Fox-Fordyce disease: report of two cases with perifollicular xanthomatosis on histological image*

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Abstract: Fox-Fordyce disease is a relatively infrequent pathology of the apocrine glands that affects almost exclusively young women. The disease is characterized by the presence of pruritic follicular papules mainly in the armpits that respond poorly to treatment and severely affect the patient's quality of life. We report two cases with clinical diagnosis and histopathological confirmation, presenting perifollicular xanthomatosis on histological examination, recently described as a distinctive, consistent, and specific feature of this disease.

Keywords: Apocrine glands; Fox-Fordyce disease; Miliaria

INTRODUCTION

Fox-Fordyce disease (FFD), also known as apocrine miliaria or chronic pruritic papular eruption of the pubis and armpits, affects areas where apocrine glands are found predominantly, such as the pubic, axillary, and anogenital regions.¹,² The pathogenesis remains unknown, and the disease affects primarily young women.³ Commonly used treatments are poorly or partially effective, as the lesions frequently recur and the symptoms persist.

We present two cases with both clinical and histopathological diagnosis of perifollicular xanthomatosis.

CASE REPORTS

CASE 1

A 33-year-old female patient, resident of Mexico City, previously healthy, reported a one-month history of multiple mildly pruritic papules in both armpits. Patient reported hyperhidrosis and no prior treatment.

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CASE 2
A 24-year-old female patient, resident of León, Guanajuato, Mexico, presented intensely pruritic papules in both armpits and the genital area with two years’ evolution. Patient had received pri-

![Figure 1: Fox-Fordyce Disease. Case 1. Yellowish-brown punctate papules with follicular distribution coalescing in plaques and affecting both armpits](image)

![Figure 2: Fox-Fordyce Disease. A. Histological section with infundibular dilation and corneal plug (Hematoxylin & eosi

![Figure 3: Fox-Fordyce Disease. Immunohistochemistry. A - CD68 intensely positive in peripheral xanthomatous histiocytes. B - Negative membrane epithelial antigen C - Negative carcinoembryonic antigen in histiocytes](image)

or treatment with antihistamines and emollients with no improve-
ment. Patient reported that other females in her family had present-
ed this skin condition in the armpits, although less severe.

Patient had a 12-year history of comedogenic acne on the face and trunk as well as menstrual alterations with amenorrhea of up to 2 months. Therefore, pelvic ultrasound was ordered, showing polycystic ovaries.

Physical examination showed a disseminated dermatologi-
cal condition affecting the axillae and genitalia, in hairy areas, char-
acterized by skin-colored punctate papules 1 to 2 mm in diameter with follicular distribution and some crusts (Figure 4).

Histopathology showed dilated follicular infundibula with hyperkeratosis, as well as xanthomatous histiocytes with perifollic-
lar distribution and discrete inflammatory lymphocytic infiltrate. Intrafollicular mucin deposits were also observed (Figure 5).

FFD was diagnosed, and combined oral contraceptives (cy-
proterone with ethinylestradiol) and topical hydrocortisone were prescribed, with partial improvement of lesions and pruritus.

DISCUSSION
Fox-Fordyce disease was first described in 1902 by Amer-
ican authors George Henry Fox and John Addison Fordyce.1,2 The pathogenesis of this condition remains unknown, although pro-
posed theories suggest that hormonal factors, hair removal, and inheritance may be involved in the apocrine obstruction, sweat re-
tention, and inflammation.3,4

This disease entity presents characteristic clinical data, af-
fecting areas of the body where apocrine glands are found, such as armpits, pubis, and the anogenital region. However, less frequent locations on the thorax, areolas, abdomen, and legs have been de-
scribed.5 The disease occurs mainly in women 15 to 35 years of age and usually remits in menopause.6 In the current cases, we report typical lesions affecting the axillary region and genitals, with no les-
ions on other parts of the body surface. Both patients were child-
bearing-age women.

 Clinically, FFD is characterized by the presence of multiple skin-colored follicular papules, slightly yellowish or brown, dome-
shaped, with a smooth surface, which may be accompanied by mild to moderate pruritus or even be asymptomatic. Exacerbating symp-
toms include heat, moisture, physical activity, friction with cloth-
ing, and excessive sweating.7 Laser hair removal and intense pulsed light have also been described as triggers.8,9 The lesions tend to dis-
play chronic evolution, described as lasting weeks to years.⁷
Differential diagnoses include Graham-Little-Piccardi-Las
seur syndrome, trichostasis spinulosa, Darier’s disease, syringo-
mas, lichen nitidus, lichen amyloid, and papular mucinosis.⁹,¹⁰
Definitive diagnosis is made by histopathological exam-
ination in which nonspecific findings such as intrafollicular corneal
plug, hyperkeratosis, spongiosis, retention vesicles, glandular dil-
ation with mucin deposits, and perifollicular lymphohistiocytic in-
flammatory infiltrate can be observed.¹¹,¹² The presence of infundib-
ular dyskeratotic cells, vacuolar changes, and parakeratosis similar
to cornoid lamella have also been described.¹³ However, Borman et
al. recently described the presence of foamy or xanthomatous his-
tiocytes (perifollicular xanthomatosis) as a distinctive, consistent,
and more specific feature of this pathology.¹⁴ This was corroborated
in the histopathology of our cases, as both presented the previously
described findings and xanthomatous histiocytes as well as the
presence of intrafollicular mucin.

Treatment response tends to be limited or partial; the lesions
and symptoms may recur or persist. First-line treatments include
topical and oral retinoids, benzoyl peroxide, topical calcineurin in-
hibitors, clindamycin, intralesional or topical steroids, and oral con-
traceptives, the latter reported with complete resolution of lesions.¹⁴
In our first case, the patient was treated with topical clindamycin,
achieving partial improvement of the lesions and symptoms. In the
second case, the patient was treated with combined oral contracep-
tives and topical hydrocortisone, achieving partial improvement of
lesions and pruritus.
Alternative therapies as second-line treatment or in severe
cases, such as botulinum toxin, phototherapy, electrocoagulation,
copper vapor and CO₂ laser, liposuction, curettage, and microwave
have been described with favorable results.¹⁴,¹⁵
We have reported two cases here, both with perifollicular
xanthomatosis on histology, supporting the position that this is the
most specific and distinctive feature of this relatively rare disease.⁷
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AUTHORS CONTRIBUTION

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