Successful Treatment of Eccrine Angiomatous Hamartoma With Botulinum Toxin

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

We present the case of an eccrine angiomatous hamartoma in a 12-year-old girl. The lesion caused profuse sweating and lowered her quality of life because of clothes drenching. It was successfully treated with botulinum toxin, and therapeutic response was maintained for several months.

REPORT OF A CASE

A 12-year-old girl was referred to our department for evaluation of a 6-cm erythematous, brownish, indurated plaque that has been present on the sacral area since birth (Figure 1). The gluteal cleft was not deviated, and the lesion was not tender to palpation. The patient complained of profuse sweating that would drench her clothes. These symptoms were distressing and unrelated to emotional stress or physical exercise. A magnetic resonance imaging study revealed no lumbosacral spine abnormalities or cord tethering. A skin biopsy specimen demonstrated benign fibrovascular proliferation with a hyperplasia of the eccrine sweat glands in the dermis (Figure 2), which is consistent with an eccrine angiomatous hamartoma (EAH). The hamartomatous component was 2 mm below the epidermis and extended 4 mm into the dermis. In view of the symptoms, surgical excision was proposed, but the patient and her family preferred a different therapeutic approach.

CLINICAL CHALLENGE

Eccrine angiomatous hamartoma is a benign tumor that does not require aggressive treatment if it remains asymptomatic. When the lesion causes pain or hyperhidrosis, or is cosmetically distressing, surgical excision is curative. Pulsed-dye laser and Nd:YAG laser treatment have been performed without much success. To our knowledge, no further therapeutic approaches are currently available.

SOLUTION

Because of the specific symptoms, the location of the lesion, and the parents’ refusal of surgical intervention, we proposed the administration of botulinum toxin to suppress the excessive sweat production of the hyperplastic eccrine sweat glands in the hamartoma. Because we used botulinum toxin for a nonapproved indication, we obtained written consent from the patient’s parents when they were informed about the proceeding. The Minor starch-iodine test was performed to assess the area to be

Figure 1. Clinical aspect of the lesion. Note sweat drops over the lesion.

Figure 2. Microscopic aspect of the lesion (hematoxylin-eosin, original magnification ×10).
treated, and 2.5 U per injection of botulinum toxin type A was infused in a single course of 14 injections spaced 1.5 cm apart. Botulinum toxin was diluted with isotonic sodium chloride solution to a concentration of 2.5 U per 0.1 mL. A total dose of 35 U was infused using an insulin (1-mL) syringe. Injections were applied superficially, forming wheals, and avoiding the administration of botulinum toxin into the vascular component of the lesion situated 2 mm beneath the epidermis. Hyperhidrosis disappeared soon afterwards, and the effect lasted for 5 months. The patient’s quality of life improved significantly, and she was very satisfied with the results. When hyperhidrosis reappeared at 5 months, she requested a second treatment, and the therapeutic response was again rapid (Figure 3).

**COMMENT**

Eccrine angiomatous hamartoma is a benign malformation composed of capillary channels and mature eccrine gland structures. It usually arises in the distal parts of the limbs at birth or during childhood, and rarely develops during puberty or adulthood. There is no preference related to the patient’s sex. The lesion typically shows proportional growth since birth and presents as a solitary nodule or a plaque that may be red, blue, violaceous, brown, yellow, or skin colored, although macular or papular presentations are also possible. It may be hypertrichotic or painful or cause excessive sweating. Pain may be the result of swelling and compression or infiltration of neural structures of the hamartomatous tissue. A multiple, noninherited variant has been described.

The etiology of EAH is unknown. It is, however, thought to be the product of an anomalous tissular organogenesis due to defective biochemical interactions between the epithelium and mesenchyma, leading to an abnormal proliferation of vascular and adnexal structures.

Histologically, EAH is characterized by mature normal eccrine sweat glands and ectatic vascular channels in the dermis and subcutaneous tissue within a dense fibrocollagenous stroma that separates the sweat gland lobules. The secretory portion of the eccrine glands is composed of an eosinophilic and clear cell layer. The angiomatous portion is composed of thin-walled capillaries and ectatic thick-walled vessels set in the fibrocollagenous stroma between the eccrine apparatus. Occasionally, apocrine glands may be found. Cavernous channels and venous and/or arteriolar structures are also found in the upper dermis or in the fat. Mucinous, lipomatous, nervous, and/or pilosebaceous components can also be present in the dermis. The epidermis is usually spared and shows no abnormalities. According to the definition by Pelle et al., diagnostic criteria for EAH includes the following symptoms: (1) hyperplasia of normal or dilated eccrine glands; (2) close association of the eccrine structures with capillary angiomatous foci; and (3) the variable presence of pilar, lipomatous, mucinous, and/or lymphatic structures. Cytologic atypia and mitotic figures are not included in the EAH histological picture.

The immunohistological pattern of EAH does not differ from that of normal eccrine glands and capillary channels. Eccrine sweat apparatuses stain positive for S-100 protein, carcinoembryonic antigen, epithelial membrane antigen, and CAM5.2 antibody, and the vascular component shows positivity for CD34, CD44, human nerve growth factor receptor, and Ulex europaeus and factor VIII–related antigens. The surrounding stroma show positive results for anti-CD36 immunostaining.

Clinical differential diagnosis includes vascular malformations, eccrine nevus, tufted angiomata, smooth-muscle hamartoma, glomus tumor, and blue rubber bleb nevus syndrome. These lesions can be ruled out histologically. Sudoriparous angiomata and eccrine nevus are harder to differentiate by microscopic examination.

Although EAH is a benign hamartoma and aggressive treatment is not recommended, complete surgical excision may be considered when the lesion is progressively enlarging or reducing the quality of life because of pain, local hyperhidrosis, or unpleasant aesthetics. Excisional biopsy may be curative for small tumors, but amputation of a finger or toe may be required for symptom control in the case of larger lesions. Spontaneous regression has only been reported in 1 case. Some authors recommend a “wait and see” policy if EAH remains asymptomatic or if the excisional procedure is too traumatic because pain associated with the lesion may spontaneously resolve.

To our knowledge, this is the first report of successful treatment of EAH with botulinum toxin. Botulinum toxin causes a temporary chemodenervation at the presynaptic nerve terminals, impeding the release of acetylcholine and thus reducing the activity of the target striated muscular and autonomic structures, decreasing muscle tone and eccrine gland sweat secretion. All botulinum toxin serotypes are highly specific in targeting cholinergic presynaptic fibers. They block the SNAP-25 synaptosomal protein complex, which mediates the fusion of the synaptic acetylcholine vesicle with the plasma membrane. The duration of the neurotransmission blockade effect varies by the botulinum toxin serotype: type A has longer blocking properties and its action can persist for 4 to 10 months, depending on the dosage, technique, and the area of application. The main clinical indications for botulinum toxin are painful conditions.
are hyperhidrosis and diseases in which excessive neuro-muscular activity is the major feature. A cosmetic use of botulinum toxin is also feasible, acting as a wrinkle reducer. When treating hyperhidrosis, it is first recommended to practice a starch-iodine test to delineate the region involved, keeping in mind that areas of denervation may reach about 2.5 to 3.0 cm for each injection owing to toxin spread. Standard botulinum toxin dosage for treating hyperhidrosis is not defined, and it varies from 50 U per axilla to 60 to 100 U per palm. Touch-ups 2 weeks after the first injections are not uncommon. Botulinum toxin is injected intradermally, producing small wheals spaced 1.5 to 2.0 cm apart. Complications are scarce and may include local weakness, injection site reactions (eg, pain, edema, erythema, ecchymosis, hyperesthesia), generalized idiosyncratic reactions (eg, nausea, fatigue, malaise, flulike symptoms, cutaneous eruption) and toxin resistance. Hyperhidrosis treatment with botulinum toxin has been shown to be rapid, effective, well tolerated, and more satisfactory for the patient compared with any other therapeutic option, increasing the patient’s quality of life.

In view of the refusal for surgical management of EAH in the case presented herein, botulinum toxin infiltration was administered, providing excellent results. In conclusion, botulinum toxin may be a novel therapeutic approach for hyperhidrotic lesions of EAH.

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