WHAT'S NEW IN THE MANAGEMENT OF FOX-FORDYCE DISEASE

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Summary

Fox-Fordyce disease is known to be a chronic and uncommon skin disease that affects regions with a high density of apocrine glands. This disease affects women between 13 and 35 years. It may be considered that hormonal imbalance play a key role in the pathogenesis, but the exact cause is still unclear.[1] Other cause may be a history of trauma caused by laser hair removal may be a trigger of this disease. Pruritus can be present and it may be caused by the extravasion of glandular content. Due to the severe itch, the patient may develop infection or hiperpigmentation in the affected regions. The clinical features are monomorphic, dome-shaped, skin-colored, follicular papules that invole the axillary, pubic, perineal and areolar areas, pruritus and hair loss in the affected regions. Histopathology is in many cases non-specific.[2] Terapeutic options are varied and may include topical steroids, topical retinoids, topical clindamycin, topical calcineurin inhibitors, oral retinoids, oral contraceptives, intradermal infiltration of botulinum toxin or triam-cinolone, excision, electrocoagulation and laser.

Key words: *Fox-Fordyce disease, papules, electro-coagulation.*

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Introduction

Fox-Fordyce disease is deffined as a chronic skin disease that affects the apocrine glands. It affects women between 13 and 35 years and it is considered that hormonal imbalance play a key role in the pathogenesis, but the exact cause is still unclear.[1] Pruritus may be caused by the extravasion of glandular content. The exact pathophysiological mechanism has not been discovered. As clinical manifestations present monomorphic, dome-shaped, skin-colored, follicular papules that invole the axillary, pubic, perineal and areolar areas. Histopathology is frequent non-specific.[2] Terapeutic options include topical steroids, topical retinoids, topical clindamycin, topical calcineurin inhibitors, oral retinoids, oral contraceptives, intradermal botulinum toxin or triamcinolone, excision, electrocoagulation and laser.

Clinical cases

Our aim is to create a review of the literature about the Fox-Fordyce disease, starting with two cases of this rare dermatologic condition treated in our clinic. As clinical presentation both patients are young women, who developed monomorphic, dome-shaped, skin-colored, follicular papules that invole the axillary region, the surrounding skin is spared. Only one of the patients associates pruritus. General evaluation

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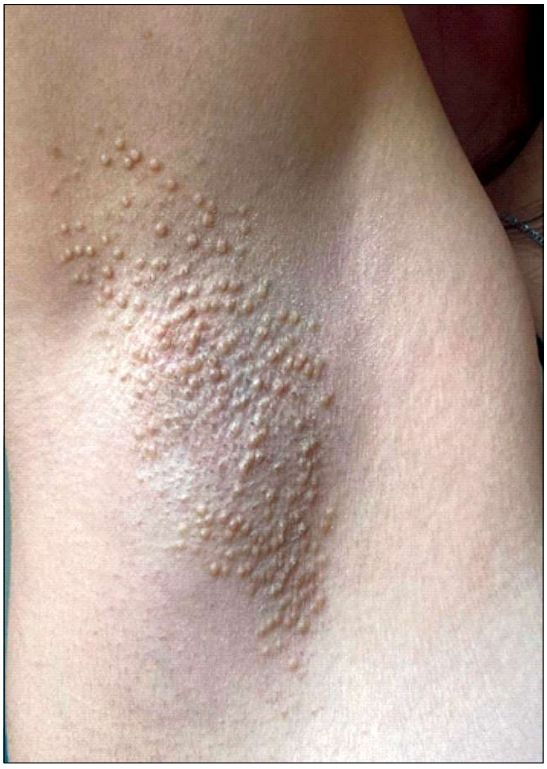

Figure 1. Case 1

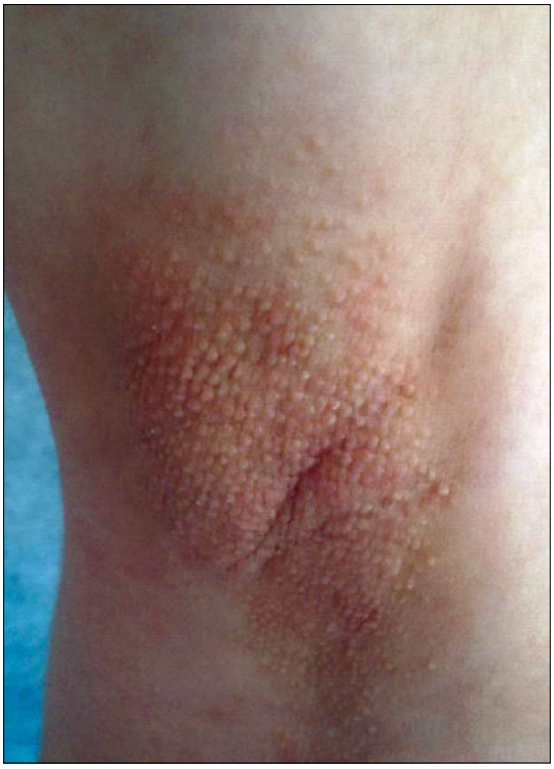

Figure 2. Case 2

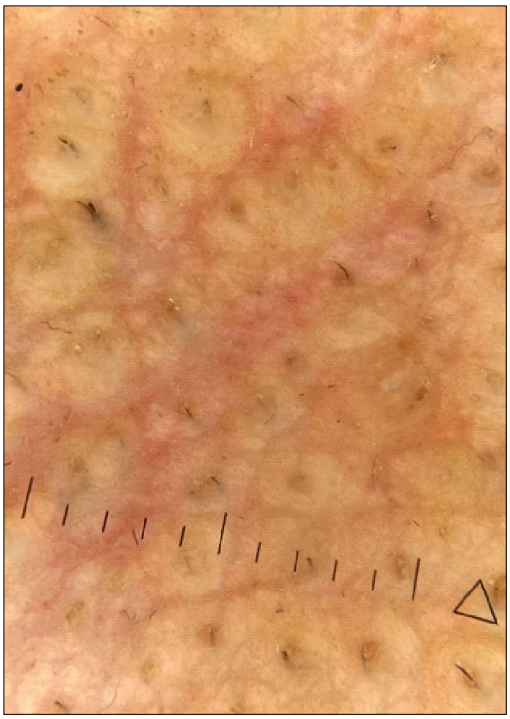

Figure 3. Dermoscopic evaluation of Fox-Fordyce disease

showed no other changes, no lymphadenopathy has been revealed. Dermoscopy has an important role to facilitate the diagnosis of Fox-Fordyce disease. This method using the polarized mode will show light to dark brown structureless areas, without any specific pigmentary network, as well as folliculocentricity and central hyperkeratotic plugs, traumatised terminal hair and blackheads. Using the non-polarized mode, it can be noticed the loss of dermatoglyphics of the skin surface.[2] The examination under Wood's lamp won't show any fluorescence.[3]

In order to aquire a final diagnosis, it is recommended to perform a histopathologic examination. The result will show the existence of dilated follicular infundibulum with hyperkeratosis, a central keratin plug and a lymphocytic inflammatory infiltrate around the apocrine duct. Less frequent histopathological findings may be: spongiosis, dyskeratosis of the infundibular epithelium, vacuolar degeneration of the dermo-epidermal junction, periadnexial lymphocytic inflammatory infiltrate. A characteristic histopathologic feauture has been discovered to be the presence of parakeratosis in the infundibular epithelium in the form of cornoid lamellae. A key histological finding may be the perifollicular xantomathosis with the presence of the foamy cells. In some cases the histopathological result will be non-specific, and also very variated. Despite this variety the clinical findings are always the same.

The biopsy results taken from one of the patients showed a skin biopsy covered by hyperkeratotic epidermis with dermal fibrosis, discrete chronic inflammatory infiltrate and polypoid formation lined by hyperkeratotic epithelium, interpapillary bridges, embedded squamous turbinates, fibrovascular chorion, laxer parcel. The other patient's histopathological result showed a skin biopsy covered by a keratotic epidermis, with dermal fibrosis, without the presence of cutaneous appendages. discrete chronic inflammatory perivascular inflammatory infiltrate. Both of this result were non-specific and variable to this rare skin condition called Fox- Fordyce disease.

For our patients we chose the electrocoagulation procedure because the onset was a few years ago, they had little inflamatory lessions and one of them had mild pruritus. The outcome was the one expected with the disaperance of the lessions at 3 weeks postprocedure. The side effects were minimal with a little swelling and scarring but they were satisfied with the aestetic result.

Discussions

Fox-Fordyce disease is known to be difficult to treat and the different methods of treatment are not yet been widely studied, because the rarity of the disease. Though there is no definitive cure for Fox-Fordyce disease, there are several treatment options available to manage the symptoms.

First of all, the simple suportive methods include using cool compresses to the affected areas can help alleviate itchiness and discomfort, wearing loose-fitting clothing and breathable fabrics can reduce friction and sweat accumulation.

Topical and intralesional steroids are first-line treatment options in this rare skin condition. Using them on long term can lead to the risk of cutaneous atrophy and striae. In early stages of the disease intralesional triamcinolone 5 mg/ml may have benefit.[6]

Calcineurin inhibitors like tacrolimus an pimecrolimus are also used as therapeutic options. In literature there are many articles that shown beneficial effects of pimecrolimus in Fox-Fordyce disease, but there are less reports about the use of tacrolimus. One article showed positive results using tacrolimus pomade 0,1% on patients twice a day. It is known to have strong anti-inflammatory effect and less side effects than the topical steroids. The results showed that tacrolimus was effective on the patient with an early onset and more inflammatory disease with newer lesions, intense pruritus and less keratinization.[6]

Topical clindamycin is an antibiotic used in the treatment of acne vulgaris for the anti-bacterial and anti-inflamatory effects. The efficacy of topical clindamycin use in Fox-Fordyce disease was described in one study and it included patients topical clindamycin 1% lotion twice daily for 8 weeks. It was reported improvement in pruritus and clinical improvement in

majority of the patients. An histological analysis showed a decrease in lymphocytic infiltration following treatment, suggesting anti-inflammatory effects.[22]

Topical retinoids are considered to be another method of treatment for the Fox- Fordyce disease due their effect of reducing the keratinization. Some report cases from the speciality literature showed an benefficial effect using the topical 0,1% adapalene gel with a smaller irritative side effect compared to the tretinoin. It was observed a reduction of the papules, improvement of the itch and hair growth.[15]

The hormonal imbalance may play a key role in the pathogenesis of this disease. Studies showed the efficiency of the oral contraceptives for the young patients. The results were very encouranging with the relief of the symptoms and amelioration of the papules but they did not dissapeear entirely.[25] Another oral treatment proposed is the use of oral retinoids due to their keratolytic effect. The outcome was not the one expected, it was observed only the temporary relief of the symptoms.[26]

Botulinum Toxin-A is used in Dermatology for the treatment of hyperhidrosis and for aestetic purposes. It is effective on sweat reduction, which is a known as a trigger of pruritus in Fox-Fordyce disease. Other effects thet may lead to the antipruritic effect are to stabilize mast cells and inhibit their degranulation. In literature were reported two cases of refractory Fox-Fordyce disease showed successful treatment results with Botulinum Toxin A injections.[10]

Laser therapy, including the fractional CO2 laser type, have been used for recalcitrant lesions which do not respone to medical treatment. The results were remarkable with a clinical response in 3 months. However,using this method for axillary hair removal have been shown to induce Fox-Fordyce disease. [11] An analysis of the laser treatment method was used and the results showed that the laser is considered fairly effective and safe and there were observed minimal complications. The 1550 nm fractionated erbium glass laser is a newer laser based on infiltration of the deep skin layer, where the target sweat glands exist, and will produce thermal injury to the glands. It can be used for the treatment of less severe lesions.[12]

A novel therapeutic option called MiraDry that uses a microwave device that is recommendes for the treatment of primary axillary hyperhidrosis. The apocrine sweat glands are target in addition to hair follicles by actioning using electric heating on the dermal-hypodermal junction. There is reported a case of axillary Fox-Fordyce disease treated with this novel non-invasive microwave technology. The patient developed expected sequelae from the procedure like temporary pain, swelling, and bruising.on the short term Altered sensation in the skin of the axillae may be a long ther effect. Marked improvement was observed after the second treatment including resolution of the pruritus. No evidence of recurrence was remarked at 4 months.[13]

There are a few published articles specifically focused on the use of electrocoagulation for Fox-Fordyce disease. However, some studies and case reports have shown positive outcomes with this treatment method. The articles reveals that the procedure resulted in significant improvement in symptoms, including reduction in pruritus and disappearance of lesions, in the majority of patients.[24] They show thatb this procedure is a safe and effective treatment option for Fox-Fordyce disease with a few side effects like swelling, redness, scarring and hyperpigmentation in the treated area. The use of electrocoagulation has shown promising results in the treatment of Fox-Fordyce disease. We have used this method of treatment to our patients with great results like disapearance of the papules and pruritus at 3 weeks after the procedure. The side effects were minimum with hyperpigmentation and reduced scars.

Another method of treatment used for Fox-Fordyce disease is liposucion assisted by curettage. It was found to be usefull in the treatment of axilary hyperhidrosis but a modified technique of liposuction will permanently destroy the apocrine sweat glands. The secretory part of the apocrine glands is placed in deeper part of the dermis. An action at the deep dermis level is necessary to induce inflammation and finally fibrosis, eliminating the apocrine glands completely. The data from the case reports reveal that

this method was beneficial to the patients, but it can be used only for the Fox-Fordyce disease with the involvement of the axila that did not respond to other therapeutic methods.[23]

Conclusions

The Fox-Fordyce disease is a very difficult to treat because it is not studied enough. There are many treatment options from topical to oral and interventional procedures. The method of treatment should be chose individually for each patient in order to have positive outcomes. Topical treatments like topical corticosteroids may be prescribed to decrease inflammation and pruritus. Topical retinoid creams such as adapalene can help unclog affected sweat ducts, resulting in relief from symptoms. In severe cases, oral medications like hormonal contraceptives or isotretinoin may be prescribed to regulate sweat gland activity or reduce inflammation. The are more invasive options like laser therapy, electrocoagulation, liposuction and curettage, we consider them for those patiens with a refractary form of the disease.

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Conflict of interest
NONE DECLARED

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