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Letter

Glycopyrrolate-induced craniofacial compensatory hyperhidrosis successfully treated with oxybutynin: report of a novel adverse effect and subsequent successful treatment

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Abstract

Hyperhidrosis, or abnormally increased sweating, is a condition that may have a primary or secondary cause. Usually medication-induced secondary hyperhidrosis manifests with generalized, rather than focal sweating. We report a 32-year-old woman with a history of palmoplantar hyperhidrosis for 15 years who presented for treatment and was prescribed oral glycopyrrolate. One month later, the palmoplantar hyperhidrosis had resolved, but she developed new persistent craniofacial sweating. After an unsuccessful trial of clonidine, oxybutynin resolved the craniofacial hyperhidrosis. To our knowledge, this is the first case of compensatory hyperhidrosis secondary to glycopyrrolate reported in the literature. The case highlights the importance of reviewing medication changes that correlate with new onset or changing hyperhidrosis. It also demonstrates a rare drug adverse effect with successful treatment.

Keywords: Hyperhidrosis; Craniofacial; Glycopyrrolate; Compensatory

Introduction

Hyperhidrosis is characterized by excessive sweating beyond normal parameters of thermoregulatory need. Hyperhidrosis may be classified as primary or secondary. Primary hyperhidrosis occurs without an identifiable cause, whereas secondary hyperhidrosis is a result of an underlying medical condition or drug [1]. Compensatory hyperhidrosis is a type of secondary hyperhidrosis characterized by decreased sweating in the original problem area coupled with hyperhidrosis in a new area [2]. This type of hyperhidrosis is most often seen following endoscopic thoracic sympathectomy (ETS) for treatment of refractory palmar hyperhidrosis [3]. Hyperhidrosis may also be classified by location as either generalized or focal. The most common focal locations include the axillae, palms, soles, and craniofacial region [1,4].

There is no recent data regarding the prevalence of hyperhidrosis in the US, but a country-wide mail survey in 2004 estimated approximately 2.8% of the US population suffers from the disease [5]. Recent data from a survey of over 14,000 German patients reported a prevalence of 16%, suggesting that perhaps the US prevalence has been underestimated [4]. In a retrospective chart review of almost 400 patients with hyperhidrosis, 7% were found to have secondary hyperhidrosis [1]. More epidemiologic data is needed to assess the frequency of secondary hyperhidrosis and its underlying causes.

Case synopsis

A 32-year-old woman presented to the dermatology clinic with constant, daily hyperhidrosis of the palms and soles for fifteen years. She denied any family history of hyperhidrosis. Her past medical history was significant for polycystic ovarian syndrome and insulin resistance, and she was diagnosed with prediabetes five years before presentation. A review of systems yielded no other significant findings and thyroid function tests were within normal limits. The patient was diagnosed with palmoplantar primary hyperhidrosis and prescribed oral glycopyrrolate 1 mg twice daily and 20% aluminum chloride topical solution.

Upon return to clinic, the patient reported dramatically decreased sweating on the palms and soles, but had developed excessive sweating of the head and face. The craniofacial sweating began approximately one month after the patient started using glycopyrrolate. No other medication changes were made during this time. On physical exam, the patient had noticeably dripping sweat on both the face and the scalp, but the palms and soles were dry, along with the rest of her body. She had never experienced craniofacial sweating before starting glycopyrrolate.

Given that the craniofacial sweating began following glycopyrrolate treatment and there were no other potential triggering factors, glycopyrrolate was identified as the offending agent and discontinued. The patient was diagnosed with compensatory hyperhidrosis. After counseling regarding treatment options, the patient was started on clonidine 0.1 mg BID to address the new craniofacial distribution of sweating. Aluminum chloride 20% topical solution was continued to the palms and soles. Six weeks later, the craniofacial hyperhidrosis persisted, despite clonidine therapy. Next, two rounds of Botox were injected into a limited area of the scalp two months apart, with little improvement of the hyperhidrosis. Finally, a trial of oxybutynin was given to attempt to treat the craniofacial compensatory hyperhidrosis. Oxybutynin was titrated up as follows: week 1, 2.5 mg at night; weeks 2-3, 2.5 mg twice daily; weeks 4-6, 5 mg twice daily. After six weeks of oxybutynin at the aforementioned dosing schedule, the patient returned to clinic with resolution of the craniofacial compensatory hyperhidrosis. She was extremely happy with the results and was continued on oxybutynin 5 mg twice daily.

Discussion

Over ninety medications have been implicated as causes of secondary hyperhidrosis [2]. Common drug classes associated include anticholinesterases, psychiatric medications, opioids, antihypertensives, hormones, antibiotics, antiglaucoma agents, and many others [2, 6]. Although numerous medications have been shown to cause generalized secondary hyperhidrosis, there is no report in the literature of any medication causing focal secondary or compensatory hyperhidrosis. Given that the patient's palmoplantar hyperhidrosis resolved with glycopyrrolate treatment and new craniofacial hyperhidrosis began concurrently, this case likely represents compensatory hyperhidrosis. It is also possible that aluminum chloride treatment of the palms and soles resolved her palmoplantar hyperhidrosis and the oral glycopyrrolate caused an unrelated secondary focal hyperhidrosis. However, this presentation would be unusual considering glycopyrrolate is often used to treat craniofacial hyperhidrosis [7].

Typically, glycopyrrolate acts as a competitive antagonist of muscarinic receptors and causes decreased sweating by inhibition of the M3 receptor [7]. One possible explanation for this patient's reaction to glycopyrrolate is that inhibition of M3 receptors in the palms and soles caused downregulation of negative feedback to the hypothalamus, leading to increased sweating in the craniofacial region. A similar mechanism has been proposed for compensatory sweating after ETS [8]. However, the pathway or pathways explaining how compensatory sweating occurs has yet to be elucidated.

Compensatory hyperhidrosis has been recognized in a number of conditions affecting the neurological system. Nerve and spinal cord injury, Parkinson disease, post sympathectomy, cerebral malformations and lesions, and neuropathy have all been associated with compensatory hyperhidrosis or secondary focal hyperhidrosis [1, 2]. In diabetics with poorly controlled hemoglobin A1c (HbA1C) levels, there is a measurable increase in sweat production of the upper body that correlates with a simultaneous decrease in sweat production of the lower body. This change reflects early symptoms of autonomic neuropathy [9]. However, our patient did not meet criteria for diabetes and had no other symptoms of neuropathy. Additionally, the distribution of sweating was isolated to the craniofacial region, making autonomic neuropathy an unlikely cause of her hyperhidrosis.

Given that secondary hyperhidrosis may be caused by a wide variety of medications, this case illustrates the importance of gathering a thorough history of any new medication use that coincides with onset of new or different hyperhidrosis. Regardless of whether there is a documented association between hyperhidrosis and a new medication, a trial of medication discontinuation may be warranted given the right clinical indicators. If hyperhidrosis continues, treatment with another oral medication indicated for hyperhidrosis such as oxybutynin or clonidine may be effective [7, 10]. This case also documents a rare reaction to glycopyrrolate and demonstrates the possibility that some medications may cause compensatory hyperhidrosis. Although hyperhidrosis is not a life threatening condition, it can dramatically decrease quality of life and has an impact on personal and professional development [11]. Therefore, recognition of any possible secondary causes is critical to provide superior patient care.

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