Two Cases of Multiple Eccrine Hidrocystomas with Good Response to Botulinum Toxin

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Multiple eccrine hidrocystomas of the face are rare benign cystic lesions characterized by numerous asymptomatic, flesh-colored, mild, and translucent facial papules in middle-aged women. The condition often runs a chronic course, which may be exacerbated by seasonal change or heat exposure. Topical application of 1% atropine is the conventional treatment option, but the results are not always satisfying. Here, we present the clinicopathological features of and treatment modality for two middle-aged female patients with multiple eccrine hidrocystomas. They achieved rapid clearing of the skin lesions (<1 week) on treatment with the first course of botulinum toxin injection. (Dermatol Sinica 27: 186-191, 2009)

Key words: Multiple eccrine hidrocystomas, Botulinum toxin type A

INTRODUCTION

Eccrine hidrocystoma is a benign cyst of eccrine duct origin, which can be classified into two types according to the number of lesions: solitary type (the Smith and Chernosky type), and multiple type (the classic Robinson type). The solitary type constitutes 80% of all eccrine hidrocystomas, affecting both males and females equally. By contrast, the multiple type is a relatively rare condition, the majority of the patients being middle-aged women, with a male to female ratio of 1:8. Multiple eccrine hidrocystomas (MEHs) are a condition characterized by multiple translucent skin-colored, dome-shaped papules of 2-5 mm with a predilection for the mid-face region, especially the periorbital and malar areas.

The diagnosis of MEHs is based on the clinical appearance and histopathology. Here, we present the clinicopathological features and treatment modality of two middle-aged female patients with MEHs who achieved rapid clearance (<1 week) after injection of botulinum toxin type A (BTX-A) (Botox®; Allergan, Irvine, CA).

CASE REPORT

Patient 1

A 64-year-old Taiwanese housewife presented with a 15-year history of multiple small shiny lumps around the eyes. The lesions increased in number and size during the summer and after a hot bath or heavy exercise. Physical examination showed multiple, dome-shaped, bluish to skin-colored papules,
some of which were translucent, over the periorbital areas (Fig. 1A, 1B). Histopathologic examination showed solitary dermal cysts lined by two layers of small cuboidal cells, consistent with the features of eccrine hidrocystoma (Fig. 1D).

As the patient requested nonscarring and nonsurgical therapy, we offered treatment with BTX-A. A 100-U vial of BTX-A was diluted with 2.5 mL of saline solution without preservative, and a 2-U/cm² dose was injected intradermally, provoking skin blanching in the bilateral cheek and nose wing area. However, because of the initial unequal amounts of facial lesions (right side > left side) in the patient (Fig. 1A, 1B), we injected more doses (34 U) into the right side of the face and only 26 U into the left. The patient was evaluated 7 days later, and her skin looked smooth and glossy. The lesions in the injected areas had resolved, and lesions located at untreated areas remained unchanged (Fig. 1C). No obvious adverse side effects such as injection site bruising, headache, eyelid ptosis, brow ptosis, ectropion, and strabismus were reported. However, the patient noticed mild facial asymmetry especially while smiling about 3-4 days after the injection. A neurologist was consulted and the possibility of stroke or other neuromuscular diseases was ruled out by serial neurological examinations in the neurology outpatient clinic. Suspecting botulinum toxin-related transient facial asymmetry, observation was suggested and the symptom resolved gradually in 3 weeks after the first injection. Six months after the treatment session, no recurrent cystic lesions were observed. To date, the patient has received BTX-A injections annually for 3 years because of the long-term efficacy, convenience, and good tolerability. The adverse effect of facial asymmetry was not seen in subsequent treatment sessions after injecting 30-U BTX-A evenly into each side of the face.

**Patient 2**

A 53-year-old Taiwanese woman presented with a 20-year history of numerous small, dome-shaped, skin-colored to pale-blue papules on her lower upper eyelids and cheeks. (Fig. 2A, 2B) The lesions in the injected areas were resolved in 1 week after injection and recurrences were not observed 6 months postoperatively. (Fig. 2C) The cyst wall consisted of two layers of cuboid cells or flattened cells. (H&E stain, original magnification x200)
blue papules on both eyelids and cheeks (Fig. 2A, 2B). Lesions were exacerbated by sun exposure and elevated temperature, and were cosmetically unappealing to the patient, prompting her to seek treatment. Laboratory parameters including complete blood count, electrolytes, and thyroid-stimulating hormone (TSH) were within normal limits. Findings on tissue biopsy were consistent with eccrine hidrocystoma (Fig. 2D). Totally, 40 U of BTX-A was injected evenly into both cheeks and the periorcular area at a dose of 1 U/cm². Lesions in the injected areas were resolved in 1 week after injection, and recurrences were not observed within 6 months (Fig. 2C). The patient was satisfied with the results and received her second BTX-A injection at a half-year interval for maintenance therapy.

DISCUSSION

MEHs are characterized by multiple translucent papules around the eyelids appearing in warm weather and remitting spontaneously during winter. Although not serious, they represent a troublesome and cosmetically unpleasant condition. Avoidance of hot environments and factors that increase perspiration may prevent worsening of the condition.

The etiology and pathogenesis of MEHs remain unclear. They are usually localized cutaneous tumors without associated systemic involvement; however, Graves’ disease may develop before or concurrently with MEHs in few cases.5 The rapid disappearance of skin lesions after normalization of thyroid function suggests the etiologic role of hyperthyroidism in the development of MEHs. Neither of our patients showed evidence of Graves’ disease, and had no symptoms of hyperthyroidism such as exophthalmos and goiter.

Treatment of MEHs is difficult and unsatisfactory because of minimal improvement or significant side effects. Although multiple treatment modalities have been reported, these approaches are not universally successful. Local drainage by simple needle puncture induces only transient improvement, and recurrences are often observed within 4-6 weeks. Although a solitary eccrine hidrocystoma can be treated easily with conventional surgical excision, the elimination of multiple lesions is problematic because of their multiplicity and cosmetic location. Complete excision or aggressive destruction may lead to unacceptable scarring.

The reported topical regimens with anticholinergic properties, such as 1% atropine4,7,8 and scopolamine,8,10 may induce transitional or complete resolution of the lesions, but side effects such as nausea, photophobia, and blurred vision limit the clinical use of anticholinergics. Daily application of atropine or scopolamine is not always convenient for everyone, and the results are variable.7,8,10

Ablative laser systems such as carbon dioxide (CO₂) laser and erbium: YAG laser have been attempted, but these are accompanied with a risk of scarring, ectropion caused by improper practices, excessive dermal damage due to the nonselective nature, and too aggressive destruction. These are considered to be limiting factors in the choice of treatment. Nonablative laser system such as pulsed-dye laser11 is reportedly effective, but treatment has not been universally successful.12 Purpura, pigmentary change, and the need for multiple sessions are the major concern of and disadvantage for the patient.

BTX-A injections are the fastest-growing cosmetic procedure in the industry, according to the American Society for Aesthetic Plastic Surgery. In 2007, more than 2.7 million people received injections, an increase of 1.5-fold over that in 2000. More popular than liposuction and breast-enhancement surgery, BTX-A is regarded by some as the ultimate fountain of youth. Cosmetic applications of BTX-A for facial aesthetics, in
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general, have recently been reviewed\textsuperscript{13-16} and have confirmed the overall positive clinical experiences.

Although much attention has been paid to the cosmetic application of BTX-A, there are a number of other valuable uses of this agent. One important and widely used therapeutic modality is the treatment of axillary and palmar hyperhidrosis.\textsuperscript{17} The toxin might work by blocking cholinergic terminals of the parasympathetic nervous system governing sweat gland secretion. To date, by negative S-100 protein staining of the tumor cells, some studies have shown that MEHs exist as a retention cyst derived from the ductal part of the eccrine sweat gland,\textsuperscript{4, 18, 19} but still little is known about the pathogenesis. Hyperhidrosis may play a role in the formation of MEHs because both conditions show good response to BTX-A treatment through the blockage of the nervous system governing sweat gland secretion.

The benefits of BTX-A treatment for MEHs has been documented by Blugerman \textit{et al.} as a new and safe therapeutic option.\textsuperscript{6} They described a case of MEHs of the face in a cook man who received a total dose of 15U of BTX-A in the affected areas with excellent results in 1 week after injection, and recurrences were not observed within 6 months.

Only small doses and very superficial intradermal injections should be applied to prevent paralysis of key muscles of facial expression. The adverse effect of facial asymmetry, observed for a short duration in patient 1, can be prevented by injecting equal doses of BTX-A into each side of the face. In addition, aesthetic treatment for aging facial features with glabellar, frontal, and periorcular rhytids can be provided by blocking specific muscles at the same session according to the patient’s desires and preferences. Patients should be informed about the potential adverse effects of BTX-A in the management of MEHs, and also made aware of the fact that most adverse effects are mild and transient. It is important to remember that not only is technique important for ensuring good results but also is the need for a confirmatory diagnosis of MEHs and evaluation of the suitability of candidates, to avoid unnecessary complications and patient dissatisfaction.

BTX-A therapy for MEHs is safe and convenient, and was well tolerated by our patients, although favorable results depend largely on injection technique of the operator and the cost of BTX-A therapy is higher than other topical medication. Because MEHs are known to wax and wane in relation to temperature or seasonal change, we suggest periodic injection of BTX-A (total 40-60 U annually) at a dose of 1-2 U/cm\textsuperscript{2} as an alternative therapy for MEHs during the hot seasons. Additional BTX-A injections can be given depending on the clinical response in 6 months. Further controlled studies including larger case numbers are necessary to confirm the long-term efficacy of BTX-A in the treatment of MEHs.

REFERENCES
二個多發汗腺囊瘤的病例對於肉毒桿菌治療的良好反應

劉達儒  何宜承
高雄長庚紀念醫院皮膚科

臉部多發性汗腺囊瘤是一個罕見的良性臉部囊性病變。特色是中年婦女，在臉上產生許多膚色到些微透光而無症狀的丘疹，通常是一個慢性的病程，且會隨著季節變化或是氣溫的高低而病況有所起伏。傳統的建議治療方式為塗抹局部1%的atropine，但效果並非總是顯著有效。我們報告兩位出現多發性汗腺囊瘤的中年女性病人其臨床、病理特色以及治療方法。她們臉上的病灶在單次肉毒桿菌素治療之後的一週內成功的快速消除。（中華皮誌：27: 186-191, 2009）