previously treated with ointments and/or suppositories for hemorrhoids; 13 were treated for penile or perianal warts with cryotherapy by a dermatologist and four for penile warts with electrocoagulation by a urologist. Only in 5 cases did dermatologists direct their patients for proctoscopy. Half of the patients included in the study had no previous treatment for anogenital warts.

In 80% (57/71) of cases general or spinal anesthesia was required for removing widespread primary anogenital warts. Recurrent warts were usually removed under local anesthesia with electrocoagulation or cryotherapy. A close follow-up prevents the spread of disease in the major area in most cases. During the follow-up period no recurrence was noticed in only 31 patients. The recurrence rate is presented in Table 3.

Multiple treatment procedures and the long recovery period can have a negative impact on patients' social and sexual life, and so consultations on psychological and sexual problems were part of follow-up visits. However, depression requiring antidepressant treatment developed only in 3 patients with multiple recurrent disease. Receptive anal intercourse was painful and avoided in the majority of patients up to 6 weeks after the intra-anal operation.

During the last 2 years, the author has also recommended intra-anal and perianal application of imiquimod to reduce the rather high recurrence rate. Adjuvant therapy with imiquimod, starting 14 days after the surgical removal of warts, was introduced for 3 months in twenty-two cases with intra-anal dysplasia and/or more than two intra-anal and/or perianal recurrences. No major side-effects were noticed despite intra-anal use. Only three patients had a burning sensation that caused interruption of treatment for a few days. Only in one case did an influenza-like syndrome with leucopenia occur; the patient had used two imiquimod sachets instead of one, and the side effects disappeared when he applied only one sachet and cleaned the lubricated area after 8 hours. There were no other signs of systemic side-effects. In 10 cases further recurrences occurred despite adjuvant therapy.

Despite close follow-up, 13 patients needed general or regional anesthesia for removal of recurrent intra-anal disease. Two patients needed three operations under general anesthesia within 6 months for extremely aggressive intra-anal and perianal recurrence. Further recurrences were stopped in one of them with adjuvant therapy with imiquimod applied intra-anally and perianally for 4 months, but the other also needed systemic interferon alpha s.c. 5 million units three times weekly for another 3 months. Both were HIV-negative but had minor dysplasia intra-anally.

In three cases with a mucopurulent discharge and signs of proctitis in MSM, *Proteus vulgaris* was determined in one HIV-positive MSM, in the other two the

cause could not be detected. Histological examination in these three cases excluded ulcerative proctitis or Crohn's disease. Proctitis caused by *Proteus vulgaris* was successfully treated according to an antibiogram with ciprofloxacin 500 mg twice a day for 14 days. In the other two cases high index of suspicion warranted empiric treatment with azithromycin 1.g p.o. as a single dose and ciprofloxacin 500 mg twice a day for 10 days. Proctitis was under control in both cases before negative culture results were obtained.

Discussion

Because it is impossible to determine the sexual orientation of a patient by their history and behaviour (8), the practicing physician must enquire about sexual orientation. A negative attitude toward homosexuality depends on the physician's ability to obtain an appropriate personal and sexual history.

Seventeen patients with anal warts were previously treated by ointments and/or suppositories for hemorrhoids prescribed mainly by family physicians. Most of them did not perform anal examinations because the examining physicians assumed that pruritus and/or minor hemorrhage after defecation in young men were due to hemorrhoids. Many diseases including perianal dermatitis, which seem to be common disorders of the anogenital area (9), can cause symptoms similar to condylomata acuminata. On the other hand, coexistence of two or more anogenital diseases (condylomata acuminata and hemorrhoids or perianal dermatitis and condylomata acuminata, etc.) is possible. Even if physicians do perform a digital rectal examination they cannot confirm the diagnosis without proctoscopy and a biopsy, if the lesions are located at the dentate line or above. A similar impression may result from palpation of anal papillae, polyps, or warts. Slightly elevated lesions above the dentate line are usually undetectable by palpation (Fig. 1) including a carcinoma in situ, as was the case of the 29-year-old HIV-positive man in this study.

Dysplasia and/or carcinoma in situ were detected in 5 of 13 patients with intra-anal warts. They mentioned only minor occasional bleeding or no symptoms at all.

The majority of dermatovenereologists and urologists that had previously treated external anogenital warts in patients included in this study did not suggest a proctological examination. The proctologist should also examine the penis and scrotum and direct the patient for urethroscopy if meatal warts are found. One may expect intraurethral warts in 17 to 22% of such cases (10). Sixteen percent of patients in the Abcarian study (11) as well as in this study had penile as well as intra-anal warts. Six of them were previously treated by a dermatologist, and intra-anal warts with dysplasia were found in 4 of them. Therefore the author strongly dis-

agrees with the recently published article in the *American Journal of Clinical Dermatology* (12) that denies the importance of genital warts, calling them merely a cosmetic nuisance. One should not forget that Buschke-Loewenstein tumors, characterized by invasive growth, recurrence, and possible malignant transformation, are always preceded by condyloma acuminatum (13) (Fig. 2). In 14 out of 71 patients, dysplasia was detected by intra-anal examination. The reported recurrence rates of anogenital warts averaged from 10 to 75% (14), and it is known that condyloma in the anal canal has a higher risk of recurrence compared to extragenital warts (15), whereas in HIV-positive MSM the intra-anal dysplasia could be as high as 71% (16).

Adjuvant therapy with imiquimod has been recommended (15, 17). In a study of 211 patients that received topical imiquimod after laser ablation of external anogenital warts, only 11% of patients developed recurrences in the treated areas (16).

In a small number of patients, application of imiquimod intra-anally by suppositories effectively prevented recurrence after ablation of anal canal condyloma (15). However, this study's results from using imiquimod were less effective, possibly because it was recommended only in inveterate cases, with the use of lubrication instead of suppositories, so further studies are needed.

In patients with evident proctitis and a history of recent unprotected insertive anal sex, culture and biopsy of rectal mucosa is recommended as well as prompt treatment with ciprofloxacin and azithromycin, a combination which is recommended in cases of rectal gonorrhoea and suspected coinfection with chlamydia (18). This combination was also effective in the two patients in this study with proctitis, for whom the cultures were negative. Negative results of the cultures can be falsely negative because many lubricants contain antibacterial agents and proctologists routinely lubricate the proctoscope prior to insertion. However, swabs taken blindly have only a 34 to 55% positive yield in culture-positive rectal-gonorrhoea patients (19).

Conclusion

Proctological problems are frequent in MSM. All patients with external anogenital warts should have proctoscopy and histological examination of all intra-anal lesions. Long-term follow-up after treatment is necessary, especially in the case of intra-anal dysplasia. Elimination of intra-anal and perianal warts is also important in reducing the risk of possible transmission of HIV and other STDs because warty tissue is fragile and easily bleeds through friction during anal sex, and is not merely a cosmetic nuisance. Preventive proctological examinations for MSM can be beneficial because detection of intra-anal warts, dysplasia, and even carcinoma in the asymptomatic stage is possible.

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A U T H O R S ' A D D R E S S E S

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