

Vaginal intraepithelial neoplasia: report of 102 cases

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Summary

Background: Vaginal intraepithelial neoplasia (VAIN) is a rare asymptomatic disorder. The aims of the current study were to profile patients with VAIN and to evaluate the response to treatment.

Material and Methods: We reviewed the records of 102 patients with VAIN diagnosed from 1990 to 2000.

Results: Patients with VAIN₁, VAIN₂ and VAIN₃ had the following mean ages 44.5, 47.8 and 61.8 years, respectively ($p < 0.001$). All patients with VAIN were found to have abnormal Papanicolaou smears. Localization of the lesions to the upper third of the vagina was observed in 80% of the cases. Recurrences following laser ablation and partial vaginectomy reached 21%. Patients with minimal VAIN lesions from whom punch biopsies were obtained had the lowest recurrence rate. Multifocality significantly affected the risk of recurrence ($p = 0.03$).

Conclusion: VAIN most often involves the upper third of the vagina and is often multifocal. Patient selection and operator skill have a significant influence on the treatment outcome.

Key words: Vaginal intraepithelial neoplasia; Treatment; Laser; Surgery; Vaginectomy.

Introduction

Vaginal intraepithelial neoplasia was first described by Hummer in 1933. It is an uncommon clinical entity that accounts for approximately 1% of intraepithelial neoplasias in the lower genital tract [1].

Little is known of the natural history of VAIN although it is probably similar to that of CIN. However, a few studies have shown a progression from VAIN to invasive carcinoma [2]. VAIN is usually asymptomatic and is usually diagnosed by abnormal cytologic testing, but infrequently women complain of postcoital staining. Unusual lesions may occur in the upper third of the vagina, on the posterior wall and these lesions may be either single and discrete or multifocal.

Successful treatment of VAIN is difficult and no consensus exists on the most effective treatment. Initial methods of therapy for VAIN were irradiation or surgery, but the complications of potential vaginal stenosis [3] made these treatments less suitable for younger patients and resulted in trials of other treatments. These include topical chemotherapy [4], local laser ablation [5] and surgical excision. The aim of this study is to report on the outcome of treatment in 102 patients with VAIN.

Patients and Methods

This retrospective study involves 102 cases from the card index of the Colposcopy and Laser Surgery Unit, Alexandra Hospital, Athens, Greece over a 10-year period (1990-2000).

In all cases the diagnosis was based on a histologic specimen which had been processed by the Pathology Department of

Alexandra Hospital. Colposcopy with the application of 3% acetic acid and Schiller's test were used. In all cases, complete assessment of the vagina and cervix, when present, was carried out. Postmenopausal women or women previously irradiated were given oral estrogen therapy ten days prior to their examination.

Patient's charts were reviewed for the following information: age, menopausal status, history of human papillomavirus (HPV), history of hysterectomy, history of cervical surgery for dysplasia, history of gynaecologic cancer, history of pelvic radiation therapy, Papanicolaou smear results, colposcopic findings, location of VAIN, multifocality of VAIN, recurrence of VAIN and development of vaginal cancer.

Patients with vaginal intraepithelial neoplasia were treated by various means. Young patients with VAIN₁ received no further treatment after initial biopsy because their lesions, most of which were small and unifocal went into remission after the biopsy. Criteria for laser ablation included a completely visualized lesion with no suspicion of invasive cancer. Upper vaginectomy was performed for grade 2-3 VAIN when the lesion was confined to the upper one-third to upper one-half of the vagina in hysterectomized women.

Follow-up consisted of colposcopic and cytologic control examination every three months during the first year, every six months during the second year and then yearly for a prolonged period.

Results

The age of the patients ranged from 19 to 68 years with a mean age of 52.5 years. For patients' characteristics see Table 1. Patients with VAIN₁, VAIN₂ and VAIN₃ had the following mean ages of 44.5, 47.8 and 61.8 years, respectively, and the difference between the mean ages of patients with different grades of VAIN was found to be statistically significant ($p < 0.001$).

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Table 1. — Patient characteristics

Number	102
Age (mean)	52.5
History of CIN	30 (29%)
History of total hysterectomy	37 (36%)
History of gynaecologic cancer	17 (17%)
History of radiation therapy	6 (6%)
History of VIN	7 (7%)

All patients with VAIN were found to have had abnormal Papanicolaou smears. Colposcopic examination revealed acetowhite epithelium (80%), punctation (15%) and mosaicism (3%) and most of these patients were asymptomatic (96%). However, three patients had abnormal vaginal bleeding (3%) and one patient had recurrent vaginal discharge (1%).

Localization of the lesions to the upper third of the vagina was observed in 82 cases (80%) and to the lower third in 20 cases (20%). VAIN lesions were multifocal in 62% (63/102) of the cases and single and discrete in 38% (39/102). The distribution of grades was VAIN₁ 49% (50/102), VAIN₂ 15% (15/102) and VAIN₃ 36% (37/102). The frequency with which the various therapeutic modalities were used as the first measure, were CO₂ laser 57% (58/102), surgical excision (partial or total) 24% (24/102) and in 20% (20/102) of cases the lesions were followed-up by observation only (cytology and colposcopy).

The median follow-up for the 102 patients was 25 months. Among these patients, 20 had recurrences and two patients developed invasive vaginal cancer (Table 2).

It was found that the grade of VAIN did not affect the risk of recurrence and recurrence rates among patients with VAIN_{1,2} and 3 were found to be 14%, 26%, 27% ($p = 0.272$), respectively.

Patients with minimal VAIN₁ lesions from whom punch biopsies were obtained had the lowest recurrence rate compared to those (with VAIN_{2,3}) treated with laser or vaginectomy, but the difference is not statistically significant (15%, 21%, 21%, respectively; $p = 0.4$).

We found also that multifocality significantly affected the risk of recurrence. In 17/63 patients with recurrence the lesion was multifocal, whereas in 3/38 it was unifocal ($p = 0.03$).

Table 2. — Vaginal intraepithelial neoplasia recurrence according to the method of treatment

Treatment modality	Recurrence (%)
Punch biopsy (VAIN)	3/20 (15%)
Laser	12/58 (21%)
Surgical excision	5/24 (21%)

Discussion

The vagina is the least frequent location for genital neoplasia. From 1990 through 2000 we examined about 17,000 patients at the Colposcopy and Laser Surgery Unit of Alexandra Hospital. We encountered 102 patients

with vaginal intraepithelial neoplasias (0.6%). In the literature, the incidence of VAIN accounts for approximately 0.4%-1% of lower genital intraepithelial neoplasias [1].

The mean age of women with VAIN in our study was 52.5 years which is similar to that reported by Benedet *et al.* [5] and Lenehan *et al.* [6]. In our study, we also found increasing mean patient age with increasing grade of VAIN. In the literature Dodge *et al.* [7] did not find a statistically significant difference between the mean ages of patients with different grades of VAIN, while other authors reported increasing mean patient age with increasing grade of VAIN (Silman *et al.* [8]). In our study, 29% of patients with VAIN had a history of cervical intraepithelial neoplasia and 36% of the patients had had a total hysterectomy for other gynaecological conditions. Confirming the findings of other authors, [6, 7, 8] we found that most women with VAIN were asymptomatic, with the diagnosis being made following colposcopy and biopsy for abnormal Papanicolaou smears. The results of this study give an answer to the dilemma of whether or not to perform periodic vaginal cytologic samples on all posthysterectomy patients.

In a recent study, Saraiya *et al.* [9] have demonstrated that continued Papanicolaou screening of women without intact uteri may result in excessive use of resources in time and money with minimal impact on decreasing cervical cancer. One reason for continuation of Papanicolaou smear screening after hysterectomy includes screening for vaginal neoplasia. In our study 36% of women with VAIN had had a hysterectomy for other reasons and were asymptomatic.

Because of the retrospective nature of our study it is not possible to identify factors that influenced choice of treatment modality in all the patients. In our department, a specialized dysplasia-gynaecological oncology unit, we managed all the cases of VAIN from 1990 to 2000 with upper colpectomy or laser ablation or follow-up by Papanicolaou smear and colposcopy after punch biopsy on the basis of careful patient selection. As demonstrated in Table 2, we found that women with VAIN₁ who were followed-up with Papanicolaou smears and colposcopy after the punch biopsy of small lesions had a recurrence rate of 15%. Spontaneous regression of VAIN appears to be more common in cases with grade 1 than with more advanced VAIN lesions [2].

A wide variety of treatment has been used in other situations, most commonly consisting of local excision, partial or total vaginectomy, radiotherapy, laser vaporization or topical 5-fluorouracil administration. Each of these treatment methods has advantages and disadvantages. In this study, we have treated patients usually with laser ablation or vaginectomy. Criteria for laser vaporization included a completely visible lesion of VAIN₁₋₃ that had been sampled as indicated and in which invasive carcinoma had been excluded and that could not be managed by small local excision. Upper colpectomy was performed for grade 2-3 vaginal intraepithelial neoplasia when the lesion was located in the upper 1/3 of the vagina in women having had a hysterectomy. As demonstrated in Table 2, we did not find any statistical difference in the

recurrence rate between vaginectomy and laser ablation. This study has also shown that high-grade VAIN is a percutaneous lesion. Also, two cases with VAIN₃ progressed to invasive cancer. Other authors have also reported progression of VAIN₃ to invasive cancer [2, 10].

In conclusion, VAIN is a rare asymptomatic disorder and the diagnosis is made by colposcopic examination after an abnormal Papanicolaou smear. VAIN₁, depending on the extent of the lesion, will most likely regress after initial treatment, however patients with VAIN require careful monitoring because of the risk of recurrence and even progression to invasive carcinoma [12]. Patient selection and operator skill have a significant influence on the treatment outcome [13]. In post-hysterectomy patients with VAIN₃ at the vaginal apex in the region of a vaginal cuff scar, upper vaginectomy is the treatment of choice [11], while multifocal VAIN_{1,3} or colposcopically well-defined lesions involving large areas of vaginal mucosa could be successfully managed by laser CO₂ ablation [12].

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