

Giant Molluscum Contagiosum: Does it Affect Truly Immunocompetent Individuals?

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Sir,

Molluscum contagiosum (MC) is a skin infection caused by a double-stranded DNA virus of the family *Poxviridae* manifesting clinically as asymptomatic single or multiple skin-coloured papules with umbilicated centres. It is a universally distributed and very common disease affecting mainly young children, sexually active adults and immunocompromised patients (1). In conditions with altered immunity such as atopic dermatitis, corticosteroid and immunosuppressive therapy, sarcoidosis, leukaemias, Wiskott Aldrich syndrome and AIDS, atypical lesions of MC may occur, often reaching a large size (2). We present here a case of disseminated giant molluscum contagiosum in a patient without past history of immunodeficiency.

PATIENT AND METHODS

A 21-year-old man was admitted to our hospital with a 10-month history of disseminated lesions. Physical examination showed multiple skin-coloured papules and nodules measuring from 4 to 19 mm on the dorsum of the right foot and disseminated umbilicated papules mainly localized in the axillae, trunk and thighs. The foot lesions coalesced to form a large plaque (Fig. 1). He also presented with two verrucous papules on his fingers clinically diagnosed as verrucae vulgaris. The patient denied having any medical condition or current use of immunosuppressive drugs.

Histopathological examination of a biopsy specimen from a nodular lesion of the foot showed a classic picture of MC.

Several tests to investigate for an underlying immunodeficiency were performed, including HIV 1-2 and HTLV 1-2 serologies by ELISA and complete blood count. Lymphocyte phenotyping and chemokine receptors expression were assessed by flow cytometry with Coulter and Pharmingen monoclonal antibodies in a Coulter XL-MCL flow cytometer. Lymphoproliferative assays were as follows. Peripheral blood mononuclear cells (PBMC) were cultured in RPMI-1640 medium (Sigma) with 10% of human AB+serum (Sigma), and stimulated either by *Candida* metabolic antigen (Institut Pasteur, France), tetanus toxoid (Instituto Butantan, Brasil), *Mycobacterium tuberculosis* purified protein derivative (NIBSC, UK), cytomegalovirus antigen and Varicella-Zoster virus antigen (Virology Laboratory, Instituto de Medicina Tropical) or pokeweed mitogen (Sigma) for 6 days, or by phytohaemagglutinin (Gibco) for 3 days. Eighteen hours before harvesting, cells were pulsed with 1 μ Ci of 3 H-TdR, then harvested and counted in a Beta Plate scintillation counter (Wallac). The results are presented as stimulation index.

RESULTS

HIV 1-2 and HTLV 1-2 serologies were negative. Peripheral blood lymphocyte count and T, B and natural



Fig. 1. Multiple umbilicated skin-coloured papules and nodules on the dorsum of the right foot.

killer (NK) cell phenotyping, as well as CD4/CD8 ratio were within normal limits. Conversely, there was a striking imbalance between naïve (90.57%) and memory (9.42%) CD4⁺ T cells identified by the expression of CD45 RA and CD45 RO, respectively, with very low counts of memory cells for age (normal value 51–68%). There was normal expression of chemokine receptors CXCR4 and CCR5 on T cells. Lymphocyte proliferation assay of mitogens was normal but the response to antigens was clearly abnormal, showing no proliferation to *Candida* (0.7, normal 3.35–91.4), *M. tuberculosis* (0.06, normal 4.17–129.4), tetanus toxoid (0.72, normal 3.0–37.4), cytomegalovirus (0.66, normal 2.7–62.8) and Varicella-Zoster (0.65, normal 2.9–16.6).

DISCUSSION

To the best of our knowledge, there are only five reports of giant MC occurring in immunocompetent patients. However, except for HIV serology, no further investigation of immunodeficiency was performed in these patients. Two of the patients were children aged 3 and 5 years, presenting with an atypical scalp mass and a solitary nodular lesion on the sole, respectively (3, 4).

The third patient, a 21-year-old paraplegic man, also had a lesion on his sole. The paraplegia was considered as a contributing factor to the lesion (5). The fourth patient was a 57-year-old woman with giant MC lesions on the forehead and concomitant actinic granuloma on the chest. Both lesions were attributed to sunlight exposure (6). The last patient, a 68-year-old man with multiple cystic tumours on the scalp, face, neck and upper trunk previously considered immunocompetent, died 1 year later due to a lung infection (7).

Host cell-mediated immunity has been considered to play a vital role in controlling and eliminating MC infection. According to Heng et al. (8), immunocytochemical staining of histopathologic samples of persistent MC lesions demonstrated the absence of T-lymphocyte and NK-cell subsets in the underlying dermis, thus suggesting a lack of recognition by the host cellular immunity to the MC viral glycoproteins. Electron microscopy and immunocytochemistry studies have led to two potential explanations for this lack of recognition by cell-mediated immunity. First, on electron microscopy, lipid-like material distributed between the keratinocyte cell membrane and the intracytoplasmic viral inclusions has been demonstrated. In addition, cross-reactivity of antigens of MC bodies with antigens normally present on macrophages has been demonstrated by immunocytochemistry. The expression of viral glycoproteins on the surface of keratinocytes could be hampered by these two non-exclusive ways resulting in an immunologic ignorance.

In this particular case, the findings of normal expression of chemokine receptors CXCR4 and CCR5 on T cells exclude the possibility of increased susceptibility to infection as has already been described for papilloma virus (9). However, the absence of specific lymphoproliferative response to several antigens characterized an anergic status, re-inforced by the very low counts of memory CD4⁺ T cells in our patient, suggests a disturbance of the activation/differentiation of memory T cells, warranting further evaluation.

As illustrated by this case report, atypical or giant molluscum lesions may herald an underlying immunodeficiency, which could be overlooked without a thorough immunologic work-up. Based on previous case reports of 'immunocompetent' patients with only a partial evaluation of their immune system, it remains to be seen whether or not these atypical molluscum lesions can occur in truly immunocompetent patients. Future advances in the field of immunology may elucidate the mechanisms of immunodeficiency in such patients and may lead to the development of additional testing for such defects.

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