FOX-FORDYCE DISEASE WITH HIDRADENITIS SUPPURATIVA*

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Poral closure is a feature of both Fox-Fordyce disease and hidradenitis suppurativa. Shelley (1, 2) has demonstrated histologically the poral closure phenomenon in both diseases. Sulzberger† has stated that there is a relationship between Fox-Fordyce disease and hidradenitis suppurativa, with both having obstruction of the follicle. It might be logical to suspect that the two diseases would be found together with considerable frequency; however, the English literature has been surveyed and hidradenitis suppurativa as a complication of Fox-Fordyce was mentioned in only one report (3). We are reporting three instances in which Fox-Fordyce disease and hidradenitis suppurativa occurred together.

Fox-Fordyce disease is a rare, itchy disorder of unknown etiology, affecting primarily women (4) and characterized by a persistent eruption of small, discrete, dry papules located symmetrically in the axillary, areolar, pubic, and sternal regions. The two original cases of this rare, papular disease involving the axillary region were described by Fox and Fordyce (5) in 1902, with one case occurring in a female and one in a male. Fordyce's (6) early impression was that this process was a variety of neurodermatitis, probably toxic in origin, and the clinical manifestations were secondary to scratching. After Schiefferdecker's (1, 7) monumental treatise on sweat glands in 1922, many accepted that Fox-Fordyce disease is a functional derangement of the large apocrine sweat glands based on some endocrine disorder. Most writings on this disease have been case reports (8–16), hypothesis as to etiology (17), interesting associated conditions (18, 19) and histochemical and histopathologic studies (20, 21). Attention at the present time seems to be focused on pathogenesis, with speculation as to whether the primary pathology is an obstruction of the apocrine ducts or a change in the apocrine glandular activity with secondary factors contributing to the total pathological picture.

Hidradenitis suppurativa is a deeply seated acneform or furuncular inflammation of the apocrine glands described in 1864 by Verneuil. Sutton (22) believes that two diseases manifest abscesses of the apocrine sweat glands; apocrine acne and apocrine furunculosis. He says the apocrine acne is not primarily parasitic, but bears marked resemblance to acne conglobata, some cases of acne keloidalis, and perifolliculitis abscedens et suffodiens. The apocrine furunculosis may be a primary or secondary bacterial adenitis. Ormsby and Montgomery (23) state that hidradenitis is fundamentally an infection of the apocrine glands, but genetic and hormonal factors may be implicated in its etiology. Hidradenitis was reviewed in 1933 by Lane (24), and in 1939, Brunsting (25) stressed the relation to acne conglobata. Most subsequent writings have been about therapy, relation to acne, and pathogenesis.

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† Sulzberger, Marion B. in a discussion (3).

SUMMARIES OF CASES

Case 1. (Figures No. 1 and No. 2) E. M., a 33 year old colored patient, came to the clinic for treatment of a few, deep, painful, nodular lesions of hidradenitis suppurativa. This developed in November of 1954, shortly after beginning the use of a new deodorant. An incidental finding was the presence of numerous, small, flat-topped, papular lesions in the axillae, about the nipples, and in the vulvar region. She stated that these lesions had been present for 10 to 12 years and that they produced considerable itching. Hair was scanty in the axillae.

The hidradenitis suppurativa responded promptly to therapy. It is of interest that the pruritis associated with the Fox-Fordyce disease was relieved by oral Terramycin; however, various forms of treatment had no objective effect on the papular lesions. These included 150,000 units of Vitamin A per day, antihistamines, Gantrisin, and topical hydrocortisone.

Laboratory work-up, including examination of the blood and urine, was normal. The chest x-ray revealed no pathology.

Pathological examination (Figures No. 3 and No. 4) showed the stratum corneum to be irregular, with alternate areas of normal thickness and hyperkeratosis. In an occasional area there was poral closure with keratinous material plugging the duct. Underlying the keratinous plug there

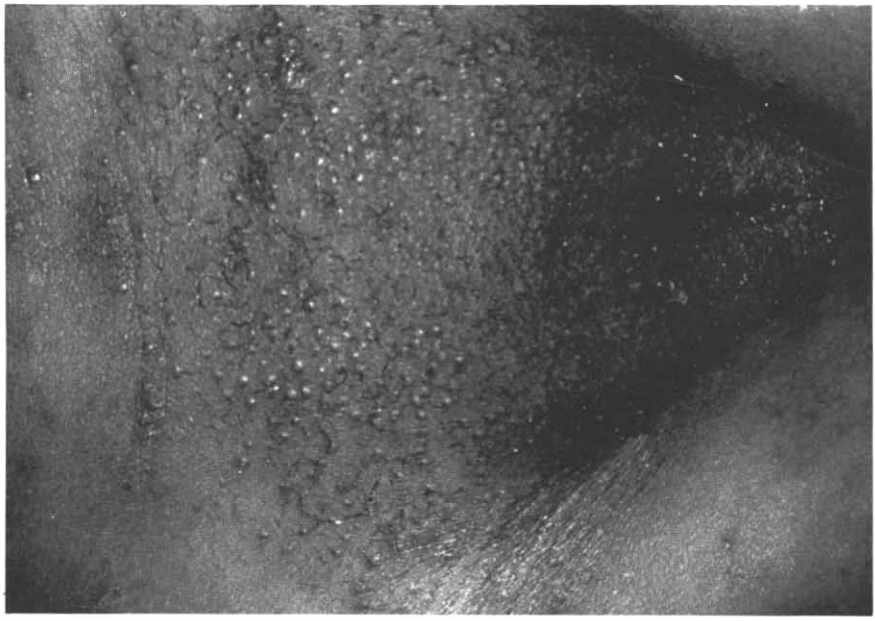

FIG. 2

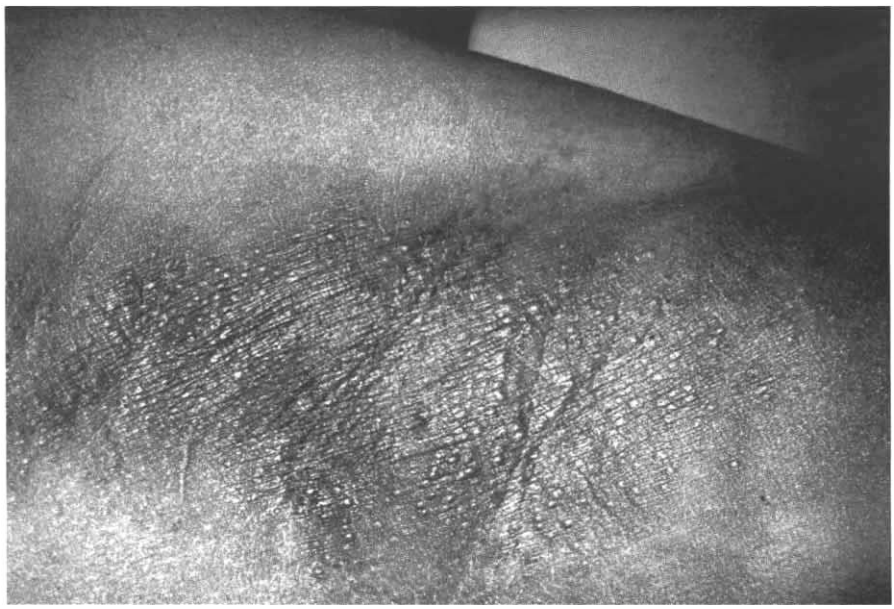

FIG. 1

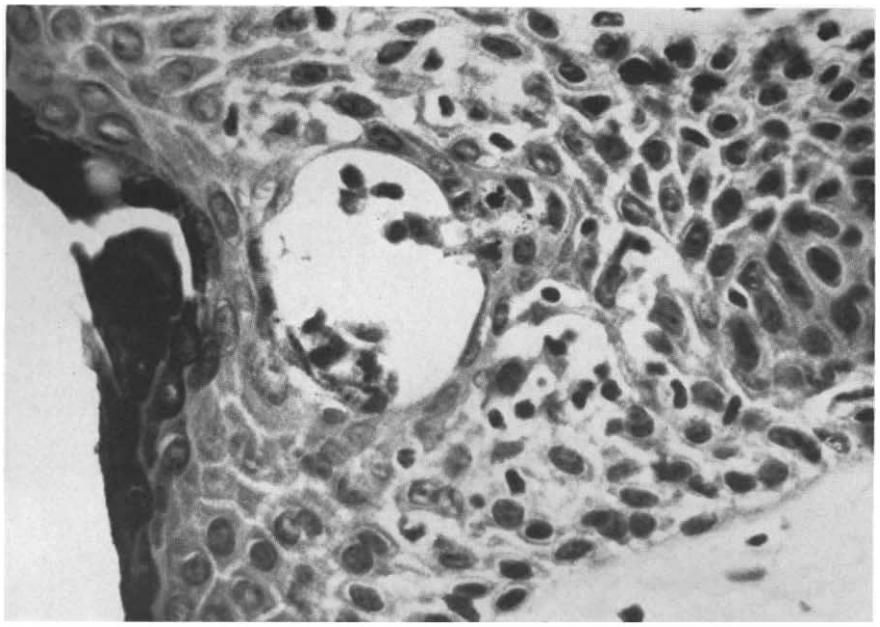

FIG. 4

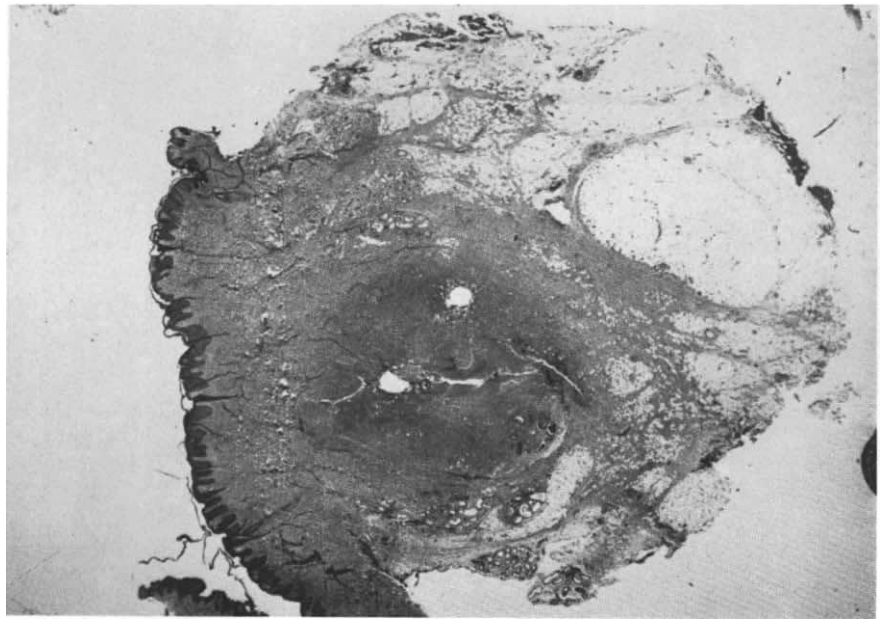

FIG. 3

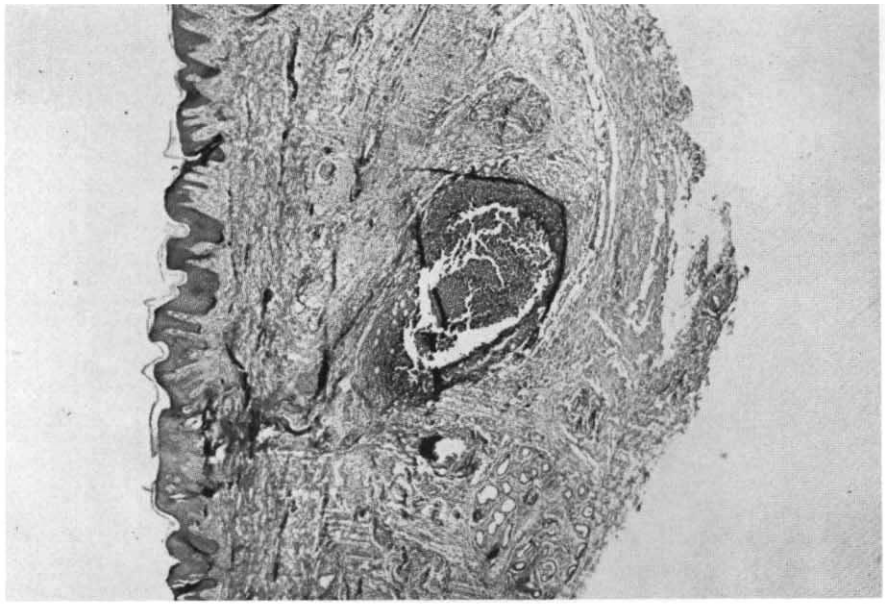

FIG. 6

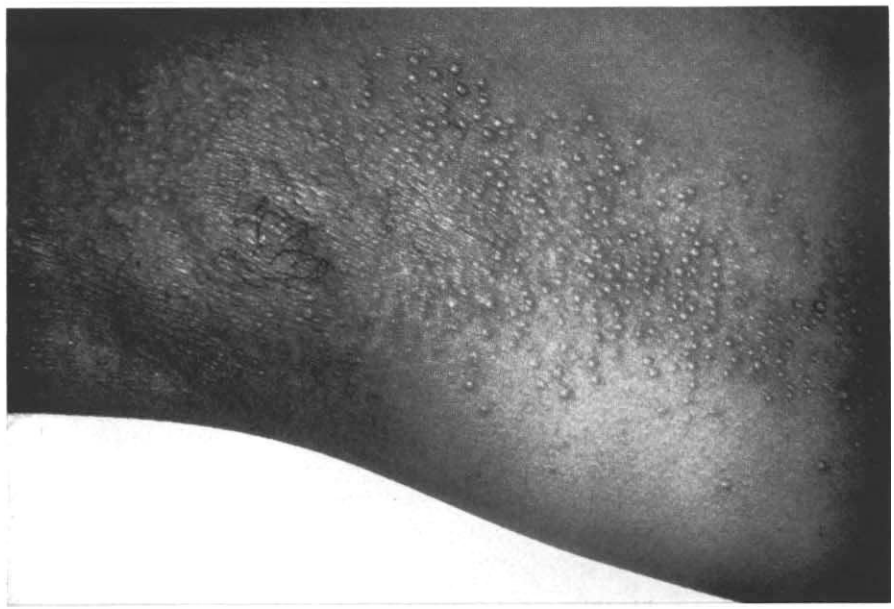

FIG. 5

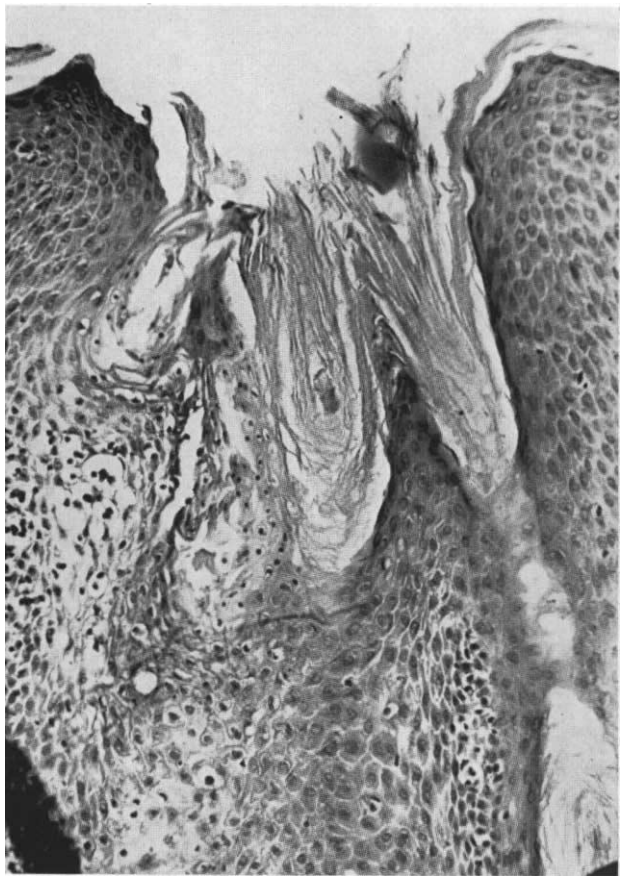

FIG. 7

was dilatation of the duct and surrounding intracellular and intercellular edema. The rete ridges were both elongated and broadened. The superficial dermis was normal. From the mid-dermis to the base of the specimen submitted for examination, there were numerous foci of inflammatory cells. These were primarily located about eccrine sweat glands and apocrine sweat glands. In general, there was more inflammation about the apocrine sweat glands. In some sections there was a large abscess in the deep dermis. Necrotic debris filled the center of the abscess. Connective tissue and appendages were destroyed throughout a large area. Polymorphonuclear leukocytes predominated in the inflammatory infiltrate. Around the periphery of the abscess, lymphocytes and fibrocytes were numerous.

The superficial histopathologic changes were those of Fox-Fordyce disease and manifested clearly the classic sweat retention vesicle in the proximity of the poral outlet. The large abscess in the dermis was non-specific, but characteristic of those found in hidradenitis suppurativa. The central area of necrosis and inflammation was quite large and extensive.

Case 2. (Figure No. 5) I. F. J., a 19 year old colored female, manifested the typical papular lesions of Fox-Fordyce disease with the eruption located in the axillary, areolar, periumbilical, and perineal regions. The disease began at the age of 16 and since onset, had been constant and unchanged. The lesions itched only when she was tense, nervous, or excited, and the pruritus would eventually subside spontaneously. In addition, the patient had periodically developed tender, swollen, subcutaneous nodules in the axillae, breasts, and on the labia. The latter lesions brought the patient to the physician.

On physical examination, the patient had tender, swollen, subcutaneous nodules in the axillae and on the labia underlying areas of Fox-Fordyce disease.

On routine laboratory examination, the urine

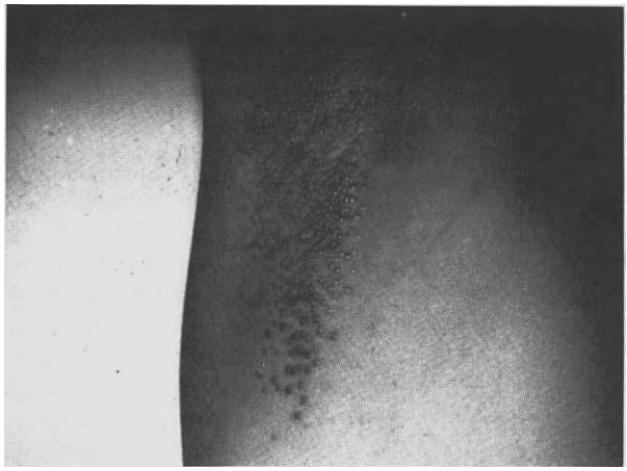

FIG. 8

was normal. The blood was normal except for a leukocytosis of 11,800.

Pathological examination (Figures No. 6 and No. 7) showed that, except for a slight hyperkeratosis, the stratum corneum was normal. The granular cell layer manifested no significant histologic changes. The malpighian layer was acanthotic with elongation and broadening of the rete ridges. In one large, pilosebaceous structure there was a massive keratin plug that produced follicular and poral closure. There was intracellular and intercellular edema about the apocrine sweat ducts. Developing sweat retention vesicles were noted. Inflammatory cells, primarily lymphocytes, were also present. In the mid-dermis there were foci of inflammatory cells, located primarily about small blood vessels and appendages. In the deeper dermis there was a large abscess filled with necrotic debris and polymorphonuclear leukocytes. This abscess was sharply localized at the level of the apocrine and eccrine sweat glands. In the vicinity of the abscess, appendages and connective tissue were destroyed and polymorphonuclear leukocytes were numerous. In adjacent areas, some of the apocrine and eccrine sweat glands were completely normal. Others were surrounded by a few inflammatory cells which were mainly mononuclear with lymphocytes predominating. A few plasma cells were also noted. The deepest portions of the dermis were normal except for the presence of a few inflammatory cells.

The superficial histologic changes were those of acanthosis with keratotic plugging of pilosebace ous openings. Sweat retention vesicles were found in these areas. These changes are characteristic of Fox-Fordyce disease. The sharply localized abscess in the dermis confirmed the clinical diagnosis of hidradenitis suppurativa. This abscess was confined to the level of the sweat gland coil.

Case 3. (Figure No. 8) This 22 year old colored woman was diagnosed as having Fox-Fordyce disease in February 1956. For the previous two months she had noted pruritus of the axillae, sternal areas, and perineal area. This pruritus was most pronounced in hot weather. Since October 1955, the patient had also complained of recurrent episodes of tender nodules in the axillae with suppuration and drainage. She also gave a history of having tender nodules on the external genitalia on one occasion.

The past medical history revealed two items of possible significance. In September of 1955, the patient was diagnosed as having carbuncles in the auditory canals and an associated external otitis media. This was accompanied by pruritus and excoriation of the external auditory canal. In December 1955, the patient was seen in the Gynecology Clinic for the sudden onset of dyspareunia. There was pain during, but no pain after intercourse. On pelvic examination there were definite, freely movable nodules palpable in the vaginal wall. This pelvic disease was not followed as the patient did not return to the Gynecology Clinic.

On physical examination, the patient presented pinhead-sized, papular lesions of Fox-Fordyce in the axillae, surrounding the areola, and over the pubic region, together with deeper nodules of hidradenitis in the axillae. There was axillary alopecia bilaterally.

Laboratory examination revealed a leukocytosis of 12,000. The urine was normal.

The histopathology (Figure No. 9) showed a minimal hyperkeratosis with slight concomitant increase in the thickness of the granular cell

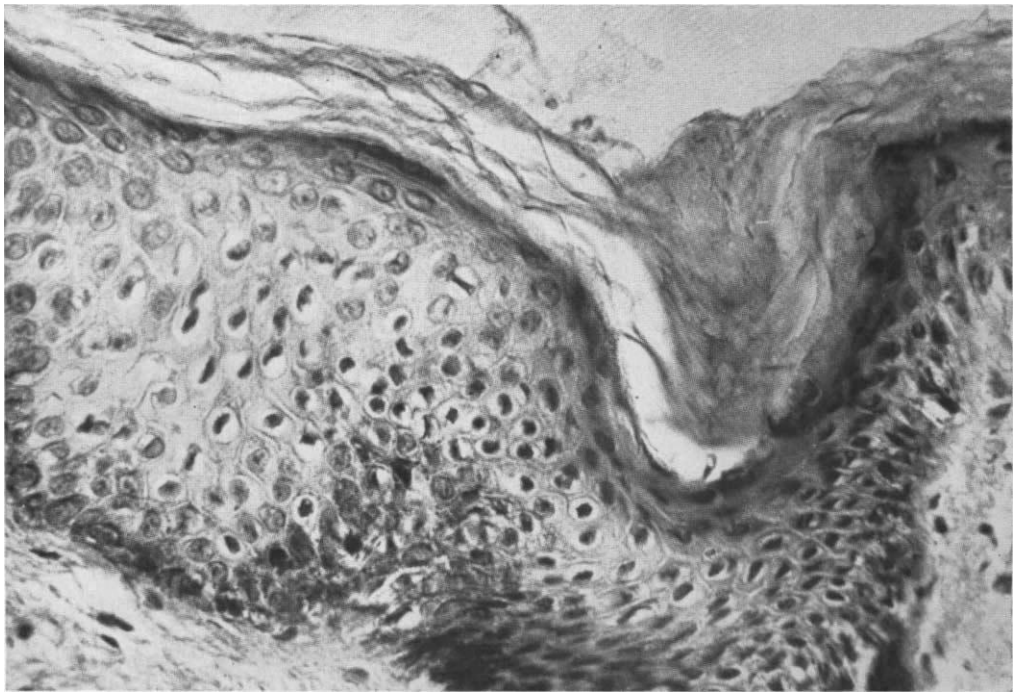

FIG. 9

layer. The malpighian layer manifested some elongation and broadening of the rete ridges. In an occasional area poral hyperkeratosis was noted, and underlying this there was some intracellular and intercellular edema periductally in the epidermis. Inflammatory changes were absent in the sections examined. The biopsy specimen did not extend deep enough for evaluation of sweat glands.

The above described histopathologic changes are nonspecific and not diagnostic of Fox-Fordyce disease. The intracellular and intercellular edema in the vicinity of the epidermal sweat ducts, however, is suggestive of and compatible with Fox-Fordyce disease. (Note: This patient manifested classic hidradenitis suppurativa with indurated subcutaneous nodules and draining sinuses. In this case a biopsy specimen was not taken from the area of hidradenitis suppurativa.)

COMMENT

In hidradenitis suppurativa there is acute purulent inflammation with cystic dilatation of the deep part of the gland with destruction of the epithelial lining and micrococci in the pus. The infection may spread throughout the subcutaneous tissue. Destruction of the sweat glands may occur with recurrence and chronicity. In less severe forms of hidradenitis suppurativa, it might be preferable to employ the term "apocrinitis" as used in the book "Dermatology" by Pillsbury *et al.* (26). Two of our cases were mild and could be considered to be apocrinitis, but one was severe with the scarring and chronicity of classic hidradenitis suppurativa.

In Fox-Fordyce disease, the pathology of previously recorded cases has varied as to whether or not there was an inflammatory reaction present around and in the apocrine glands. Fordyce's (6) histologic report was: (1) hyperkeratosis of the poral orifices; (2) acanthosis, with altered sweat ducts and hair follicles; edema and minute vesicles contiguous to the duct; (3) mechanical dilatation of the sweat glands with degeneration of the epithelial lining; and (4) inflammation of a chronic character in the corium. Knowles (27), in his cases of Fox-Fordyce disease, describes a cellular infiltration, dilatation, and degeneration of the wall of the sweat gland coil. Pick (28) included an inflammatory focus in the region of the glands as part of the pathologic picture in Fox-Fordyce disease. Roxburgh's (29) case had normal apocrine glands with inflammation about the hair follicle. Shelley (3) considers the disease an apocrine miliaria with a distinct pathology. He

does not include the inflammatory reaction around the glands as part of the diagnostic pathologic picture of Fox-Fordyce which, he says, "is characterized by apocrine anhydrosis, pore closure, and sweat retention vesicles in the epidermis". He further says, "Many apocrine glands do become large, cystic structures, but this is asymptomatic and is a common finding in normal skin. It is only when intraepidermal rupture occurs that Fox-Fordyce changes develop". Several cases in the literature on Fox-Fordyce disease describe retention cysts histologically, but few refer to the occasional inflammatory swelling as was mentioned in the axilla of the patient of Zakon and Goldberg (30). This was a clinical description, but it might suggest that there was an association of hidradenitis suppurativa with the Fox-Fordyce disease in their patient. Other reports have not associated these two conditions except as both being diseases of apocrine glands and perhaps responsive to similar types of therapy (31).

Abnormalities of the axillary and pubic hair are commonly associated with Fox-Fordyce disease and hidradenitis suppurativa. Cornbleet (32) says that this "is no wonder" since most apocrine ducts empty through the follicle and it would seem logical that diseases involving the glands would affect the adjacent hair growth also. He says that the hair at affected sites becomes stunted or disappears in Fox-Fordyce disease and that patches of alopecia may occur over the surface of an abscess of hidradenitis. The papules of Fox-Fordyce disease have been described as being most numerous in the areas where hair is sparse (33, 34). One wonders what role the deficiency of hair (congenital or acquired alopecia) might play in the development or perpetuation of Fox Fordyce disease, since the hair normally acts as a stylette in keeping the pore open (35). This may be analogous to the hypothesis that absence of an effective hair in the follicular orifice precipitates comedo formation (36). Shelley and Cahn (2) had to pluck the hair in producing hidradenitis suppurativa experimentally.

It is interesting that Case 3 had pathologic processes occurring in the axillae, ears, perineum, and breasts; suggesting that all of these conditions were related to apocrine gland abnormality. Perhaps even the nodules in the vaginal wall were aberrant apocrine glands.

It is possible that these two apocrine gland diseases may have a similar pathogenesis. The anatomic location of the obstruction or the extent of secondary infection might determine whether Fox-Fordyce or hidradenitis suppurativa, or both diseases develop. This might be somewhat analogous to miliaria rubra and miliaria profunda in which the clinical picture is determined by the location of the obstruction (37). Shelley has suggested the name "apocrine miliaria" for Fox-Fordyce disease (3).

SUMMARY

Three cases with Fox-Fordyce disease and hidradenitis suppurativa occurring simultaneously in the same patient have been presented. In reviewing the literature, we have found only one similar case mentioned. It was emphasized that poral closure is of prime importance in the pathogenesis of both Fox-Fordyce disease and hidradenitis suppurativa. The anatomic location of the obstruction or the presence of secondary infection may determine whether Fox-Fordyce disease, hidradenitis suppurativa, or both diseases develop.

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