LEUKOPLAKIA VULVAE
A CLINICO-PATHOLOGICAL REVIEW

THESIS

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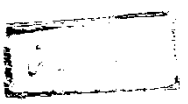

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A C K N O W L E D G E M E N T

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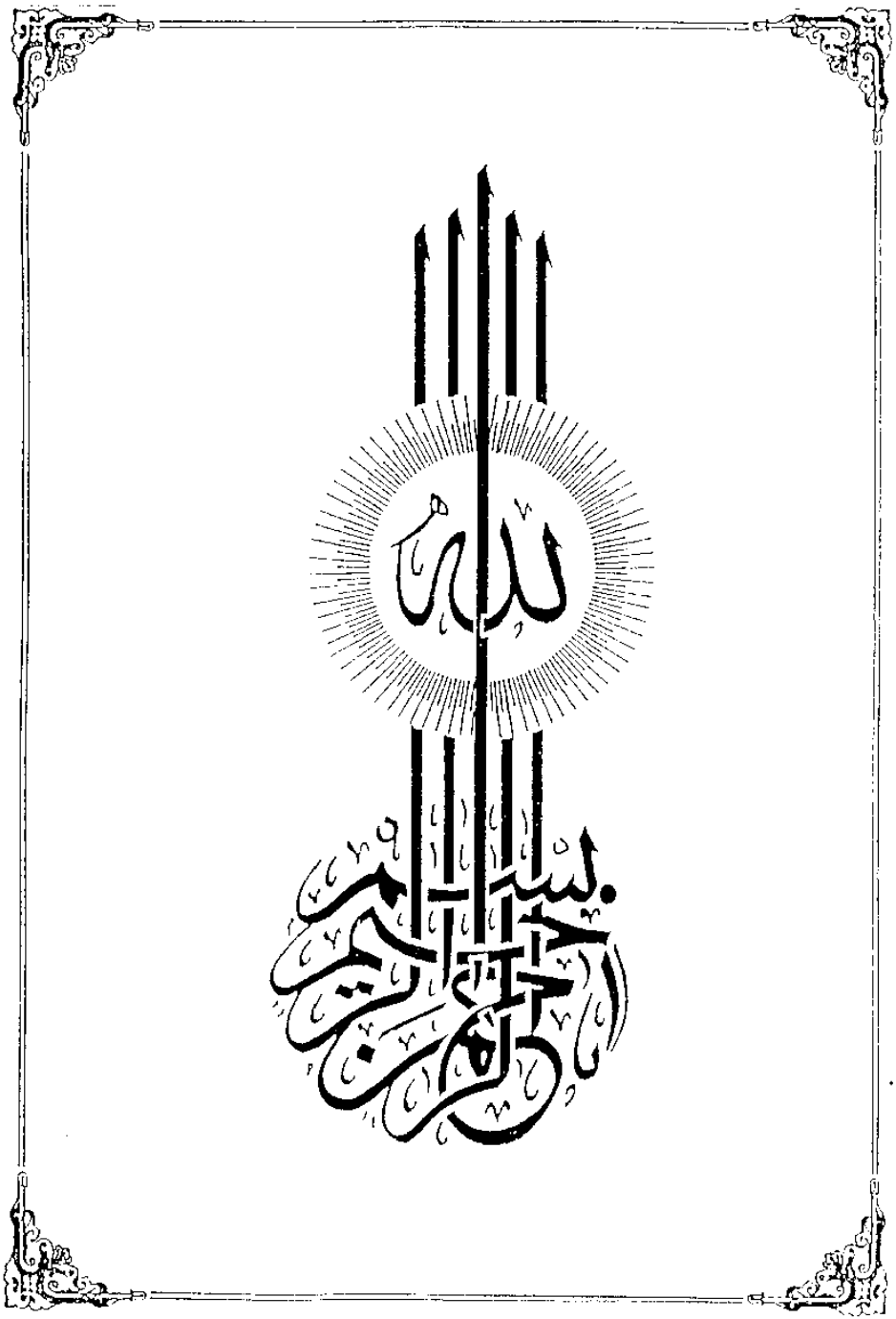

Introduction

I N T R O D U C T I O N

Leukoplakia vulvae means a white patch of the vulva that excites both clinicians and pathologists. White lesions of the vulva have traditionally set apart as a group because of an unwarranted fear of their premalignant potential. Three factors , operating independently or in concert , account for the white appearance : KERATIN , DEPIGMENTATION , and RELATIVE AVASCULARITY (Friedrich , 1976).

Any hyperkeratotic area which is constantly moist will eventually become white (Woodruff and Beans , 1963). The thicker the keratin layer , the more this is true , the sole of the foot after lengthy water immersion is the prime example of this phenomenon. For the same reason , any skin lesion which is hyperkeratotic (thickened keratin layer) appears white if located in an area of constant moisture such as the vulva. Depigmentation occurs when the basal layer melanocytes are lost or destroyed , or when because of chemical malfunction , they are unable to manufacture melanin pigment. Skin appears pale whenever superficial blood vessels are constricted , when the interposing distance between them and the surface is

increased , or when they are numerically decreased by a sclerotic process (Friedrich , 1976).

When the histologic examinations of radical vulvectomy specimens became possible , white areas of skin with disordered epithelial architecture were sometimes found adjacent to the carcinomatous growth. Early observers concluded that the white change preceded the cancer and led to its development. Thus evolved the concept that white patches (leukoplakia) on the vulva were premalignant. The same logic could be used in the reverse interpretation ; that the presence of carcinoma caused the surrounding white change. But , in fact , there is no good evidence to substantiate either theory. White changes are common ; cancer is rare. Occasionally both are found to coexist on the same vulva , but such coincidence does not imply a causal relationship (Friedrich , 1976).

AIM OF WORK

Review of Literature

HISTORICAL REVEIW AND TERMINOLGY

Breisky in 1885 , used the term kraurosis vulvae to describe a condition of progressive atrophy affecting the labia majora and minora , in which the skin became shiny , dry , and white. He recognized only one stage. Clinically and histologically the appearances were essentially identical with Taussig's atrophic stage of leukoplakic vulvitis described in 1929. Berkeley and Bonney (1909) considered it as a separate entity to leukoplakic vulvitis , while Taussig (1929) considered it as the end stage of 50 percent of cases of leukoplakia.

In 1887 , the dermatologist Hallopeau described as lichen planus atrophicus an atrophic skin lesion which he believed to be a late stage of lichen planus. Subsequently this became known as lichen sclerosus et atrophicus and , more recently , as lichen sclerosus.

The word "leukoplakia" , derived from the Greek leukos = white and plax = plate , was said in 1909 by Sir Comyns Berkeley and Victor Bonney of the Middle sex Hospital in London.

It was firmly in gynaecological literature in 1909 when Berkeley and Bonney defined " leukoplakic vulvitis " as a chronic inflammatory disease which was invariably premalignant , affecting the labia majora and minora , perineum , perianal region and thigh . They believed that the vestibule and urethra were never affected by the disease .

In 1929 , Taussig , in U.S.A.,held that leukoplakic vulvitis could affect any part of the vulval skin from the mons veneris to the anus . The gross stages of the disease as described by Taussig were as follows : (1) erythema , oedema , excoriation , and dryness ; (2) thickening and flattening of whitened vulvar folds ; and (3) cracking and superficial ulceration with parchment - like appearance to white or bluish white skin . The microscopic stages were : (1) minimal hyperkeratosis and acanthosis with inflammatory infiltrate , (2) hyperkeratosis and acanthosis with epithelial hypertrophy and round cell infiltration , and (3) hyperkeratosis , flattened rete pegs and a frayed basement layer with dermal collagen and inflammatory infiltrate . Like Berkeley and Bonney , Taussig believed that " leukoplakia " was thus altered from its original connotation of simply

" white plake " to carry a more sinister implication of " precancerous white plaque " .

McAdams and Kistner (1958) emphasized that the presence of acanthosis (of any degree) , irregular rete ridges , or hyperkeratosis was not believed sufficient to warrant a diagnosis of leukoplakia . Certain important epithelial changes to diagnose leukoplakia , were ; (1) poor orientation of cells and variations in nuclear size ; (2) extremes of atypicality with bizarreness of size and shape ; (3) individual cell hyperchromatism ; (4) dyskeratosis , a term used in the restricted sence to imply an abnormality of keratinization .

In 1966 , Jeffcoate introduced the term " dystrophy " into the nomenclature to describe abnormal epithelial proliferation . Since that time , there have been various interpretation of the malignant potential for the individual case of " vulvar dystrophy " .

In 1976 , the International Society for the Study of Vulvar Disease had deleted the following terms : lichen sclerosus et atrophicus , leukoplakia , neurodermatitis , leukeratosis , Bowen's disease , erythroplasia of Queyrat ,

carcinoma simplex , leukoplakic vulvitis , and kraurosis vulvae . To replace these terms , the following terms had been adopted : vulvar dystrophies , squamous cell carcinoma in situ , and Paget's disease of the vulva .

ANATOMY AND HISTOLOGY OF THE VULVA

The vulva is an ill-defined area which in gynaecological practice comprises the whole of the external genitalia and conveniently includes the perineum. It is therefore , bounded anteriorly by the mons veneris , laterally by the labia majora and posteriorly by the perineum. The labia majora pass from the mons veneris to end posteriorly in the skin over the perineal body. They consist of folds of skin which enclose a variable amount of fat and are best developed in the child-bearing period of life. In children before the age of puberty , and in postmenopausal women the amount of subcutaneous fat in the labia majora is relatively small and cleft between the labia is therefore conspicuous. At puberty the pudendal hair appears on the mons veneris , on the outer surface of the labia majora and in some cases on the skin of the perineum as well. The inner surfaces of the labia majora are hairless and the skin of this situation is softer , moister and pinker than the outer surfaces .

The labia majora are covered with squamous epithelium and contain sebaceous glands , sweat glands called

apocrine glands which produce a characteristic aroma and from which the rare tumour of hidradenoma of the vulva is probably derived. The presence of all these structures in the labia majora renders them liable to the common skin infections , folliculitis , boil , and sebaceous cysts (Howkins and Baurne , 1978) .

Histological variations of the vulvar skin and its significance :

Structural variations of the vulvar stratum corneum could be classified into five categories : orthokeratosis , hyperkeratosis , parakeratosis , dyskeratosis and tumour penetration. Orthokeratosis , hyperkeratosis and parakeratosis were present in the normal vulvae as well as in benign conditions ; they were characterized cytologically by anucleated horny squames or by parakeratotic cells. Dyskeratosis usually indicated precancerous or malignant conditions but was also observed, although in mild form only , in certain benign lesions , e.g. , acute inflammation and condyloma acuminatum. Nevertheless , evidence of dyskeratotic cells in vulvar smears should cause concern because vulvar cancer frequently is covered by a continuons horny (dyskeratotic)

layer. Only half of the malignant vulvar lesions showed tumour penetration through this superficial layer , with subsequent exfoliation of tumour cells. It is well known that parakeratosis indicates a proliferating tendency of the epidermis and occurs in vulvar changes associated with increased cellular turnover (psoriasis , eczema , inflammation , dysplasia , carcinoma , etc). It should be noted that parakeratosis indicates nuclear uniformity , while dyskeratosis indicates nuclear polymorphism (Nauth and Schilke , 1981) .