OBSERVATION

Idiopathic Localized Unilateral Hyperhidrosis

Case Report of Successful Treatment With Botulinum Toxin Type A and Review of the Literature

Oliver P. Kreyden, MD; Peter Schmid-Grendelmeier, MD; Günter Burg, MD

Background: Localized unilateral hyperhidrosis (LUH) is a rare disorder of unknown origin. We describe a patient with LUH on the forearm, where a fracture was identified as a past injury.

Observations: We treated the patient with botulinum toxin type A injections, and he was complaint free during the 6 months after treatment. In addition, the initially strong positive results of the iodine starch test (Minor sweat test) were negative in the affected region after treatment.

Conclusions: This relatively new therapeutic modality already established for axillary, palmar, and plantar hyperhidrosis seems to be efficient in LUH. As the former therapeutic approaches are rather disappointing, and as botulinum toxin type A locally applied shows limited adverse effects, we think a trial of botulinum toxin type A is justified in cases of LUH, even as a first-line treatment. In addition, the literature considering localization and causes of LUH is reviewed.

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From the Praxis Methininserhof, Muttenz (Dr Kreyden), and the Department of Dermatology, University Hospital of Zurich (Drs Schmid-Grendelmeier and Burg), Zurich, Switzerland.

SWEATING IS an important mechanism in the regulation of a constant body temperature. Hyperhidrosis is defined as an excess of sweating beyond the amount required to return elevated body temperature to normal, with a distinction between primary and secondary forms of hyperhidrosis. The primary or essential form arises mainly from emotional factors (nervous sweating) and is located in most cases in the axilla, on the palms of the hands, or on the soles of the feet. In the secondary form, an underlying neurologic or endocrinological disease is the cause of the usually diffuse sweating. Besides these quite common forms of hyperhidrosis, rare disorders such as Frey syndrome[1] or Ross syndrome,[2] which also have an underlying neurologic cause, can produce localized hyperhidrosis.

A few cases of localized unilateral or segmental hyperhidrosis (LUH)[3-8] are described in the literature that do not fit into the mentioned categories. Hyperhidrosis in these cases is located mainly on the forearm or the forehead and is restricted to an area of less than 10×10 cm.[4,6] Localized unilateral hyperhidrosis has none of the typical triggering factors found with essential hyperhidrosis. The attacks occur with no apparent cause, even during the night while the patients are asleep. The pathogenesis of LUH remains unclear. Some authors have related the disease to neurologic disturbances or malignant disease. Herein, we describe a patient with LUH in whom the cause may be a past trauma in the affected area. We used botulinum toxin type A (Botox; Allergan Inc, Irvine, Calif) as a successful therapy, to our knowledge a treatment not yet reported for LUH.

REPORT OF A CASE

A 35-year-old patient had had a sharply demarcated area of hyperhidrosis on his right forearm (**Figure 1**) since puberty. Two years before onset, he had been treated for a fracture in this area. Family and personal history were otherwise uneventful. The patient could not identify any triggers for the hyperhidrosis that occurred in isolated attacks. A dependence on emotions, environmental temperature, or physical efforts was denied. Treatment of the area with a carbon dioxide laser by his general physician worsened the sweating. Apart from a slightly hyperpigmented scar of 2×3 cm that remained due

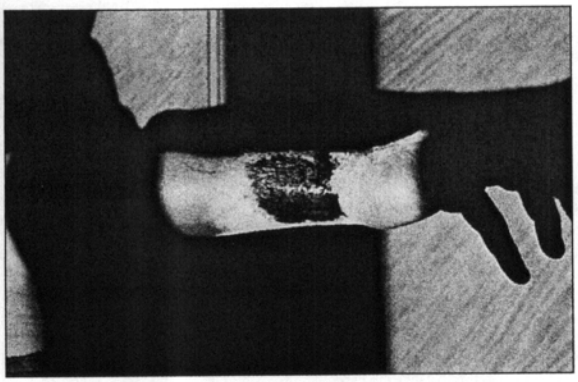

Figure 1. Localized unilateral hyperhidrosis on the right forearm documented with results of the iodine starch test (Minor sweat test) as a sharply demarcated area during an attack.

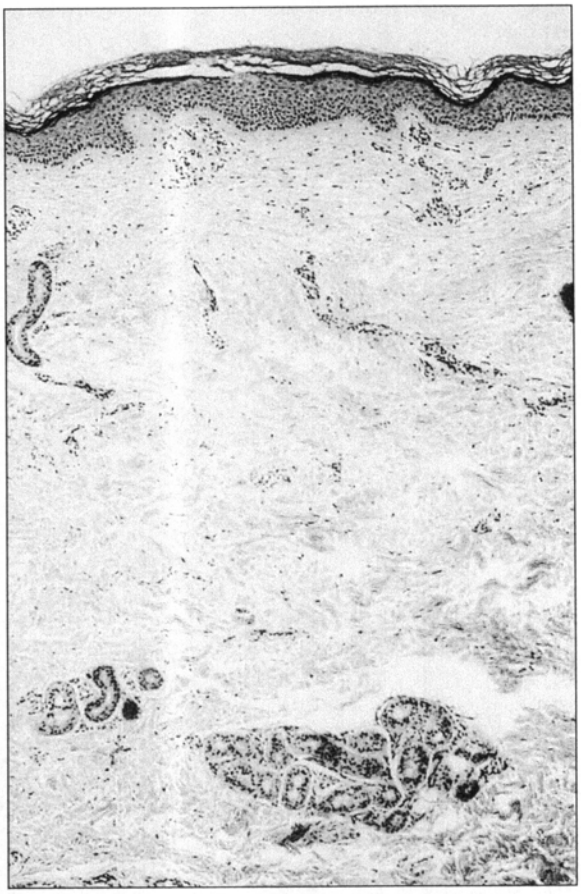

Figure 2. A biopsy specimen showed no increase of sweat glands in the hyperhidrotic area (hematoxylin-eosin, original magnification ×200).

to this laser treatment, the skin was normal. Results of laboratory tests, including endocrinological examination, and neurologic tests, including electromyography, were normal. Results of a biopsy showed no increase of sweat glands in the hyperhidrotic area (**Figure 2**), thus excluding an eccrine nevoid lesion. The sweat glands were no larger than the sweat glands of a control biopsy specimen. Normal results of the iodine starch test (Minor sweat test) were found during symptom-free intervals. The patient was instructed to perform this test at home, and was able to document a sharply demarcated area of focal hyperhidrosis 4×9 cm in diameter on the forearm during attacks (Figure 1). Topical treatment with aluminium chloride produced an unsatisfactory response. Systemic therapy using an anticholinergic preparation (atropini sulfas, 0.5 mg) had to be stopped because of adverse effects. Iontophoresis was not performed due to logistical problems. Therefore, we treated the patient with 15 injections (30 U) of botulinum toxin type A (Botox; Allergan, Inc) in the affected area in a single session. During follow-up, the patient was free of any complaint. However, after 6 months, the effect of the treatment decreased, so the patient elected a second treatment that gave again a full satisfactory result.

Cases of Localized Unilateral Hyperhidrosis in Literature

Reference	Location	Cause
Baker[9]	1 Leg and foot	Buerger disease
Boyvat et al[3]	Hemifacial and scalp	Idiopathic
Cunliffe et al[4]	Forearm (n = 2) and forehead (n = 1)	Increased size of glands
Fernandez and Armijo[10]	Facial circumscribed	Idiopathic
Kempermann et al[11]	Hemifacial	Gustatoric
Kopera and Soyer[12]	Forearm	Eccrine hamartoma
Köse and Baloglu[5]	Forearm	Idiopathic
Kreyden et al (present study)	Forearm	After injury
Labar et al[13]	Face and arm	Cerebral infarction
Lambert et al[14]	Face, trunk, and upper extremities	Myelomatous tumor
Parslew and Lewis-Jones[15]	Left hand	Eccrine hamartoma
Rufli et al[6]	Forehead	Idiopathic
Ruiz de Erenchun et al[16]	Right side of thorax and abdomen	Eccrine hamartoma
Sakashita et al[17]	Right side of body	Ischemic stroke
Takase et al[7]	Left side of the face and scalp	Idiopathic
van de Kerkhof et al[8]	Forehead left side	Central nervous system disorder
Verbov[18]	Face and scalp	Idiopathic
Yamauchi et al[19]	Hemifacial	Pancoast tumor

COMMENT

Localized unilateral hyperhidrosis is a rare but well-defined special form of localized hyperhidrosis with unknown pathogenesis that occurs in otherwise healthy individuals.[3] All cases of LUH found in the literature, to our knowledge, are summarized in the **Table**.[3-5,7,8-19] Localized unilateral hyperhidrosis is attributed to neurologic factors, underlying tumors, or unknown causes. In one case of LUH, a subclinical increase in evaporative water loss from other areas of the body with a left-right gradient in the sweating rate was also found. Because of the widespread sweat gland dysregulation, a more central involvement of the autonomic nervous system was concluded in this case.[8] Localized unilateral hyperhidrosis has also been reported in association with organic diseases of the nervous system such as cerebral

infarction,[13] spinal cord injuries,[20] or peripheral neuropathy.[21] In addition, segmental hyperhidrosis associated with intrathoracic neoplasmas such as bronchial or pleural carcinomas has been reported.[22-25] In all of these cases of nonidiopathic unilateral hyperhidrosis, the spread of the disorder was much more extensive than in our case (ie, face, upper extremities, and thorax), or the localization was on the trunk. Our patient had had a forearm fracture in the area that later became hyperhidrotic, and the situation was subsequently exacerbated by laser treatment. Some authors have identified an eccrine hamartoma as a cause of LUH.[12,15,16] An eccrine nevus, however, could be excluded by means of biopsy in our patient.

In cases of LUH where the affected area is very limited, a former injury should be considered as a potential cause. A possible mechanism would be a misdirected reconnection of the sympathetic nerve fiber network after injury, similar to Frey syndrome, and not detectable by means of conventional neurologic examination. Frey syndrome or gustatory sweating is a well-known consequence of operation on the parotid glands or other parotitis. The syndrome was first described by Lucja Frey (1889-1943), a Polish neurologist.[26] Frey syndrome is characterized by hyperemia of the head and neck and abundant sweating of the hyperemic skin in respect to gustatory stimuli. After surgery, misdirected resprouting of parasympathetic fibers may occur, and the fibers come into contact with sweat glands that are normally innervated by sympathetic fibers. Typically, gustatory sweating develops within 6 months of parotid gland or neck surgery[27] or after other lesions such as infection or trauma.[28]

Ross syndrome is another focal hyperhidrotic disorder. In 1958, Ross,[29] a neurologist from Indianapolis, Ind, reported for the first time a case of progressive, selective sudomotor denervation. He described a 32-year-old patient with the triad of symptoms consisting of unilateral tonic pupils, generalized areflexia (Holmes-Adie syndrome), and progressive segmental anhidrosis with a compensatory band of excessive perspiration. Patients with Ross syndrome usually do not perceive the hypohidrosis, but finally notice compensatory segmental hyperhidrosis. In addition to the triad, some authors[2,6] have reported several symptoms of vegetative dysfunctions such as palpitation, stenocardia, orthostatic hypotonia, and disturbance of intestinal motility (irritable colon), which are believed to be characteristic features of Ross syndrome. The pathogenesis of Ross syndrome is unknown. In the literature, multiple neuropathies of the autonomic nervous system[29] or a failure in the syntheses or release of neurotransmitters have been suggested. Recently, Bergmann et al[30] used immunofluorescence to show a selective reduction of nerve fibers innervating the sweat glands in the anhidrotic areas, whereas epidermal innervation remained normal.

The iodine starch test was helpful in the diagnostic procedure, and we recommend using this simple, easy, and risk-free investigation in cases of localized hyperhidrosis.

Treatment of LUH has been disappointing until now. Botulinum toxin type A injections offer an effective new therapeutic modality for this condition. This therapy is more and more established and successfully used for the treatment of focal hyperhidrosis of the axilla, palms, and soles. The ophthalmologist Scott[31] together with Schantz and Johnson[32] first developed the poison botulinum toxin type A into an useful therapeutic tool. Later Bushara et al[33] found a good anhydrotic effect of the drug when treating patients with blepharospasmus. Many reports of the excellent effect in the treatment of hyperhidrosis followed.[34-38] Botulinum toxin type A can easily be administered in cases of LUH. Our patient was treated only with 30 U of botulinum toxin type A (Botox; Allergan, Inc) and was free of symptoms for 6 months. Even after that time, the symptoms were much less distinctive. Because the patient wished not to wait until full hyperhidrosis was reestablished, we treated him again with the same amount of botulinum toxin type A. He has been free of symptoms since then. As botulinum toxin is locally applied and shows limited adverse effects (pain during injection, potential weakness of the underlying muscles), we believe botulinum toxin type A in cases of LUH, even as a first-line treatment, is justified.

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Corresponding author and reprints: Oliver P. Kreyden, MD, Praxis Methininserhof, Baselstrasse 9, 4132 Muttenz, Switzerland (e-mail: kreyden@hin.ch).

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News and Notes

The Fourth International Days on Pediatric Dermatology will take place from April 25 to April 27, 2002, in the Auditorium of the Catholic University of the Sacred Heart in Rome, Italy. The congress is organized by the International Center for Study and Research in Dermatology of the University's Department of Dermatology and the Italian Group of Pediatric Dermatology (GIDEP), with the patronage of the Italian Society of Dermatology and Venereology (SIDEV) and the European Society for Pediatric Dermatology (ESPD). Illustrious university professors from all over the world will take part in this scientific event where 500 to 600 congress members are expected from all over Europe. For information, contact Professor Giuseppe Fabrizi, Department of Dermatology, Catholic University of the Sacred Heart, Largo A. Gemelli 8, 00168 Rome, Italy. Phone/fax: 39063013250 (e-mail: fabrizi.unicat-derm@ntt.it).