Interferon α treatment of molluscum contagiosum in immunodeficiency

Jonathan Hourihane, Elizabeth Hodges, John Smith, Martin Keefe, Alison Jones, Gary Connett

Abstract
A sister (aged 6 years) and brother (aged 8 years) presented four months apart with severe molluscum contagiosum. Both children demonstrated clinical and laboratory evidence of combined immunodeficiency. The extent of skin involvement by molluscum contagiosum precluded conventional treatment as well as intralesional interferon α (IFNα). Both subjects responded well to subcutaneous IFNα.

Keywords: immunodeficiency; molluscum contagiosum; interferon α

Molluscum contagiosum (MC) is a cutaneous pox virus infection that is common in normal children. It is usually a self limiting disease, requiring local treatment, usually only for cosmetic reasons. Patients with primary immunodeficiencies or HIV infection may have “giant” MC or MC that is widely disseminated and difficult to treat.1–3 Interferon α (IFNα) has been used successfully (intravenously and then subcutaneously) in the treatment of papillomatosis of the respiratory tract4 and subcutaneously in chronic hepatitis B in children.5 In patients with HIV, MC can be difficult to treat conventionally.3,6 IFNα has been administered intralesionally with some success.7 We report two siblings with features of combined immunodeficiency who both suffered extensive MC that was treated successfully with subcutaneous IFNα.

Case reports
Case 1 (aged 6 years) is the second child of unrelated white parents. She weighed 3230 g at birth (50th centile) but failed to thrive. She was immunised fully. She was frequently wheezy in the first year of life and was intolerant of cows’ milk and allergic to egg. Asthma is now well controlled by inhaled corticosteroids. Her weight and height have followed the third centile.

From age 1–5 years she had diarrhoea. Eczema herpeticum caused admission to hospital when she was aged 2 years. A right middle lobe pneumonia with effusion was diagnosed at age 3 years (no organism isolated). Immunological testing on several occasions around 5 years of age showed a low CD4 count (absolute CD4 count 300/ml, fifth centile for age) and poor T cell proliferative response to phytohaemagglutinin (PHA). She had a low IgM and raised IgA. She had a normal antibody response to Haemophilus influenzae type b (Hib) immunisation. Tests for HIV infection were negative.

MC developed at age 4 years and 2 months (preceding her brother’s onset by 4 months). The MC was considered too extensive to benefit from cryotherapy. IFNα (Wellferon, Wellcome, Uxbridge, UK) 3 MU subcutaneously three times a week was started at age 5 years. She was started on intravenous gammaglobulin (IVIG) at aged 5½ years because the spectrum of abnormalities of immunological tests was so similar to her clinically more severely affected brother. Despite IVIG treatment, computed tomography of the chest showed progressive bronchiectasis on occasions.

Case 2 (aged 8 years) is more severely affected by immunodeficiency than his sister. He developed eczema at 6 weeks of age and had cows’ milk, peanut, and lentil allergy before the age of 1 year. He received the normal course of immunisations in infancy. At aged 2 years and 5 months he had septic arthritis of his right knee. Hib biotype I was isolated from blood. He had chronic diarrhoea between the ages of 3–5 years and a single isolate of cryptococci was identified at age 4 years and 11 months. Right middle lobe and right upper lobe pneumonia developed at age 5 years and haemophilus was isolated again. Chest computed tomography showed bronchiectasis in the middle lobe.

At age six years he developed a left lower lobe pneumonia complicated by pericardial effusion (haemophilus was isolated from blood). Clinical deterioration despite appropriate antibiotics prompted bronchoscopy and Pneumocystis carinii was isolated from the lavage fluid. Repeated tests for HIV infection have been negative. He has remained on cotrimoxazole prophylaxis since the episode of P carinii pneumonia (PCP) with only one recent recrudescence of PCP (at age 7 years and 5 months), which was responsive to an increased dose of cotrimoxazole. Chest computed tomography at 6½ and 8 years showed progression of bronchiectasis.

He has a low absolute CD4 count (200/ml, less than fifth centile for age), poor response to PHA, low IgM, and raised IgA. There was no specific antibody response to routine immunisations against Hib or diphtheria, although antibody responses to measles, rubella, and tetanus were normal. Pneumococcal vaccination elicited no specific antibody. Despite normal levels of IgG he was given IVIG treatment.
at age 7 years and 2 months because of his poor functional antibody response to bacterial infection.

At age 7 years he developed severe MC (fig 1), probably caught from his sister who had recently started treatment with subcutaneous IFN\textsubscript{a}. He was given subcutaneous IFN\textsubscript{a} and within three weeks there was considerable improvement (fig 2).

Both children achieved approximately 95% clearance of MC with 3 MU IFN\textsubscript{a} given subcutaneously three times a week for six months. Weekly injections were continued for a further three months. The residual MC has not worsened up to the time of writing, six months after discontinuing IFN\textsubscript{a}. Both children are currently awaiting bone marrow transplantation (matched unrelated donors) to correct their underlying immunodeficiency.

Their father, aged 48 years, has had recurrent genital herpetic infections and has had an absolute CD4+ count of 360/ml (just within normal limits) on several occasions. The mother has shown normal results to all tests to date.

**Discussion**

The molecular basis of the combined immunodeficiency in these children and the lymphocytopenia in their father is not known. Clinically the brother is more severely affected than his sister, with life threatening episodes of haemophilus septicaemia and two episodes of PCP. He has CD4+ lymphocytopenia but normal B cell numbers. Quantitative immunoglobulin production is preserved but dysregulated, with raised IgA and slightly reduced IgM. He has low qualitative antibody responses to specific organisms. He currently shows no features of granulomatous or autoimmune disease.

Despite having had only one significant bacterial infection, it is highly likely that his sister is affected by the same immune defect: she has had long standing failure to thrive and diarrhoea, frequent but usually minor chest infections, and similar quantitative and qualitative T cell defects and low IgM values to her brother.

Conventional treatment of MC, such as destruction of individual lesions by application of phenol, curettage, and cryotherapy were not considered feasible because of the extent of the disease. Intralesional treatment with IFN\textsubscript{a} was also considered impracticable. The sustained response of MC to subcutaneous IFN\textsubscript{a} has been dramatic in both children.

The mechanism of action of subcutaneous IFN\textsubscript{a} in these siblings is not known. Interferons are produced by nearly all eukaryotic cells in response to a range of stimuli. Receptor binding induces synthesis of effector proteins, leading to cytotoxic, immunomodulating, and direct antiviral effects. IFN\textsubscript{a} treatment of children with chronic hepatitis B infection accelerates termination of viral replication\textsuperscript{8} and clearance of HBe antigen.\textsuperscript{9} It is reasonable to propose a similar mechanism was active in our patients, although no tissue or sampling studies were done.

There has been a single case report of MC and other opportunistic skin infections developing during treatment of erythroderma, which included IFN\textsubscript{a}-2b.\textsuperscript{10} This patient had idiopathic CD T cell lymphocytopenia. The role of IFN\textsubscript{a}-2b in the treatment of MC is unproven in this patient with immunodeficiency receiving other medications and treatment (5-methoxypsoralen and UVA).\textsuperscript{10}

In immunocompetent children MC is usually a self limiting disease. Adults and children with primary or acquired immunodeficiencies may suffer severe MC, resistant to conventional treatment. Our patients with MC successfully treated with subcutaneous IFN\textsubscript{a} suggest another therapeutic option for those severely affected by MC.

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1 Ben-Amitai D, Hodak E, Garty BZ, Metzker A, Cohen I. Molluscum contagiosum in a patient with common immunodeficiency.

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Figure 1  Molluscum contagiosum in the left axilla of case 2 at the age of 7 years.

Figure 2  Appearance of the left axilla of case 2 after 3 weeks of treatment with subcutaneous IFN\textsubscript{a}.
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