A clinico-pathological study of vulval dermatoses

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SYNOPSIS  A long-term review of 108 women suffering from various forms of vulval dermatosis is described and a detailed analysis of those with chronic hypertrophic vulvitis, lichen sclerosus et atrophicus, and neurodermatitis is made. One case of neurodermatitis and two cases of lichen sclerosus progressed to carcinoma but no case of chronic hypertrophic vulvitis became malignant. It is possible that vulval dermatoses occur more commonly in the nulliparous than in the parous women and there is a slight preponderance of women who are blood group A.

It is suggested that the term 'leukoplakia' should be abandoned and that vulval lesions should be described in precise and meaningful histological terms.

Although the vulva may be regarded as part of the genital tract it is also part of one of the largest organs of the body, namely, the skin. For this reason most of its disorders are those of the skin modified only by site. However, when well defined dermatological conditions such as psoriasis and candida infections are excluded, a residue of ill-defined dermatoses remains which have been variously termed leukoplakic vulvitis, leukoplakia, kraurosis, and lichen sclerosus et atrophicus. The clinical behaviour of vulval dermatoses may be affected by the warm and moist environment and the histological appearance is modified by lichenification which follows scratching. These factors have contributed to the confusion in the diagnosis of distinct disease entities.

There are two major problems in the study of vulval dermatoses; first, the formulation of a discriminating and acceptable terminology, and second, the assessment of the malignant potential of the lesions thus defined. The object of the present investigation is to assess the risk of malignant change in various vulval disorders and to consider the consequent clinical and taxonomic implications.

Material and Methods

One hundred and eight women suffering from leukoplakia or lichen sclerosus et atrophicus of the vulva were recorded in the laboratory diagnostic file in the 19 years, 1949 to 1968, but after 1968 very few cases of leukoplakia were recorded because of uncertainty about the diagnostic criteria and these have not been investigated further. All the available histological material from the 108 cases was reviewed. The tissue varied; sometimes it was from a small biopsy but more frequently it was a specimen from a simple vulvectomy or, occasionally, from a radical vulvectomy. Each woman's clinical case history was reviewed and those who did not have a vulval cancer at the time of initial hospital attendance were traced for a clinical assessment of their present condition. For the purposes of this survey it was necessary arbitrarily to define the histological criteria of the various dermatoses. After a review of some of the literature (Berkeley and Bonney, 1909; Wallace and Whimster, 1951; Hunt, 1954; Hyman and Falk, 1958; McAdams and Kistner, 1958; Barker and Gross, 1962; Lever, 1967; Montgomery, 1967; Novak and Woodruff, 1967; Janovski, 1970; Janovski and Douglas, 1972; and Milne, 1972) and excluding simple atrophic states, three types of lesion were recognized: hypertrophic vulvitis, neurodermatitis, and lichen sclerosus et atrophicus. These were distinguished on the basis of the following criteria.

HYPERTROPHIC VULVITIS
(SOMETIMES TERMED LEUKOPLAKIA)

This is a condition affecting the glabrous skin of the vulva, namely, the inner surfaces of the labia
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Fig 1a

Chronic hypertrophic vulvitis. Note (a) normal squamous epithelium of the vulva with slight inflammatory reaction in the corium. (b) The squamous epithelium shows marked hyperkeratosis and acanthosis. The granular layer is conspicuous and the rete pegs irregular and often spiky. The corium shows a chronic inflammatory reaction. (c) Slight cellular atypia (individual cell keratinization) is present. All the sections are taken from the glabrous area of the vulva (H & E × 50).
majora, the labia minora, the clitoris, and the fourchette. It is characterized by epidermal hypertrophy with acanthosis (fig 1); mitotic activity and minor cytological abnormalities may be present, such as variation in size and shape of some cells and occasionally a few cells showing individual cell keratinization. If the abnormalities are more severe the lesion may merit the description of dysplasia or of a Bowenoid type of hypertrophic vulvitis which is more closely allied in appearance and in behaviour to carcinoma in situ. Hyperkeratosis is a feature of hypertrophic vulvitis although the variation in the degree of keratinization of the glabrous skin both with age and site in the same vulva must be borne in mind when interpreting the histological picture. In the dermis there is usually some inflammatory infiltrate and sometimes homogenization of the collagen fibres.

**NEURODERMATITIS (CHRONIC DERMATITIS OR LICHEN SIMPLEX CHRONICUS)**

This lesion (fig 2) may arise as a result of prolonged rubbing or scratching of the skin. In this survey it is defined as a lesion occurring on the hair-bearing skin. Clinically the skin is thickened with exaggerated surface markings. There is marked acanthosis with elongation of the rete ridges and slight intercellular oedema may occur. Hyperkeratosis is intermingled with areas of parakeratosis and the stratum granulosa is conspicuous. In the upper dermis there is moderate perivascular infiltration of inflammatory cells. The number of capillaries may be increased. It will

**Fig 2** Neurodermatitis of the vulva. The section is taken from the hair-bearing area. There is moderate hyperkeratosis and marked acanthosis. The underlying corium shows a chronic inflammatory reaction (H & E × 50).

**Fig 3** Lichen sclerosus et atrophicus. The squamous epithelium is thin and more than half of it is keratinized. A wide, pale zone of homogenized corium lies beneath the epithelium and below this a zone infiltrated with chronic inflammatory cells (H & E × 50).
be seen that, apart from site, this condition bears a close resemblance to hypertrophic vulvitis.

Lichen Sclerosus et Atrophicus
This affects both sexes and is not confined to the genital region. The lesions are whitish and sharply demarcated affecting both the hairy and glabrous skin of the vulva and extending to the genitocrural and inguinal folds and the perianal areas. Histologically the lesion consists of hyperkeratosis with keratotic plugging in the hair-bearing skin (fig 3). The stratum Malpighii is atrophied with hydropic degeneration of basal cells, and acanthosis, if present, may be in spikes. There is marked homogenization of the collagen in the upper dermis and infiltration of the lower dermis with inflammatory cells.

Results
Of the original 108 cases, 61 showed a dermatosis without invasive cancer. Eighteen of these 61 cases fulfilled the criteria for hypertrophic vulvitis and 31 those for lichen sclerosus et atrophicus, in five cases there was concomitant hypertrophic vulvitis and lichen sclerosus et atrophicus, and seven cases showed the changes of neurodermatitis. In a further 24 cases the dermatosis lay adjacent to invasive squamous cancer. Twenty-three cases were rejected from the series because the revised diagnosis when reviewed was psoriasis, condyloma acuminata, or Bowen's disease; or the vulva manifested no more than normal senile atrophy or the diagnosis was cancer without dermatosis or the biopsy was inadequate for diagnosis.

The ages, parity, and blood groups, where known, are summarized in table I. The number of nulliparous women aged over 40 years in this study was compared with that recorded in the 1961 census (counted as single women and married women with no live births). The number of such women with vulval dermatoses, with or without cancer, was 29 compared with an expected 21-35 women in the general population. There were 10 nulliparous women with vulval dermatoses with cancer compared with an expected 6-06. The differences are not statistically significant but they do suggest that these conditions occur more commonly in nulliparous women. It must also be remembered that some of the women in the census estimate of 'nulliparity' may have conceived. In a separate study in Manchester the average age of 109 women with invasive vulval cancer was 64-5 years which is a little older than the ages of women with vulval dermatoses in the present study. There was a preponderance of blood group A: 51% of the cases compared with 40-5% frequency in the general population.

Histological Features (Table II)
Hyperkeratosis was almost invariably present, para-
keratosis was sometimes seen. Most interest centres round the presence of cellular abnormalities. These

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Cases</th>
<th>Average Age (yr)</th>
<th>Age Range (yr)</th>
<th>Nulliparous Average Age at Menopause (yr)</th>
<th>Blood Group</th>
<th>Not Known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic vulvitis without cancer</td>
<td>18</td>
<td>61</td>
<td>47-85</td>
<td>7 (39%)</td>
<td>A</td>
<td>1</td>
</tr>
<tr>
<td>Hypertrophic vulvitis with cancer</td>
<td>12</td>
<td>60</td>
<td>38-78</td>
<td>3 (25%)</td>
<td>O</td>
<td>0</td>
</tr>
<tr>
<td>Neurodermatitis without cancer</td>
<td>7</td>
<td>57</td>
<td>51-63</td>
<td>2 (28%)</td>
<td>AB</td>
<td>0</td>
</tr>
<tr>
<td>Neurodermatitis with cancer</td>
<td>4</td>
<td>62</td>
<td>59-71</td>
<td>0</td>
<td>B</td>
<td>0</td>
</tr>
<tr>
<td>Lichen sclerosus et atrophicus without cancer</td>
<td>31</td>
<td>57</td>
<td>24-71</td>
<td>7 (22%)</td>
<td>AB</td>
<td>1</td>
</tr>
<tr>
<td>Lichen sclerosus et atrophicus with cancer</td>
<td>6</td>
<td>62</td>
<td>53-76</td>
<td>5 (83%)</td>
<td>B</td>
<td>0</td>
</tr>
<tr>
<td>Hypertrophic vulvitis and lichen sclerosus et atrophicus without cancer</td>
<td>5</td>
<td>59</td>
<td>51-68</td>
<td>2 (40%)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hypertrophic vulvitis and lichen sclerosus et atrophicus with cancer</td>
<td>2</td>
<td>72</td>
<td>70-73</td>
<td>1 (50%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rejected from study</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>108</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table I Analysis of original 108 cases

Information supplied by Dr F Stratton, Director National Blood Transfusion Service, North West Regional Health Authority.
were most often seen in hypertrophic vulvitis and least commonly seen in lichen sclerosus et atrophicus. The frequency of cytological abnormalities was very similar in each type of lesion whether cancer was concomitantly present or not. This concordance existed for all the specific histological features recorded. Mitoses were seen more commonly in hypertrophic vulvitis and in neurodermatitis than in lichen sclerosus although the presence of normal mitoses has no malignant significance and is merely an expression of growth to replace loss of keratin scales.

Homogenization of the dermal collagen was always present in lichen sclerosus et atrophicus but was seen in only a third of the other lesions. Lymphocytes predominated in the inflammatory cellular response and neutrophil polymorphonuclear leukocytes were absent.

In this study lichen sclerosus et atrophicus and neurodermatitis emerged as fairly uniform distinct lesions. Hypertrophic vulvitis did not present such a constant picture and could be subdivided according to cellular abnormalities whether absent or, if present, whether of minor or of major degree. The major cytological abnormalities were often associated with a disorderly epidermis constituting dysplasia or Bowen's disease (fig 4). Such cases have been excluded from the series because of their known tendency to undergo malignant change (Woodcock, 1973).

CLINICAL REVIEW

The initial diagnosis was made from six months to 19 years before the clinical review. Of 61 women with a vulval dermatosis without cancer, 40 were traced for examination. Five of 21 women not examined were known to have died. Two women with hypertrophic vulvitis had died of malignancy in another site: one from cancer of the ovary and the other of the endometrium. Three women with lichen sclerosus et atrophicus had died of heart failure with no vulval carcinoma known to the patient's general practitioner at the time of death. Thus 45 of the available 61 cases were effectively traced (table III). There were three women, free of malignancy at the initial presentation, in whom a squamous-cell carcinoma of the vulva later developed (cases 1, 2, 3).

Table II  Histological features observed in cases of hypertrophic vulvitis, neurodermatitis, and lichen sclerosus et atrophicus

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Total Cases Available for Review</th>
<th>Cases Traced or Examined</th>
<th>Cases Developing Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic vulvitis</td>
<td>18</td>
<td>13 (-2 died)</td>
<td>0</td>
</tr>
<tr>
<td>Neurodermatitis</td>
<td>7</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Lichen sclerosus et atrophicus</td>
<td>31</td>
<td>15 (-3 died)</td>
<td>1 (-1)*</td>
</tr>
<tr>
<td>Hypertrophic vulvitis and lichen sclerosus et atrophicus</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Total cases initially without cancer</td>
<td>61</td>
<td>45</td>
<td>3 (6.7% of total traced)</td>
</tr>
</tbody>
</table>

Table III  Clinical review of cases without cancer in initial biopsy.

*See case 3

Of 61 women without cancer, initial surgery was biopsy in 17 cases and simple vulvectomy in 44 cases. Eight women were known to have undergone further surgery or x-ray therapy, two of whom had both forms of treatment. One of these women had emigrated. The second patient is described in case 4.

Case 1

At 68 years she first presented with a history of
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Fig 4 From a woman of 38 years with chronic vulvitis and Bowen's type of epithelial dysplasia. Note the progressive changes: (a) normal squamous epithelium from this patient's vulva (H & E x 50); (b) chronic hypertrophic vulvitis in the same patient (H & E x 50); (c) much thickened squamous epithelium in which stratification is retained but a number of abnormal cells can be seen (H & E x 50); (d) at higher magnification the abnormal cells can be seen to have retracted from their adjacent cells, the cytoplasm is more eosinophilic and the nuclei are enlarged and disorganized (H & E x 300).
pruritus vulvae for two years and was treated by a simple vulvectomy for a white lesion. Microscopically this was lichen sclerosus et atrophicus, undistinguished by cytological abnormalities or mitoses. Two years later an excised vulval ulcer showed squamous carcinoma. A radical vulvectomy was performed and no residual malignancy was seen in the excised tissue but the vulva showed the changes of lichen sclerosus et atrophicus identical to that previously removed. On review five years later there was no recurrence of vulval dystrophy or malignancy.

Case 2
At age 72 years this woman complained of irritation and ulceration of the vulva. She also suffered from myxoedema and gout. A vulval biopsy showed neurodermatitis: there was hyperkeratosis, some parakeratosis, and patchy dermal homogenization. There were no cellular abnormalities. Four years later a squamous carcinoma of the vulva was removed. Microscopically the tumour was surrounded by skin showing similar changes to those observed in the first biopsy.

Case 3
One other woman developed cancer but the slides of the initial biopsy were not available. At age 40 years this patient had a simple vulvectomy for a pruritic white lesion. At 53 years a radical vulvectomy was performed for squamous carcinoma. The excised tissue showed invasive cancer adjacent to lichen sclerosus et atrophicus. The benign tissue did not show any cytological abnormalities. The patient was not traced for review.

Case 4
The vulva was irradiated with x rays for pruritus at age 48 years. At 51 years she had a biopsy soon followed by a simple vulvectomy. The histology showed hypertrophic vulvitis and lichen sclerosus et atrophicus, neither lesion showing mitoses or cytological abnormalities. Later she underwent skin grafting to the vulva to enable coitus and then further skin grafting with colostomy. On review at age 69 years, the whole perineum, both groins, and anus were taut, stenosed, white and itchy. The grafted skin had suffered the same fate as the original skin.

Discussion
Most of the controversy about vulval dermatoses centres on the nature of the conditions designated hypertrophic vulvitis in this paper. All the authors stress hyperkeratosis, acanthosis, and epidermal hypertrophy. Montgomery (1967) gives the most detailed description and speaks of 'benign' leukoplakia and also of epithelial changes going on to a 'Bowenoid' picture. McAdams and Kistner (1958) distinguish leukoplakia from benign leucokeratosis, in which cytological abnormalities are lacking. In leukoplakia they describe the following cellular abnormalities: (1) poor orientation, (2) variation in shape and size, (3) malignant dyskeratotic cells high in the prickle cell layer, and (4) individual cell keratinization. Lever (1967) regards the presence of atypical cells as a prerequisite for the histological diagnosis of leukoplakia. Both Wallace and Whimster (1951) and McAdams and Kistner (1958) base their descriptions on the epidermal lesions adjacent to invasive carcinoma. This approach is not as misleading as might be supposed since the present study has demonstrated that specific histological features in a vulval dermatosis vary little whether cancer is coincidentally present or not (table II).

The cases presented as hypertrophic vulvitis in the present study overlap the cases of McAdams and Kistner of leukoplakia and of leucokeratosis but exclude cases with a frankly Bowenoid or dysplastic appearance.

The natural history of vulval dermatoses is difficult to assess because these diseases are uncommon and affect older women with a short expectation of life. Previous studies relating to malignant change are summarized in table IV. Taussig (1940) studied vulval cancer and then identified 72 of these cases with an associated dermatosis. He found that three of these 72 women had experienced symptoms of leukoplakia for three, seven, and 12 years before the cancer first appeared; in one case the diagnosis was confirmed by biopsy. Other authors describe the development of cancer subsequent to the clinical presentation of dermatosis. The cases of leukoplakia of McAdams and Kistner (1958) with cellular and nuclear atypia show the highest rate of malignant change. These cases could loosely be grouped with those with disorderly overactive epithelium described by Jeffcoate and Woodcock (1961). The three cases from Manchester in which malignancy supervened did not show such cellular or nuclear atypia. This finding suggests that the biological potential of a vulval dermatosis, other than carcinoma in situ, cannot be predicted with certainty on morphological grounds. McAdams and Kistner (1958) selected cases with epidermal atypia and this has resulted in identifying a high risk group but should not imply that cases without these features have a benign prognosis. The apparent potential for malignant change in the cases reported in this study may be coincidental but to assess this requires a knowledge
of the incidence and age distribution of both vulval carcinoma and vulval dermatoses, and for these latter conditions such information is wholly lacking. However, the slightly younger average age of the women with both a dermatosis and cancer compared with women with vulval cancer only suggests that the dermatosis may be a predisposing factor. It is possible that factors which cause dermatoses in the vulva may be initiators of a field change which only needs a promoter to reveal its malignancy.

The term leukoplakia conjures up an emotive reaction because of the implied malignant potential. Strictly the term describes a naked-eye appearance of the vulva characterized by the presence of white patches which result from keratinization of the epithelium and an increased distance of the blood vessels from the surface. Since the pathological changes causing these white patches are various (Milne, 1972), attempts to define the term ‘leukoplakia’ have been imprecise and confusing. This diagnosis should therefore be abandoned and replaced by a precise histological description. By analogy with the cervix, terms such as carcinoma in situ and dysplasia should be used to indicate grades of cellular abnormality suggestive of potential malignancy. The cases here termed ‘chronic hypertrophic vulvitis’ and ‘neurodermatitis’ can only be distingushed on the grounds of anatomical location (see above) and should be assessed individually and described in simple histological terms, care being taken that specific dermatological conditions are not overlooked. Lichen sclerosis remains a distinct condition which may also be found elsewhere on the body but with no malignant association outside the anogenital region.

References


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Table IV  Cases of vulval cancer preceded by a vulval dermatosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Lesion1</th>
<th>Total No. of Cases</th>
<th>No. of Cases of Dermatosis progressing to a Vulval Cancer</th>
<th>No. of Years of Symptoms before Cancer Developed</th>
<th>Percentage Cases of Vulval Dermatosis progressing to Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taussig (1940)</td>
<td>Leukoplakic vulvitis</td>
<td>72</td>
<td>1</td>
<td>3</td>
<td>4-2</td>
</tr>
<tr>
<td>Langley, Hertig, and Smith (1951)</td>
<td>Leukoplakic vulvitis</td>
<td>122</td>
<td>1</td>
<td>12</td>
<td>0-8</td>
</tr>
<tr>
<td>Hunt (1954)</td>
<td>Leukoplakic vulvitis</td>
<td>96</td>
<td>4</td>
<td>0</td>
<td>4-2</td>
</tr>
<tr>
<td>McAdams and Kistner (1958)</td>
<td>Leukoplakia</td>
<td>20</td>
<td>3</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Jeffcoate and Woodcock (1961)</td>
<td>Leukoplakia with disorderly overactive epithelium</td>
<td>?</td>
<td>2</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Barker and Gross (1962)</td>
<td>Lichen sclerosus</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Leighton and Langley (this study)</td>
<td>Lichen sclerosus with leukoplakic patch</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>2-4</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic vulvitis</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Neurdermatitis</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Lichen sclerosus</td>
<td>18</td>
<td>1</td>
<td>1*</td>
<td>4 and 13</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic vulvitis and lichen sclerosus</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>6-7</td>
</tr>
</tbody>
</table>

1 The terms used to describe the lesion are those used by the individual authors quoted.

2 See case 3.

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