Fox-Fordyce disease: response to adapalene 0.1% *

Doença de Fox-Fordyce: resposta ao adapaleno 0,1%

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Abstract: The Fox-Fordyce disease is a rare inflammatory dermatosis that affects mainly young women and is characterized by multiple follicular papules, skin color or brownish, very itchy, localized in areas rich in apocrine glands. Histopathology shows focal spongiosis of the upper infundibulum with fibrosis and perifollicular lymphohistiocytic infiltrate. The diagnosis is based on clinical and histopathological examination. Many treatment options have been described; however none of them is excellent. We chose the topic adapalene 0.1% and a satisfactory improvement of the signs and symptoms of the disease was observed.
Keywords: Apocrine glands; Fox-Fordyce disease; Retinoids; Treatment outcome

Resumo: A doença de Fox-Fordyce é uma dermatose inflamatória rara que afeta predominantemente mulheres jovens e caracteriza-se por múltiplas pápulas foliculares cor da pele ou acastanhadas, muito pruriginosas, localizadas nas áreas ricas em glândulas apócrinas. A histopatologia demonstra espongiose focal da porção superior do infundíbulo, com fibrose perifolicular e infiltrado linfohistiocítico. O diagnóstico é baseado na clínica e no exame histopatológico. Muitas opções de tratamento já foram descritas, porém nenhuma delas é excelente. Optamos pelo adapaleno 0,1% tópico e foi observada melhora satisfatória dos sinais e sintomas da doença.
Palavras-chave: Doença de Fox-Fordyce; Glândulas apócrinas; Resultado de tratamento; Retinóides

Fox-Fordyce disease, also known as apocrine miliria, is a rare inflammatory dermatosis, characterized by multiple follicular papules, skin color or brownish, located in areas rich in apocrine glands, like armpits, periareolar areas, and pubic area, accompanied by itch. [1,2,3,4] It is more common in women between 13 and 35 years. [1] The histopathological findings are variable, and include infundibular plug, hyperkeratosis, acanthosis, spongiosis and unspecified inflammatory infiltrate. [2,5]

Here we describe the case of an 11 year old girl with cutaneous lesions on the armpits and pubic area for 2 years, which appeared just after menarche at 9 years of age. At examination we observed small normochromic papules measuring up to 2 mm, predominantly follicular, on the armpits and pubic area, where a rarefaction of hairs was noted.

Incision biopsy of the right armpit showed hypekeratosis, parakeratosis and irregular acanthosis over the area of the apocrine gland exit, as well as spongiosis along the epidermis also involving the hair follicle, which still showed neutrophils exocytosis.

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The dermis had a mild, superficial, perivascular and interstitial lymphocytic infiltrate. The histopathological exam was compatible with Fox-Fordyce Disease (Figure 1). [2,5]

No abnormalities were found at the laboratorial exams. Although the sexual hormones were not checked, the patient did not have any clinical sign of hormonal dysfunction, like menstrual irregularity, obesity, hirsutism or acne.

We chose the topical treatment with 0.1% adapalene gel. After 2 months there was mild decrease of the papules, growth of hairs on the armpits and moderate improvement of the itch (Figure 2). Erythema and burning sensation were evidenced after 15 days of using the retinoid on the armpits and the patient was instructed to apply the medication every other night, with resolution of the side effects.

Fox-Fordyce disease is a chronic disorder of the apocrine glands which affects mostly young women. There are few reports in prepubescent patients, although, according to more recent literature, the disease is little diagnosed in this age group. [6] In the case reported, the first signs and symptoms of the disease appeared just after the first menstruation. The typical lesions are firm, skin colored or yellowish papules, restricted to areas where there are apocrine glands like armpits, pubic area, areola and, more rarely, periumbilical and pre-sternal areas. [1,3] The face can also be involved in case of ectopic apocrine glands.

The affected areas show reduction of sweating, although the disease might be associated with hyperidrosis, as well as rarefaction or even absence of hairs. Itch is an invariable symptom, which can be aggravated by emotional factors, heat, and during the menstrual period. [1] Our patient had accentuated reduction of hairs on the armpits and worsening of the itch with warm weather.

The etiology remains unknown. It is postulated that a hormonal disturbance is involved, although no laboratorial abnormality has been detected. So far no genetic factor has been blamed either, despite the existence of familial cases. [7] Reports in pre-pubescent girls and in male patients show that the hormonal factor may not be important in all cases. [6,7,8] The patient denied similar cases in the family. Besides, her laboratorial exams were normal and there were no clinical signs of hormonal alterations. The physiopathology consists on the obstruction of the apocrine gland duct by a keratin plug in its insertion on the hair follicle wall, which causes secretion retention with consequent rupture of the glandular structure and secondary inflammation of the dermis. The extravasation of the glandular content can be the cause of the itch. [1]

The histopathological exam can show spongiosis and spongiotic vesiculation of the follicular infundibulum adjacent to the exit of the apocrine gland duct. In some cases a keratin plug can be seen above this area. An associated mild inflammatory infiltrate is described, which can be composed of chronic inflammatory cells and neutrophils. The histopathological findings of the present case were compatible with the literature, confirming the diagnosis of Fox-Fordyce

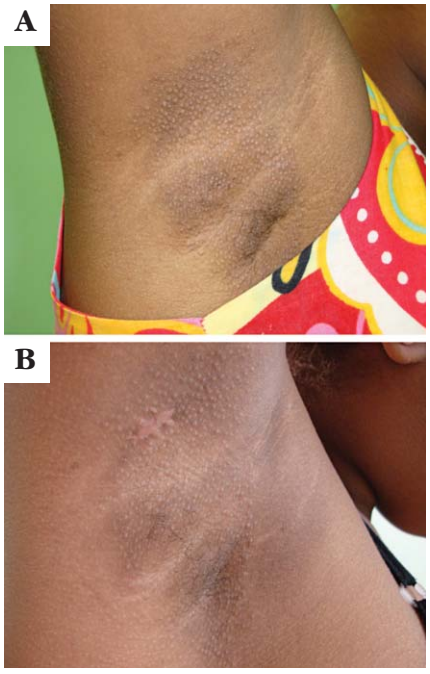

Figure 1: A. Grouped follicular papules on the armpit, with rarefaction of the hair; **B.** Decrease of the papules and hair growth after topical 0,1% adapaleno gel

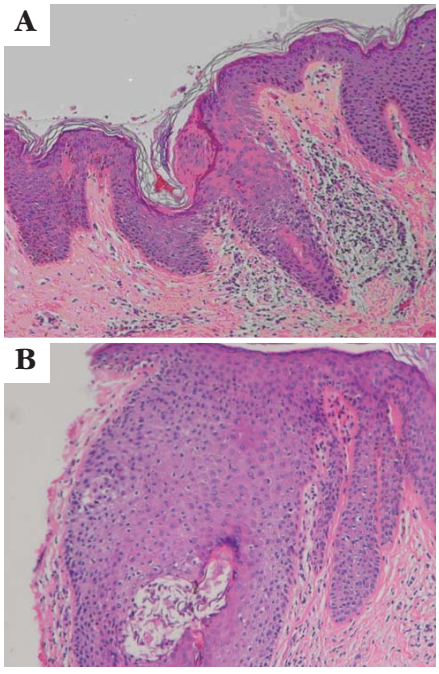

Figure 2: A. Hyperkeratosis, parakeratosis and acanthosis over the apocrine gland duct. **B.** Spongiosis and neutrophilic inflammatory infiltrate in the interior of the hair follicle

Disease. Böer described yet additional findings like vacuolar alteration on the dermal-epidermal junction of the infundibulum, disperse dyskeratotic cells on the infundibulum and parakeratosis similar to cornoid lamella with a ortokeratotic plug filling the dilated infundibulum. [5] The transversal cuts are more efficient than the conventional ones, allowing for the visualization of a higher number of follicles. [2]

On the case reported, other hypothesis were considered, like keratosis pilaris and lichen planopilaris, which were refuted by the histopathological exam. Other differential diagnoses are amyloidosis lichenoides, lichen nitidus, eruptive syringoma, contact dermatitis, infectious folliculitis and scabies.

Fox-Fordyce Disease is chronic and might have partial or complete remission after menopause, with the use of contraceptives and during pregnancy. [6] Complications are rare, although there are reports of progression to hidradenitis. [1]

Various treatments were suggested, including the administration of estrogens via oral contraceptives, topical, intralesional or systemic corticosteroids, topical and oral retinoid, topical clindamicin, pimecrolimus, phototherapy and surgical treatments like electro coagulation and curettage with liposuction. [1,3,4,6,8,9,10] There is no consensus on the literature as to the best alternative and all of them have questionable efficacy. On the reported case we preferred not to use oral contraceptives due to the age of the patient. The use of topical corticosteroid was deferred as it would be applied to a fold area and thin skin, which could cause atrophy and stretch marks. As none of the treatments is totally efficient, we opted for the topical 0,1% adapalene gel due to its smaller irritative potential in relation to the tretinoin. [11] Decrease of the papules, improvement of the itch and hair growth were observed. We know of only one other case where the 0,1% adapalene was used for this dermatosis, with partial improvement after 3 weeks of therapy. [6] The patient and her guardian were satisfied with the therapeutic result. ❑

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