Intractable Chronic Granulomatous Perioral Dermatitis in Patients Receiving Growth Hormone Therapy: A New Association between CGPD and GH

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Abstract
Childhood granulomatous periorificial dermatitis (CGPD) is a self-limiting skin condition characterized by papular eruptions around the mouth, nose and eyes of preadolescent children. We report two cases of intractable CGPD in which patients receiving growth hormone (GH) therapy showed persistent symptoms despite multiple treatment modalities. This association may suggest the role of GH in the pathogenesis of CGPD.

Key Words: Chronic granulomatous perioral dermatitis, cytokine-like action, growth hormone therapy

Introduction
Childhood granulomatous periorificial dermatitis (CGPD), a granulomatous dermatitis observed in preadolescent children, is characterized by papular eruptions around the mouth, nose, and eyes. CGPD is known to be an asymptomatic, benign, and self-limiting condition.[1]

It has been reported that complete resolution of CGPD usually occurs in a few months, either spontaneously or in response to treatment with medications, such as topical tacrolimus, or metronidazole, and systemic erythromycin or minocycline.[2]

Though peak incidence of CGPD occurs in childhood, the association of growth hormone (GH) and CGPD has not yet elucidated. Herein, we describe two cases of intractable CGPD in patients undergoing GH therapy.

Case Reports
Patient 1 was a 10-year-old girl who presented with 4-month history of tiny papular eruptions around the nose, mouth, and forehead [Figure 1a]. Patient 2 was an 11-year-old girl who presented with 8-month history of tiny papules around the nose and mouth [Figure 2a]. Both patients were otherwise healthy. The diagnosis of CGPD in both the patients was established based on histopathological finding of perifollicular noncaseating granulomatous inflammation [Figures 1c, d and 2c, d]. Patient 1 was receiving GH therapy for short stature and reported that the skin lesions appeared 18 months after initiating GH therapy. The lesions failed to respond to topical tacrolimus and oral roxithromycin. After intermittent discontinuation of GH therapy for 2.5 months, the skin lesions improved, but aggravated again 1 month after resuming regular use of GH and persisted for >2 years with continued GH therapy [Figure 1b].

Patient 2 responded well to topical tacrolimus therapy. However, she developed recurrence of CGPD 2 months after initiating GH therapy for the treatment of short stature. The lesions persisted for >20 months during GH therapy, despite various treatments [Figure 2b]. The skin lesions finally improved 1 week after the completion of GH therapy, and no further treatment was required.

Both the patients received treatment for CGPD with different modalities including topical tacrolimus,
metronidazole and benzoyl peroxide. Other modalities that were attempted in them were 830 nm LED phototherapy, indole-3-acetic acid photodynamic therapy, triamcinolone intralesional injections, and 595 nm long-pulsed dye laser. Despite various therapies, skin lesions of the two patients persisted for 19 and 31 months, respectively.

**Discussion**

The two cases of intractable CGPD in patients receiving GH therapy indicate the possibility that GH may have a role in the pathogenesis of CGPD. In patient 1, CGPD appeared 18 months after starting GH therapy, and in patient 2, CGPD recurred at 2 months after starting GH therapy. The time lag between the initiation of GH and the development of CGPD implies that GH is more likely to be an aggravating factor rather than a triggering factor of CGPD. Although GH is classically defined as a peptide hormone, recent evidence indicates that it may have a cytokine-like action.[3] Various immune cells including T-lymphocytes, B-lymphocytes, monocytes, and neutrophils produce GH, in addition to expressing GH receptors. This suggests the possibility of a paracrine or autocrine effect of GH on immune cells.[4] GH counteracts glucocorticoid-induced immunosuppression by promoting T-lymphocyte proliferation and preventing their apoptosis.[5] GH also modulates immune cell cytokine production. Short-term GH administration in short statured children reportedly increased serum concentrations of interferon-γ, IL-6β, IL-2, IL-12, and TNF-α.[6] Enhanced T-cell survival and increased secretion of Th1 cytokine in response to GH administration may have affected the clinical course of CGPD in our patients.

To the best of our knowledge, this is the first report of an association between CGPD and GH. Since CGPD occurs in the period of childhood corresponding to peak GH production, this association, if confirmed, may describe the role of GH in the pathogenesis of CGPD.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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