Case Letters

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Refractory pruritic Fox-Fordyce disease successfully treated with botulinum toxin type A

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Dear Editors,

Fox-Fordyce disease (FFD) was first described in 1902 by Fox and Fordyce[1] in 2 patients with axillary disease. FFD is a chronic, pruritic, papular eruption involving apocrine-gland–rich areas. It most commonly affects women between the ages of 15 and 35 years with a female-to-male ratio up to 13:1.[2]

A 30-year-old Saudi female presented to our dermatology clinic complaining of a 7-year history of intensely pruritic papules over both axillae. There was no hyperhidrosis or axillary chromhidrosis. There was neither fluctuation in pruritus during the day or before menstruation nor a history of laser therapy in the affected areas. Over the last 7 years, multiple treatment modalities were tried, including topical and intralesional corticosteroid, topical tacrolimus 0.1% ointment, 1% clindamycin solution, topical tretinoin 0.05%, an oral antihistamine, topical aluminum chloride hexahydrate 20%, oral isotretinoin up to 1 mg/kg for 6 months, and multiple sessions of electrosurgery. There was no significant reduction either in pruritus intensity or in the number of papules. Her main complaint was intense pruritus, rated using the Visual Analogue Scale as being 10/10. The severity of the patient's pruritus significantly affected her daily quality of life. Her Dermatology Life Quality Index was 19.

On examination, there were multiple grouped skin-colored papules involving both axillae (Fig. 1A). A dermoscopic examination showed multiple light brown to dark brown papules with hyperkeratotic follicular plugging (Fig. 2A). Histopathological analysis revealed dilated hair follicle lumen filled with lamellated keratin, acanthosis of follicular epithelium and moderate lymphoplasmacytic perifollicular inflammatory infiltrate with few foamy histiocytes and neutrophils (Fig. 2B). Based on the clinical, dermatoscopic and histological analysis, the diagnosis of FFD was made.

Treatment with intradermal botulinum toxin type A (BTX-A; Botox, Allergan, Irvine, California) 100 U for both axillae was given. The injections were marked 1.5–2 cm apart, and 2 U were injected intradermally into each point, using a 2.5 mL dilution with 0.9% preserved normal saline.

At 3 months follow-up, pruritus is almost completely disappeared, rated using Visual Analogue Scale as being 2/10. In addition, there was a marked reduction in the number of papules from the baseline, leaving few depressed scars and postinflammatory hyperpigmentation, with flattening of the remaining ones (Fig. 1B). Her Dermatology Life Quality Index 3 months after 1 session of BTX-A was 5. There were no reported adverse events after the injections. This response has been maintained after 6 months of follow-up (Fig. 1C).

Therapeutic knowledge of FFD is derived primarily from case reports. No single agent has proven particularly effective. Two case reports of refractory FFD showed successful treatment with BTX-A injections.[3,4] After a single treatment of BTX-A, our patient exhibited a marked reduction in pruritus and partial resolution of skin lesions, lasting up to 6 months. The exact mechanisms that led to the improvement of pruritus in our patient are unknown. Nonetheless, it may be explained by sweat reduction which is a known trigger of pruritus in FFD, the antipruritic effect of BTX-A through inhibiting the release of pruritogens, for example, acetylcholine, substance P, glutamate and calcitonin gene-regulating protein, stabilize mast cells and inhibit their degranulation, and downregulate the expression of transient receptor potential cation channel, subfamily A, member 1 and transient receptor potential cation channel subfamily V member 1, which may contribute toward the anti-itch effects of BTX-A.[5,6] Interestingly, we observe a significant reduction of papules after 1 session of BTX-A that could be partially explained by the inhibitory effect of BTX-A on fibroblasts through transforming growth factor beta 1, S100A4, vascular endothelial growth factor, matrix metalloproteinase-1, and platelet-derived growth factor subunit A modulation and altering apoptotic, migratory, and fibrotic pathways.[7,8]

Conflicts of interest

None.

What is known about this subject in regard to women and their families?

- Fox-Fordyce disease (FFD) is a chronic papular eruption involving apocrine-rich areas, most commonly affecting young adult women.
- FFD is usually associated with intense chronic pruritus, which affects women's quality of life at their peak reproductive age.
- There is no satisfactory treatment option for FFD.

What is new from this article as messages for women and their families?

- Treatment with intradermal botulinum toxin type A (BTX-A) injections may represent a promising treatment option for treatment-refractory FFD.
- BTX-A injection can improve the quality of life as it can alleviate the intense pruritus associated with FFD.
- BTX-A is a safe treatment option with no serious adverse events. The cost and availability are limiting factors.

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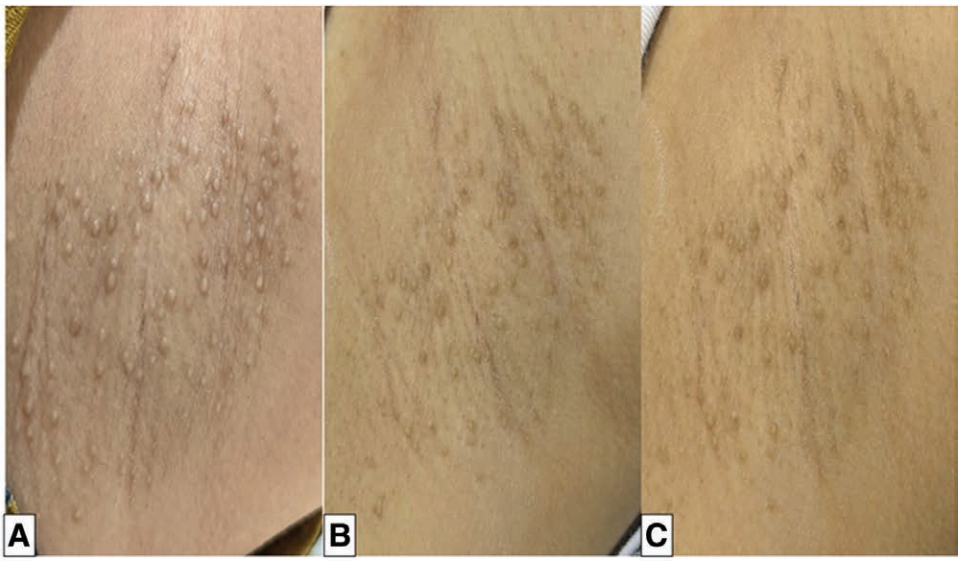

Fig. 1. Physical examination of the left axilla before and after BTX-A injections. (A) Multiple grouped skin-colored papules involving the left axilla. (B) At 3 months follow-up, marked reduction in the number of papules from the baseline with flattening of the remaining ones after 1 session of BTX-A injections. (C) At 6 months follow-up, sustained reduction in the number of papules with few depressed scars and postinflammatory hyperpigmentation. BTX-A, botulinum toxin type A.

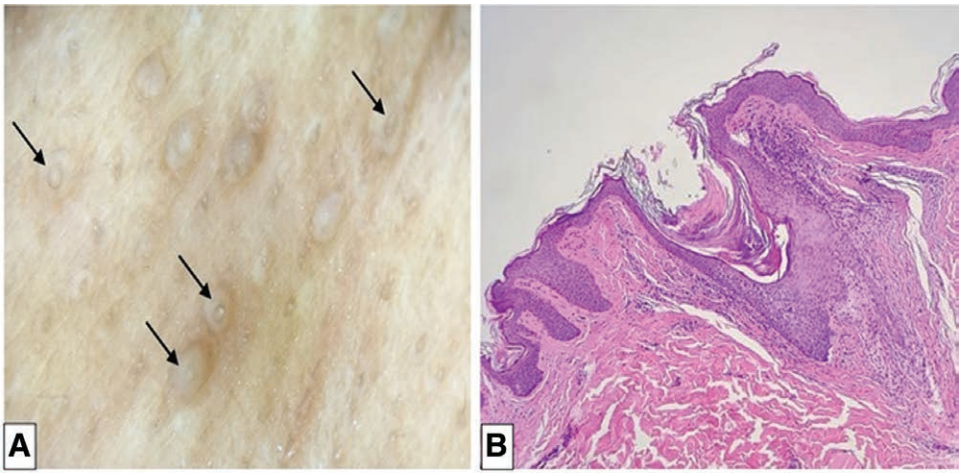

Fig. 2. Dermatoscopic and histopathological evaluation. (A) Dermoscopic examination showed multiple light brown to dark brown papules with hyperkeratotic follicular plugging (arrow) when evaluated under the polarized light. (B) Histopathological analysis revealed dilated hair follicle lumen filled with lamellated keratin, acanthosis of follicular epithelium and moderate lymphoplasmacytic perifollicular inflammatory infiltrate.

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Author contributions

MMA participated in conceptualization, methodology, investigation, writing—original draft, and writing—review & editing. MUT participated in investigation and writing—original draft.

Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

Patient consent

Informed, written consent was received from all patients and confirmed to the journal pre-publication, stating that the patients gave consent for their photos and case history to be published.

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Meshal Mohammad Alhameedy, MD*
Department of Dermatology, King Fahd Specialist Hospital, Buraydah, Qassim, Saudi Arabia

Muhammad Usman Tariq, FCPS
Department of Histopathology, Prince Faisal Cancer Center, King Fahd Specialist Hospital, Buraydah, Qassim, Saudi Arabia

*Corresponding author.
E-mail address: Meshal.alhameedy@gmail.com (M.M. Alhameedy).