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DISTINGUISHED EXPERT SERIES

ORIGINAL ARTICLES

Loop electrosurgical excision procedure in Greek patients with vaginal intraepithelial neoplasia

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Summary

Objective: The aim of our study was to evaluate the therapeutic effectiveness of the loop electrosurgical excision procedure (LEEP) in Greek patients with vaginal intraepithelial neoplasia (VAIN). *Materials and Methods:* Between January 2002 and January 2009, 23 women with histologically confirmed VAIN were included in our study. For the LEEP procedure we used a high frequency electrosurgery unit with at least 80 W output. *Results*: Complete response rate at 12 months of follow-up was 86.96%. Recurrence rate at 12 months of follow-up was 13.04%. Complete response rate at 24 months of follow-up was 75%. Recurrence rate at 24 months of follow-up was 25%. *Conclusion:* LEEP may constitute a valuable excisional method for the treatment of VAIN. It provides an interpretable specimen of the whole lesion within a few minutes. It needs a short period of training and has low cost.

Key words: Electrosurgery; LEEP; Vaginal intraepithelial neoplasia; VAIN.

Introduction

Vaginal intraepithelial neoplasia (VAIN) is uncommon, accounting for approximately < 1% of lower genital tract intraepithelial neoplasia [1, 2]. However VAIN is now being diagnosed in younger women and this rise seems to be associated with the increased prevalence of human papilloma virus (HPV) infections of the lower genital tract [3].

Generally, most patients are asymptomatic. If present, symptoms may include postcoital spotting, vaginal bleeding, unusual vaginal discharge and odor [4, 5]. The majority of lesions located in the upper one-third of vagina and are often multifocal [4, 5].

The natural history of VAIN is thought to be similar to that of cervical intraepithelial neoplasia (CIN), with risk for progression to vaginal cancer [4]. In women with VAIN, 78% may regress, 13% may persist, and 9% may progress to invasive vaginal cancer [4].

The management of women with VAIN remains controversial. Treatment protocols use surgical procedures (local excision, partial vaginectomy, total vaginectomy, loop electrosurgical excision procedure (LEEP), laser CO_2 surgery), topical medical therapy (5% 5-fluorouracil) or radiation therapy [6-11].

The aim of our study was to evaluate the therapeutic effectiveness of LEEP in Greek patients with VAIN.

Material and Methods

Between January 2002 and January 2009, about 23 women with histologically confirmed VAIN were referred to the 2nd Department of Gynecology of St. Savvas Anticancer-Oncologic Hospital of Athens. Among them, nine were treated for CIN 3 and three were treated for microinvasive cervical carcinoma Stage 1a1.

LEEP was performed in the operating room, with the patient placed in the dorsal lithotomy position. For regional anesthesia we used 2% lidocaine solution diluted with normal saline (2:1), to infiltrate the vagina lesion and separate vaginal epithelium from underlying tissue.

In all women the lesional tissue was treated with LEEP, 3 mm away from lesion margins (2 mm for free lesion margins and 1 mm for thermal effect). The tissue specimen consisted of the vaginal mucosa and a portion of the submucosal tissue. Depth was controlled by performing procedures at high magnification.

For LEEP a high frequency electrosurgery unit was used with at least 80 W output. For electroexcision we used a 10 x 4 mm loop electrode and we selected blend cut mode with 50 W power output. For electrofulguration we used a 5 mm ball electrode and we selected blend coag mode with 60 W power output.

All patients were advised to avoid intercourse during the first four to six weeks following the procedure and return for follow-up at six weeks. The post-treatment follow-up protocol included physical examination, vaginal smear and colposcopic assessment at three, six, nine and 12 months for the first year, and yearly after.

Complete response was defined as no cytologic and colposcopic evidence of any VAIN lesion. Recurrence was defined as cytologic and colposcopic evidence of a new VAIN lesion in complete responders.

When patients had more than one grade of VAIN, they were assigned the highest grade. Patients with one focus of VAIN were identified as having unifocal and those with two or more areas were identified as having multifocal disease.

The study was approved by the Ethical Committee of the Hospital. Informed consent was obtained from each woman. Statistical analyses were performed using the SPSS-13 for Windows.

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Results

The median age at diagnosis of VAIN was 55 years (range 23-80 years). The median follow-up was 34.6 months (range 16-60 months). The demographics of women are shown in Table 1.

The median operating time was 15 min (range 10-20 min) depending on multifocal and extent of the lesion. The median healing time was five weeks (range 4-6 weeks) depending on the extent of the wound. All tissue specimens had free surgical margins. In our study population we had four VAIN 1, nine VAIN 2 and ten VAIN 3.

Complete response rate at 12 months of follow-up was 86.96%. Recurrence rate at 12 months of follow-up was 13.04%. Complete response rate at 24 months of follow-up was 75%. Recurrence rate at 24 months of follow-up was 25%. None of the treated patients progressed to invasive vaginal cancer during a mean follow-up of 34.6 months. These data are shown in Tables 2 and 3.

Table 1. — *Women's demographics (n = 23).*

		Number of patients (n = 23)	Percentage (%)
Age	< 40	2	8.69%
	40-60	15	65.22%
	> 60	6	26.09%
VAIN	VAIN 1	4	17.39%
	VAIN 2	9	39.13%
	VAIN 3	10	43.48%
History of CIN	Yes	9	39.13%
	No	14	60.87%
History of cervical cancer	Yes	3	13.04%
	No	20	86.96%
History of radiotherapy	Yes	0	0%
	No	23	100%
History of immunosupression	Yes	0	0%
	No	23	100%

Table 2. — *Response at 12 months of follow-up (n = 23).*

	Complete response	Reccurence
VAIN 1 (n = 4)	4 (100%)	0 (0%)
VAIN 2 (n = 9)	8 (88.89%)	1 (11.11%)
VAIN 3 (n = 10)	8 (80%)	2 (20%)
Total	20 (86.96%)	3 (13.04%)

Table 3. — *Response at 24 months of follow-up (n = 16).*

	Complete response	Reccurence
VAIN 1 (n = 2)	2 (100%)	0 (0%)
VAIN 2 (n = 6)	5 (83.33%)	1 (16.67%)
VAIN 3 (n = 8)	5 (62.5%)	3 (37.5%)
Total	12 (75%)	4 (25%)

Discussion

Vaginal intraepithelial neoplasia (VAIN) has histopathology similar to cervical intraepithelial neoplasia (CIN) [12]. VAIN development, following HPV infection, may require a greater period of time and may occur less frequently because of the different type of epithelium from which VAIN arises [13]. The vagina lacks an active transformation zone with immature epithelial cells susceptible to HPV infection. However, HPV entry may result from vaginal mucosal abrasions (from coitus or tampon use) and reparative metaplastic squamous cell activity [12].

VAIN may occur as an isolated lesion or as a lesion on the vaginal vault after hysterectomy for CIN or invasive cervical carcinoma [4, 14]. Most VAIN lesions occur in women with a history of CIN or invasive cervical carcinoma [6, 15]. These lesions may arise at the same time (synchronous lesions) or up to several years after the initial CIN lesion (metachronous lesions) [16]. The time interval from an initial diagnosis of CIN 3 to a current diagnosis of VAIN 3 varies from two to 17 years [17]. In our study 11 patients had an isolated VAIN lesion, nine patients had a VAIN lesion on the vaginal vault after hysterectomy for CIN 3 and three patients had VAIN lesions on the vaginal vault after hysterectomy for microinvasive cervical carcinoma Stage 1a1.

The majority of VAIN lesions occur in the upper one-third of vagina. The middle and lower thirds of vagina are involved by less than 10% of lesions [6]. The majority of VAIN are also multifocal [4, 6, 17]. In our study, all women had VAIN lesions in the upper one-third of the vagina. Among them, 13 women had unifocal VAIN lesions and ten women had multifocal VAIN lesions.

Risk factors for developing VAIN are low education, low family income, previous abnormal Papanicolaou smear, genital warts, CIN or cervical cancer, immunosupression, radiation therapy and history of diethylstilbestrol exposure [18]. In our study nine patients had been treated for CIN 3 and three patients had been treated for microinvasive cervical carcinoma Stage 1a1. None of the women had any history of immunosupression, radiation therapy or diethylstilbestrol exposure.

Vaginal intraepithelial neoplasia is a rare disorder that, in most instances, will regress after initial treatment. However, patients with VAIN require careful monitoring because of the risk of recurrence and even progression to invasion [4, 5]. Risk factors for recurrence of VAIN include multifocality, association with neoplasia on other anogenital sites, histologic grade, immunosupression and treatment modality [4-6]. In our study three women treated for VAIN 3 and one woman treated for VAIN 2 recurred after initial treatment. None of the women in our study progressed to invasive vaginal cancer during a mean follow-up of 34.6 months.

The choice of treatment modality for patients with VAIN is influenced by the number of lesions, location of lesions, length of vagina, sexual activity, previous radiation therapy, previous VAIN treatment, patient preference and operator experience [6, 19]. Multifocal lesions are more difficult to treat because some lesions could be missed during treatment [6].

LEEP for VAIN lesions has been proposed with excellent results in selected groups of patients [6, 8, 9]. There are potential advantages of LEEP for treating VAIN lesions which include low cost of equipment, avoidance of the operating room, avoidance of general anesthesia, limited tissue damage, provision of a specimen, reduced

bleeding and reduced discomfort [8, 9]. LEEP may be more accurate than laser CO2 in uncovering foci of early invasion (LEEP uses excision rather than ablation) [9]. In our study all tissue specimens had free surgical margins. The operating time ranged between 10-20 min depending on multifocal and extent of the lesion. We believe that every gynecologist is capable of performing LEEP on VAIN after 10-15 supervised applications with a high index of confidence.

There are potential complications of LEEP for treating VAIN lesions which include bleeding, infection, vaginal perforation, bladder injury, rectal injury, vesicovaginal and rectovaginal fistulae [8, 9, 20, 21]. In our study population, there were no complications. Only in a few cases did spot bleeding occur during surgery. The newly formed vaginal epithelium, after a mean period of five weeks, presents excellent topography. None of the women complained of post-treatment sexual dysfunction.

It is clear that current treatments for VAIN are suboptimal and continue to represent a clinical challenge. The best approach is individualized management based on clinical presentation, extent of disease and patient preference. LEEP may constitute a valuable excisional method for the treatment of VAIN. It provides an interpretable specimen of the whole lesion within a few minutes. It needs a short period of training and has low cost.

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