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Scleroderma in the Setting of Long-term Intermittent Phentermine Use

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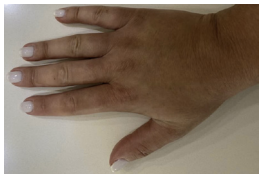
Scleroderma is a relatively rare, heterogeneous disease, often involving multiple internal organs that are frequently associated with progressive cutaneous manifestations. The disease occurs predominantly in women, who tend to present at a younger age with more limited disease.[1] We report a case of diffuse cutaneous systemic sclerosis in a patient receiving long-term, intermittent phentermine. The relationship between the patient's use of phentermine and the onset of scleroderma symptoms is considered.

REPORT OF A CASE

A 32-year-old woman presented with new-onset edematous hands and difficulty flexing her fingers. She also noted puffiness of her eyelids and darkening of the skin of her face. She had no significant past medical history. However, she has been prescribed 15 mg/day phentermine on an intermittent basis for several years as an adjunct agent to help her weight loss. She is overweight, but not obese. On review of systems, she complained of reflux symptoms, and endorsed new-onset Raynaud's phenomenon. She denied any shortness of breath.

Physical examination revealed bilateral edematous hands with a waxy appearance, extending just proximal to the metacarpophalangeal joints. She had mildly decreased oral aperture, and faint hyperpigmentation of periorbital skin with mild edema. A biopsy was performed from the right hand, which demonstrated dermal fibrosis consistent with early scleroderma (Figure 1). Antibody testing was borderline positive for an anti-nuclear antibody at a titer of 1:1280, nucleolar pattern. Anti-Scl-70, anti-centromere, and anti-RNA polymerase III antibodies were negative. She was started on amlodipine and mycophenolate mofetil and referred for pulmonary and gastrointestinal evaluation and screening.

FIGURE 1.



DISCUSSION

Phentermine is a sympathomimetic amine, which has been used as an adjunct weight loss agent since its initial approval in 1959. In the 1990s, it was widely used with fenfluroxamine in the combination drug "Fen-Phen". This combination, particularly fenfluroxamine, has been associated with a series of adverse effects, particularly cardiac valvular fibrosis leading to valvular heart disease.[2] While fenfluroxamine was withdrawn from the market after these findings, phentermine was not and since its approval, phentermine has been associated with a series of other adverse reactions including primary pulmonary hypertension, psychosis, and ischemic events.[3]

To date, there has not been a described relationship between phentermine and scleroderma. However, the pathogenesis of scleroderma is not clearly understood, but is thought to occur as a result of abnormalities in vascular, fibrotic and inflammatory pathways. Specifically, systemic sclerosis has been associated with norepinephrine-induced fibrosis.[4] Norepinephrine activates the adrenergic receptor β2, which phosphorylates p38.[4] This induces the production of interleukin 6 (IL-6), which stimulates the production of fibroblasts in collagen, inducing the clinical features of scleroderma.[4] Phentermine has been shown to increase norepinephrine.[3] This norepinephrine release may trigger the onset of fibrosis and a progression to scleroderma. The patient described could be an index case demonstrating a potential link between the two and both of these have fibrosis as a common pathology.

While phentermine has been banned in certain forms, it is still heavily prescribed in the United States as a Schedule IV substance. Phentermine is one of the most widely used anti-obesity drugs, with many patients using it for periods greater than 90 days.[5] Use of this drug is presently limited by the FDA to short-term treatment. As illustrated in the patient presented, phentermine has the potential to easily be prescribed incorrectly. In this case, an overweight patient was prescribed phentermine for long-term use, which may have been a triggering event for her development of scleroderma.

DISCLOSURES

The authors have no conflicts of interest to declare.

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