Interferon-α Treatment of Molluscum Contagiosum in a Patient With Hyperimmunoglobulin E Syndrome

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ABSTRACT

We report widely disseminated molluscum contagiosum that occurred in a 9-year-old boy secondary to hyperimmunoglobulin E syndrome, a primary immunodeficiency disorder. Cutaneous examination revealed numerous, widespread, skin-colored to translucent, firm, umbilicated papules of varying sizes. They were distributed throughout the perineal and gluteal areas and bilaterally over his lower limbs. A biopsy specimen from his skin lesion demonstrated lobulated epidermal growth that consisted of keratinocytes with large intracytoplasmic eosinophilic inclusion bodies and a central crater. These findings were consistent with the diagnosis of molluscum contagiosum. Many treatments for his skin lesions were ineffective, including physical destruction or manual extrusion of the lesions; cryotherapy; curettage; and topical therapies with phenol, trichloroacetic acid, and imiquimod. The patient was treated successfully with subcutaneous interferon-α for 6 months without any adverse effect.

HYPERIMMUNOGLOBULIN E (HYPER-IGE) syndrome, a rare idiopathic primary immunodeficiency, consists of a severe dermatitis with recurrent abscess formation, respiratory tract infections, and very high titers of serum IgE. Immune dysregulation of these patients leads to recurrent staphylococcal skin abscesses; mucocutaneous candidiasis; pneumonia with pneumatocele formation; extreme elevation of serum IgE; eosinophilia; and distinct abnormalities of the connective tissue, skeleton, and dentition.[1] Although the genetic basis is not known and the central immunologic defect is largely undefined, a genetic linkage was detected between hyper-IgE and chromosome 4. Most cases are sporadic, whereas autosomal recessive or dominant inheritance patterns are seen on many pedigrees.[2]

Molluscum contagiosum (MC) is an infection that is caused by a poxvirus that gives rise to small; benign; white, pink, or flesh-colored; umbilicated; raised papules or nodules located in the epidermal layer of the skin. The prevalence of MC is especially high in immunocompromised individuals. Children with a weakened immune system not only are at greater risk for secondary inflammation but also are prone to lesions that typically persist for prolonged periods.[3] The options for therapy are manifold, including physical destruction or manual extrusion of the lesions, cryotherapy, curettage, imiquimod, retinoids, and interferon-α (IFN-α).[4] We report a patient who has hyper-IgE syndrome associated with extensive MC and was treated successfully with subcutaneous IFN-α.

CASE REPORT

A 9-year-old boy with a long history of severe atopic dermatitis developed widespread, marked MC at the age of 5 years. This persisted and increased in severity such that he was referred for immunologic assessment at the age of 6 years. He first was admitted to the Department of Pediatric Immunology in Uludag University School of Medicine with the complaints of recurrent pneumonia, extensive MC and oral candidiasis. It also was noted that recurrent suppurative otitis media and multiple episodes of pustular and pruritic eczematous lesions, which had left scars on his body had been occurring since infancy. He was an adopted child, and the family history was not known. On physical examination, his height was 124 cm (5th percentile), his weight was 22 kg (3rd percentile),

Key Words: hyperimmunoglobulin E syndrome, Job's syndrome, molluscum contagiosum, interferon-α

Abbreviations: Ig, immunoglobulin; hyper-IgE, hyperimmunoglobulin E; MC, molluscum contagiosum; IFN, interferon

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and his head circumference was 51 cm (25th–50th percentile). His facial skin was rough and thick with pruritic eczematoid rash on his lips (Fig 1). He had scrotal tongue associated with chronic moniliasis. There was a severe eczematoid rash all over the extremities. He also had multiple papular lesions (0.5–1.0 cm in diameter) scattered on the genital region, gluteal areas, and bilaterally over his lower limbs (Fig 2). Discrete, pearl-like, skin-colored, smooth papules had a central umbilication from which a plug of cheesy material can be expressed.

The laboratory results were as follows: hemoglobin, 12.8 g/dL; white blood cell count, 9×10^3 μL with 58% polymorphonuclear cells, 20% lymphocytes, 2% monocytes, and 20% eosinophils on peripheral smear; and platelets, 350 000/mm^3. His serum IgG, IgA, and IgM levels were normal, with an elevated IgE of 65 000 IU/mL (4–269 IU/mL is normal for age). Lymphocyte subset analysis revealed normal ratios of CD3, CD4, CD8, CD19, CD16, and CD56 surface markers. Antibody response to tetanus antigen and the nitroblue-tetrazolium test were found to be normal. The Boyden chamber assay repeatedly disclosed defective neutrophil chemotaxis.

Diagnosis of MC was confirmed by a biopsy that was taken from his skin lesion. The biopsy specimen demonstrated lobulated epidermal growth that consisted of keratinocytes with large intracytoplasmic eosinophilic inclusion bodies and a central crater.

Despite normal levels of IgG, he had been taking intravenous Ig treatment (400 mg/kg every 3 weeks) since the age of 6 years because of recurrent bacterial infections. His past treatment of MC included a 1-year trial of phenol and trichloroacetic acid (4 months) and cryosurgery combined with local imiquimod treatment (8 months), but disease recurred within weeks of stopping treatment. The patient was treated successfully with subcutaneous IFN-α 3 million units subcutaneously 3 times a week for 6 months without any adverse effect. His lesions were crusted over, with the waxy papules replaced by scabs at the second week of the treatment, and considerably receded at the fourth week (Fig 3). There was no recurrence of his lesions within the 5 months after the cessation of the therapy.

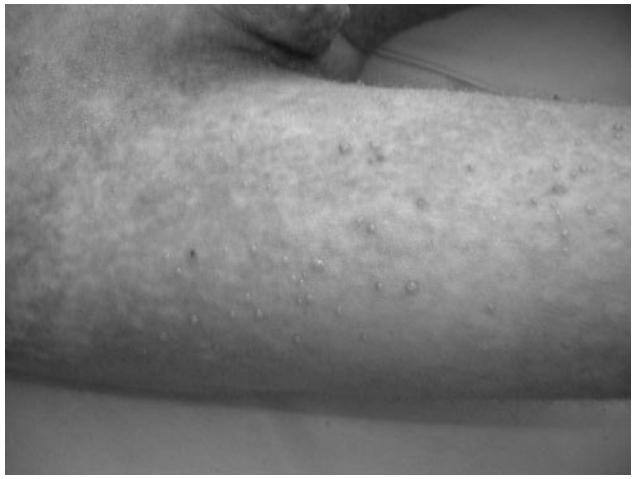

FIGURE 2
Leg of our patient showing multiple papules.

DISCUSSION

The infection of MC is common and produces benign, self-limiting lesions over the skin and mucous membranes, mainly in children and sexually active adults. However, MC can be widespread in immunocompromised states or in conditions such as atopic dermatitis,

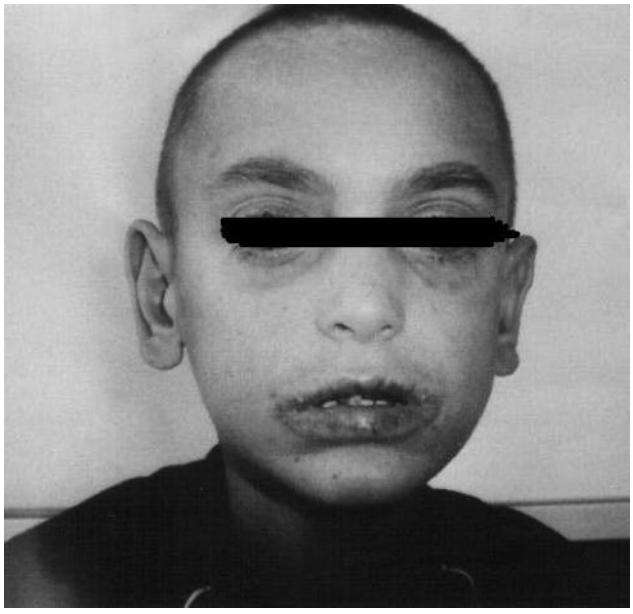

FIGURE 1
Facial appearance of our patient with hyper-IgE syndrome.

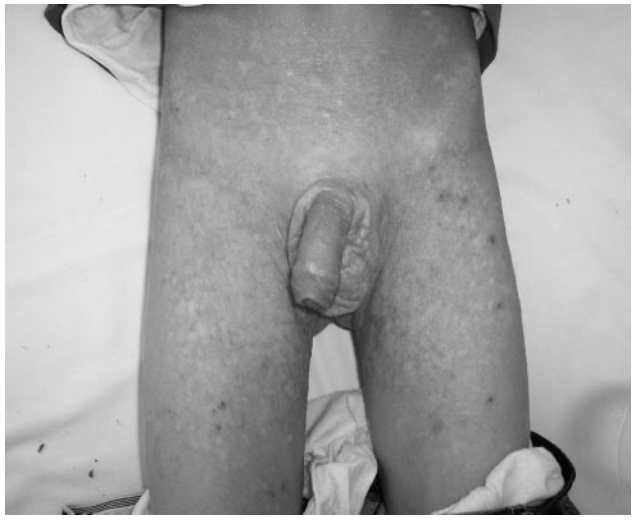

FIGURE 3
Appearance of our patient's lesions after 4 weeks of treatment with subcutaneous IFN-α.

with compromised skin barrier function. Patients with primary immunodeficiencies or HIV infection may have widely disseminated MC that is difficult to treat.[5] Hyper-IgE syndrome also may cause a genetic susceptibility for the development of severe MC infection. Most of the patients have atopic dermatitis that is more prone to MC infection and can develop eczematous areas around lesions.[6] Martins et al[7] described 1 patient with sporadic hyper-IgE syndrome and severe infection with MC. Renner at al[6] recently reported that patients with autosomal recessive hyper-IgE syndrome can develop severe MC infection that is resistant to therapy. Chronic, disfiguring MC infection suggests an increased severity and defective control of viral infection in these patients. Borges et al[8] reported that the lymphocytes of patients with hyper-IgE syndrome had an impaired response to interleukin 12, resulting in decreased IFN-γ production, which could be of key importance in the pathogenesis of the immune response abnormalities to viral antigens in hyper-IgE syndrome. In addition to susceptibility to viral infections, chronic dermatitis is a risk factor for severe MC infection in our patient.

In addition to the commonly administered treatments (physical and chemical destruction), novel treatment opportunities exist, including immunomodulated therapy with imiquimod or IFN-α.[9,10] Topical or systemic immunotherapy with immunomodulators shows potential for effective and patient-friendly treatment of cutaneous viral infections. They generate cytokine milieu biases toward a T-helper 1 cell–mediated immune response with the generation of cytotoxic effectors, and this has been exploited clinically in the treatment of viral infections, including human papillomavirus, herpes simplex virus, and MC.[11] IFN-α treatment is a glycoprotein cytokine that is produced naturally in response to viral infections. IFNs are not directly antiviral but induce production of effector proteins in cells, which inhibit various stages of viral replication. Recombinant IFN-α also has been used as the standard treatment of hepatitis B and C. It has been used both intralesionally and systemically in small numbers of patients with MC.[5,10,12] Hourihane et al[10] reported 2 siblings with combined immunodeficiency, both of whom had extensive MC that was treated successfully with subcutaneous IFN-α. Not only conventional treatment of MC, such as destruction of individual lesions by application of phenol, trichloroacetic acid, and cryotherapy, but also novel immunomodulated therapy with imiquimod cream was not effective in the treatment of our patient with widespread MC. Intralesional treatment with IFN-α also was considered impracticable. Therefore, our patient was treated with subcutaneous IFN-α and gave a dramatic response to the treatment.

CONCLUSION

Our report indicates that widespread MC infection in immunocompromised patients is an indication for subcutaneous IFN-α treatment.

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