Steroid Hormone Therapy in the Treatment of Vulvar Dystrophy

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SUMMARY: Twenty-nine patient with vulvar dystrophy were classified histologically and were subjected to a proposed protocol of treatment by steroid hormone application to the local skin. Clinical response was evaluated in twenty-three of these patients. Observation by colposcopy and toluidine blue test were the two techniques used to direct biopsies. The results showed that 4 or 5 patient with lichen sclerosus and 16 of 18 patients with Hyperplastic and mixed dystrophy had complete symptomatic response with testosterone and corticosteroid respectively. Moreover 22 (96%) had more than 50% decrease in total lesion morphologically. It is therefore concluded that for velvar dystrophy, a benign epithelial disorder of the vulva steroid hormone therapy is indeed a logical and an effective one.

INTRODUCTION

The vulvar dystrophy is an enigma and one of the most controversial topic as for the pathogenesis, clinical out-come and the malignant potentiality. Recently a more satisfactory terminology, more emphasis on histopathology, conservative approaches, more prospective studies and better knowledge were attained due to the advancement in the techniques. And clinical investigative procedure have definitely contributed to the better understanding of the vulvar dystrophic diseases. Inspite of all this advancement, to what extent the agony and morbidity of the sufferers has decreased is still an issue of persuance.

There has been very few systematic studies in Japan concerning vulvar dystrophy. In this institute a study was undertaken to evaluate the clinical outcome of vulvar dystrophies, where the patients were subjected to a proposed protocol of treatment (**Fig. 1**).

MATERIALS AND METHODS

The patients referred to the Gynecology Department of Nagasaki University Hospital with vulvar complaints with the subjective symptom of 'itching' had undergone biopsy. In all the cases toluidine blue test and colposcopy directed biopsies were obtained. In addition to the toluidine positive areas, multiple biosies were obtained from several other sites because of the multicentric nature of the vulvar dystrophic diseases.

Biopsy site and the size of the lesion were documented and photographed for references for the treatment assessment. Diagnosis being confirmed after histological examination, the patients were subjected to the proposed protocol of treatment. The steroid hormones were applied to the local skin two to three times daily for at least four weeks and the frequency of application were decreased gradually to two times per week, with the alleviation of the symptoms. The patients were examined bi-weekly

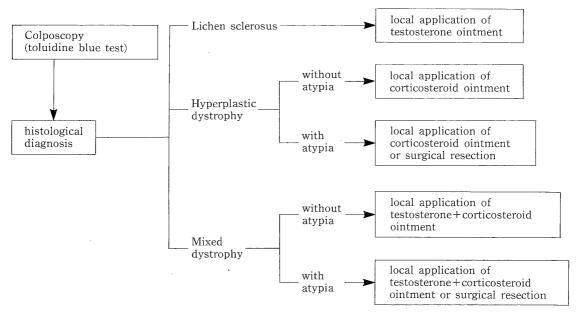


Fig. 1 Treatment protocol for vulvar dystrophy

at which time the gross appearance of vulva, symptomatic relief and side-effects were noted.

RESULTS

The patients who had undergone biopsy of epithelial lesions of the vulva were 75 in total from January 1986 till December 1990. Among them vulvar dystrophy was found in 29 cases (37.1%). The initial histological diagnosis of these 29 patients are listed in **Table 1**.

The age distribution according to histological diagnosis in lichen sclerosus was 56.4 (SD 11.4) years. The age of the patients with hyperplastic dystrophy without atypia was 54.08 (SD 12.4) years and for hyperplastic dystrophy with atypia was 50.5 (SD 14) years. The age of the patients with mixed dystrophy was quite variable, with majority of these patients being over the age of 50 years. In contrary to other frequent statements the vulvar dystrophc lesions were obtained in some patients of reproductive age group too (**Fig. 2**).

Itching was the most frequent complaint encountered in this study. Also mass, burning sensation, pain and disturbance in urination were the other symptoms commonly found. However, some of the patients were without any symptom (**Table 2**).

The frequency of vulvar dystrophy by site is presented in **Fig. 3**. Lichen sclerosus was found in the labia majora and minora and also relatively frequent in the prepuce of the clitoris and posterior labial commissure. The occurence was almost symmetrical in 4/5 (80%) of the cases. Hyperplastic dystrophy without atypia was frequent in labia majora, minora and was liable to spread to the prepuce of the clitoris and posterior labial commissure. In case of hyperplastic dystrophy with atypia was mostly localized, in the vestibule and frequently observed in the labia majora and minora.

The treatment advocated, after histological diagnosis paralleling the protocal, application of corticosteroid (Fluocinolone acetonide 0.25-mg/g in 10g) ointment in hyperplastic dystrophy without atypia and resulted in alleviation of itch. The symptomatic relief was prompt in this group, followed by demonstrable gross change of the vulva, which was evident by reduction of the size of the lesion. The final result was histological changes towards regression. In patients with hyperplastic dystrophy with atypia, corticosteroid completely removed the disease without any recurrences in 6/9 (66.7%) patients. In two other patients it was ac-

	Epithelial Lesion	Cases (%)		
Dystrophy	Lichen sclerous Hyperplastic, without aty	5 (6.4) 9 (11.5)		
	Hyperplastic, with atypia	mild-mod severe	11 (14.1) 1 (1.3)	29 (37.1)
	Mixed	3 (3.8)		
Other benign lesions	Condyloma acuminatum Hydradenoma Vulvitis and others		1 (1.3) 1 (1.3) 32 (41.0)	32 (43.6)
In situ cancerous lesion	Carcinoma in situ Paget's disease	1 (1.3) 2 (2.6)	3 (3.9)	
Invasive carcinoma	Microinvasive carcinoma Squamous cell carcinoma Invasive Paget's disease	1 (1.3) 9 (11.5) 1 (1.3)	12 (15.4)	

Table 1. Epithelial Lesions of The Vulva [Nagasaki University (Jan 1986-May 1990)]

Table 2. Symptoms of Vulvar Dystrophy

1 (1.3)

Adenocarcinoma (Skene gland)

symptoms	itching	burning	mass	pain	urinary disturbance	no symtoms
Lichen sclerosus (5 case)	80 %	40%		20 %	20 %	
Hyperplastic, (9 case) without atypia	77.8%		11.1%	11.1%	_	11.1%
Hyperplastic, (12 case) with atypia	58.3%	****	16.7%	8.3%	_	16.7%
Mixed (3 case)	66.7%	_	33.3%	_	33.3%	33.3%

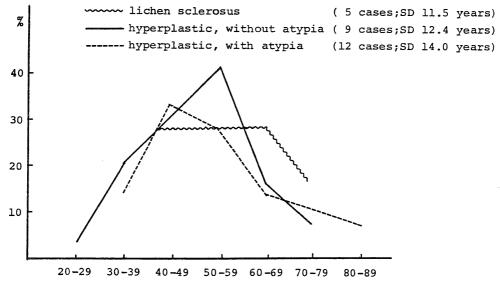
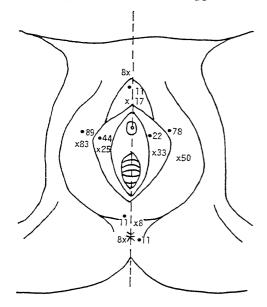


Fig. 2. Age distribution in patients with vulvar dystrophies

complished by local excision of the diseased area. In these two patients the lesion was small, localized and well demarcated, which could easily be approached for excision.

The treatment for lichen sclerosus with 2% testosterone propionate in a vaseline base applied locally has had dramatic response, noted by the symptomatic relief of itching. Subjective

- hyperplastic, without atypia
- x hyperplastic, with atypia



- lichen sclerosus
- x mixed

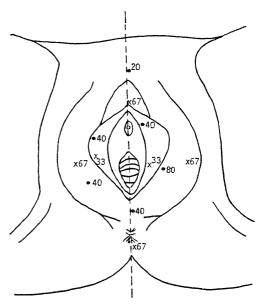


Fig. 3. Frequency of vulvar dystrophies by site (%)

Table 3. Clinical Response to Treatment

		cases	subjective (symptomatic relief)		objective (decrease of lesion)		
			complete	partial	100%	50%≦	50%>
Lichen sclerosus		5	4	1	2	2	1
Hyperplastic, without atypia		8	7	1	4	4	
	mild	3	3	_	3	_	
Hyperplastic, with atypia	moderate	5	4	1	3	2	
, , , , , , , , , , , , , , , , , , , ,	severe	1	1	_	_	1	_
Mixed		1	1	_	_	1	
Total		-23	20	3	12	10	1
			(87.0%)	(13.0%)	(52.2%)	(43.5%)	(4.3%)

symptoms disappeared or decreased in 4/5 (80%) of the cases. The improvement in the external morphology was more vivid in these patients. The treatment offered for mixed dystrophy without atypia was corticosteroid and testosterone ointment application was of great benifit. The clinical response after treatment in 23 of the vulvar dystrophic patient are represented in **Table 3**.

DISCUSSION

In the previous times the treatment of choice for vulvar dystrophy was surgery by mutilating vulvectomy. Most clinicians at that time believed that this method relieves symptoms and provides an adequate prophylaxis against the inevitable development of carcinoma. In the recent times there are several reports investigating the relationship of vulvar dystrophy to

the development of carcinoma^{1, 2, 3, 4)}. And these reports revealed that the risk of carcinoma of the vulva developing in a woman with vulvar dystrophy is approximately 2-5% at presentation with additional risk of developing malignancy from vulvar dystrophy is extremely small.

Previously, several kinds of topical agents has been tried for vulvar dystrophy. Vitamin A⁵⁾ and Mercuric Sulphide⁶⁾ were used in the early times, but they did not result in the resolution of the disease, either morphologically or microscopically. Jasionowski⁷⁾ has tried a topical application of progesterone, which resulted in a good response but the treatment was advocated in a small group of patients only. As a medical approach, intradermal injection of triamnicilone⁸⁾ and absolute alcohol⁹⁾ have been used. The result of these agents were not satisfactory.

August¹⁰⁾ employed cryosurgery on 12 patients and reported satisfactory results, without further treatment after three years in only 25% of the cases.

Surgical therapy for vulvar dystrophies has been disappointing because most patients experienced recurrences²⁾. Rettenmaier¹¹⁾ reported on skinning vulvectomy in vulvar dystrophic patients and observed recurrences in 50% of the patients at 45-96 months after initial surgery. Di Paola¹²⁾ treated vulvar dystrophy by grafting technique after vulvectomy. Two years later, the grafted skin has developed recurrence.

Recently, laser therapy has been used for the treatment of this disease¹³⁾. But a high recurrence rate has been found after this treatment. Some authorities suggest that persisting lesion after laser therapy may respond more favorably to topical steroid, but this mode of treatment has been evaluated in only small number of patients. The therapeutic value of laser therapy in vulvar dystrophies is yet to be proved.

Effective treatment of vast majority of patients can be achieved medically by steroid hormone. The local application of corticosteroid has been proved to be of great benifit in most patients becoming free of symptoms. In a prospective study by Kaufman⁸⁾ 24 out of 39 hyperplastic dystrophy without atypia had complete relief of symptoms with both morphological and histological changes to regression.

Friedrich⁶⁾ similarly reported on prompt relief of symptoms in hyperplastic dystrophic patients by the treatment using topical application of a cream containing crotamine diluted with a hydrocortisone compound.

Cinberg¹⁴⁾ was the first who noted the efficiency of topical testosterone in lichen sclerosus. His treatment was employed in a large series by several authorities^{15, 16)}. Recently Friedrich⁶⁾ in a report summarized the results of testosterone ointment for the treatment of lichen sclerosus and mixed dystrophy. In addition to his own results, he reported on the results of several authorities. Of 184 patients treated, 172 (93%) had shown improvement after testosterone therapy, both macroscopically and microscopically.

Vulvar dystrophy is a common gynecological problem causing sufferings and morbidity in large number of women. It is to be emphasized that biopsy is mandatory before advocating treatment in order to exclude malignancy during the first visit and that re-biopsy is also essential for the confirmation of regression of the disease. The present report has demonstrated the dramatic effects of steroid hormone therapy on vulvar dystrophy, irrespective of dysplasia. In the study, 4 of the 5 patients of lichen sclerosus and 16 of the 18 patients of hyperplastic and mixed dystrophy had complete symptomatic response to testosterone and corticosteroid respectively. Moreover, morphologically 22/23 (96%) of the patients had more than 50% decrease in total lesion. These data indicate that the protocol of treatment described here can eliminate the agonising symptoms without a need for mutilating surgery. It is likely that the sufferings and morbidity in vulvar dystrophic patients could be controlled by this treatment.

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