Systemic Treatment of Mollusca contagiosa with Inosiplex

GERD GROSS, CHRISTINA JOGERST and ERWIN SCHÖPF

Department of Dermatology, University of Freiburg, Freiburg in Br., Federal Republic of Germany

Gross G, Jogerst C, Schöpf E. Systemic treatment of mollusca contagiosa with inosiplex. Acta Derm Venereol (Stockh) 1986; 66: 76–80.

The ensuing regression of mollusca contagiosa in 7 of 9 children, 6 of whom were suffering from atopic dermatitis, was observed during systemic treatment with inosiplex. In our report the involutional process of mollusca contagiosa did not differ clinically from the inflammatory course observed in spontaneous healing. It is supposed that inosiplex enhances underlying defective immunological mechanisms which lead to a restoration of the host defence. (Received March 12, 1985.)

Gerd Gross, Department of Dermatology, University of Freiburg, Hauptstr. 7, D-7800 Freiburg, Federal Republic of Germany.

Mollusca contagiosa are benign infectious papulo-nodular lesions of the skin which are induced by poxvirus-mollusci, a member of the poxvirus group. Mollusca contagiosa are seen preferentially in children, whereas in adult patients they are unusual (3, 9, 10).

Widespread infections involving hundreds of mollusca contagiosa develop in patients with secondary impaired cell-mediated immunity (CMI) such as chronic lymphatic leukemia, Hodgkin's disease, and during immunosuppressive or cytochemical treatment (9). The same holds true for other viral infections such as viral warts, herpes simplex and herpes zoster (12). It has been reported that patients with atopic dermatitis too are predisposed to such infections leading to clinical pictures known as eczema molluscatum, verrucatum and herpeticatum (3, 9, 10) and chronic fungal infections (6). Increasing evidence suggests that the reason for this predisposition of atopic individuals lies in the functional defect of the host defence (at least in circumscribed areas of the skin) associated with elevated levels of serum IgE than in the chronically irritated eczematous skin itself (3, 10).

The treatment of mollusca contagiosa remains old-fashioned and non-specific. It consists primarily in surgical removal of the lesions either with a sharp curette or a pincette. In addition, a spectrum of locally applied cauterants, irritants, or chemicals such as phenol, trichloracetic acid, podophyllum, which destroy the mollusca, have been recommended (9).

These methods are unsatisfactory since they involve pain and often lead to a relapse of the disease or spreading of new lesions. General anaesthesia is necessary for children especially in cases of widespread lesions. When the mollusca are located on the facial skin, surgery or local treatment should be used with caution, since it may lead to pigmented scars.

The following report illustrates the potential efficacy of systemic treatment with inosiplex (delimmun®, Delalande, Arzneimittel GmbH, FRG) in 7 of 9 children with mollusca contagiosa. Inosiplex is an immunomodulator instigating a cellular host defence which leads to an increase in the total number of lymphocytes, the activity of natural killer cells and the total number of T-helper cells (4, 7). This chemical appears to be helpful in the treatment of subacute sclerosing panencephalitis (7), viral warts (5), herpes zoster (2) and herpes simplex virus infections (4). It was shown recently in a double-blind placebo controlled study that inosiplex plays a role in restoring cellular immunity in moderately

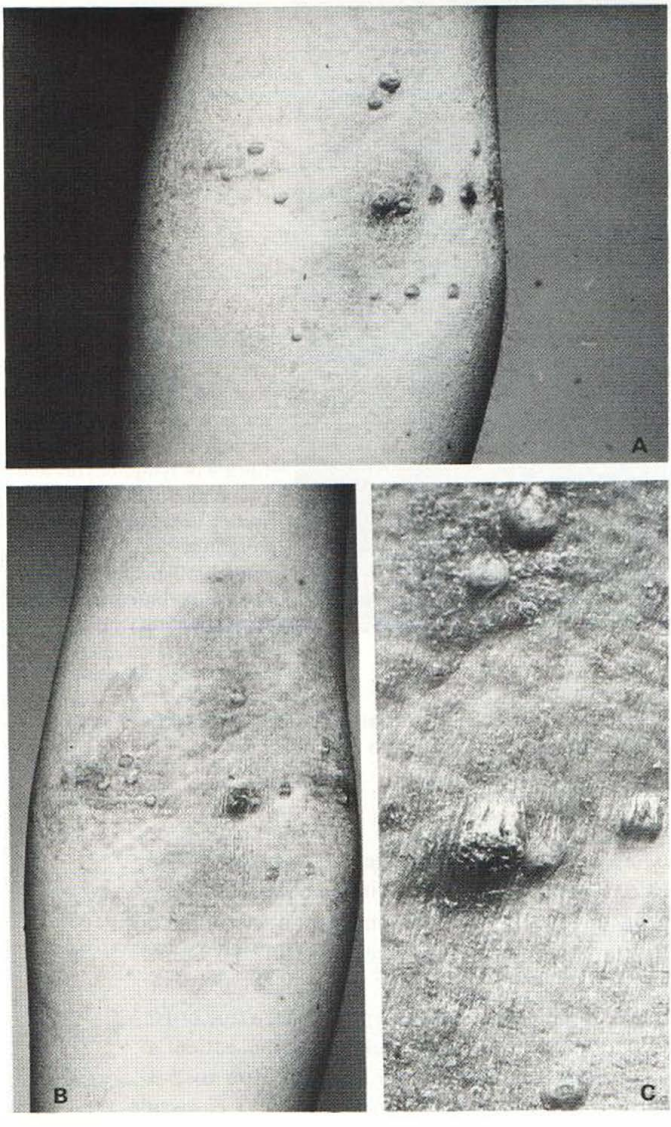

Fig. 1. Inflammatory mollusca contagiosa of the cubital space (Case 1). (A) 9 days after onset of therapy with inosiplex. (B) 2 weeks of therapy: note increase of the eczematous reaction. (C) magnification of (B): inflammation and crusting of molluscum papules.

immunodepressed individuals suffering from chronic lymphadenopathy syndrome and pre-AIDS (Wallace & Bekesi, personal communication).

PATIENTS AND METHODS

Nine children ranging from 4 to 14 years and with an average age of 7 years were treated with inosiplex. Six of these patients suffered from a moderate atopic dermatitis but were otherwise in good health. The mollusca contagiosa were situated primarily on the upper extremities (6 cases) and in one case each on the lateral thoracic wall, on the face and in the axillar fold.

On the average the lesions had developed 4 months prior to the onset of therapy. Before treatment an anamnesis and laboratory and physical examination including photodocumentation were performed. In one case a biopsy of mollusca contagiosa was taken before and after treatment for histology analysis.

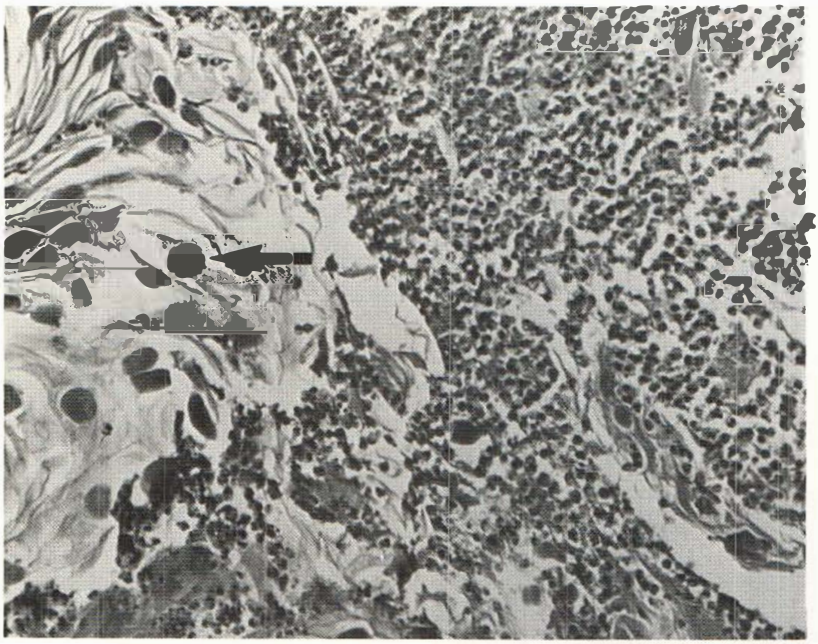

Fig. 2. Histological appearance of an inflammatory molluscum contagiosum during inosiplex treatment (patient 3, 4th week). Dense infiltrate of lymphocytes and round mononucler cells invading areas of degenerated keratinocytes. Molluscum bodies still present (arrow) (hematoxylin-eosin; original magnification, ×10).

Inosiplex was taken orally in a daily dose of 50 mg/kg body weight. The patients were seen weekly and after regression of the lesions a check-up was performed regularly up to 2 months later.

RESULTS

All the patients with the exception of two improved within an average of 3 to 4 weeks. The course of healing was as follows. The lesions were initially itchy, inflamed and in some cases even painful after approximately 10–14 days. This inflammation was confined sharply to the eczematous area, especially in regard to the older lesions (Fig. 1). Some mollusca contagiosa were edematous and increased in size. They then changed colour from pink or yellow to grey, blue-livid or black, finally flattening and producing a fine crust (Fig. 1). The mollusca contagiosa healed without scars 4 to 5 weeks after the patient's initial visit. The inflammation ("molluscum dermatitis"), however, persisted up to 2–3 weeks after successful eradication of the mollusca contagiosa. In one of the 7 cases a limited relapse was noted which responded instantly to a new application of inosiplex.

Histopathology

The biopsy specimen of one case taken during the course of healing revealed signs of an inflammatory reaction surrounding the lesions as recognized in spontaneously regressing mollusca contagiosa (8, 11, 13) (Fig. 2).

DISCUSSION

In 7 of 9 children with mollusca contagiosa regression of the lesions was observed under exclusive systemic treatment with inosiplex. In addition, atopic dermatitis in one of these 7 cases improved without topical treatment.

Thus far mollusca contagiosa have been treated with surgical methods and local irritants which involve a number of side effects such as scarring and pain (9).

The regression of mollusca contagiosa during treatment with inosiplex shows similarities to those cases that regress spontaneously (i.e. "molluscum dermatitis" (8, 11). Inflammation, subsequent blackening and necrosis of the epidermis focusses attention on possible immune mechanisms involved in this process. Histologically the accumulation of inflammatory cells, lymphocytes and histiocytes supports this hypothesis well. Viral warts too such as verrucae vulgares and verrucae planae juveniles often regress in this manner (1, 5, 13). It was demonstrated recently that the same types of warts respond well to the systemic therapy with inosiplex, whereas plantar warts (myrmecia) and conylomata acuminata seem not to be as sensitive to this treatment (5).

In view of these clinical observations one may suspect that inosiplex is helpful in the treatment of both viral warts and mollusca contagiosa. The mechanism involved, however, remains still unexplained. Patients with chronic viral warts or mollusca contagiosa are characterized by their inability to mount an adequate immunological response (1, 5, 13). It appears that immunomodulators such as inosiplex help to restore the host defence leading to eradication of the viral tumors (5).

Inosiplex should be considered a reliable systemic treatment for mollusca contagiosa. Since it is administered orally and devoid of major toxic side effects (4, 5), it can be used safely even for children. In contrast to the alternative treatments for mollusca contagiosa which consist in destroying the poxvirus-transformed epithelial cells, inosiplex seems to act indirectly mediating the immunological response of the host. Thus, one must be aware that its succcess depends on the capability of the host to respond immunologically.

Although preliminary, these findings appear to be positive enough to encourage further clinical studies and immunological monitoring of the effects obtained with inosiplex in mollusca contagiosa. Of special interest is the question why certain patients did not respond to inosiplex. Can one surmise that inosiplex leads to an interaction with the endogenous production of interferone which is shown through individual differences. Furthermore, in future studies special attention will be laid on the influence of inosiplex on the clinical course, CMI, the composition of the stromal infiltate and serum IgE level of atopic individuals with and without mollusca contagiosa.

ACKNOWLEDGEMENT

This study was supported by grants from the Deutsche Forschungsgemeinschaft — Sonderforschungsbereich 31 — Tumorentstehung und Tumorentwicklung.

REFERENCES

1. Brodersen I, Genner J. Histological and immunological observation on common warts in regression. Acta Derm Venereol (Stockh) 1973; 53: 461.
2. Bunta S, Peris E. Immunstimulierende Zostertherapie. Z Hautkrankheit 1981; 56: 1457.
3. Dupre A, Christol B, Lassere J. Dermatite atopique et surinfection à poxvirus. Ann Dermatol Venereol (Paris) 1981; 108: 829.
4. Editorial. Inosiplex: Antiviral, immunomodulator, or neither? Lancet 1982; i: 1052.
5. Gross G. Treatment of viral warts with inosiplex. Akt Dermatol 1984; 10: 197.
6. Hanifin JM, Ray LF, Lobitz WC. Immunological reactivity in dermatophytosis. Br J Dermatol 1974; 90: 1.
7. Jones CE, Dyken PR, Huttenlocher PR, Jabbow JT, Maxwell KW. Inosiplex therapy in subacute sclerosing panencephalitis. A multicentre non-randomized study in 98 patients. Lancet 1982; 1034.
8. Ogino A, Ishida H. Spontaneous regression of generalized molluscum contagiosum turning black. Acta Derm Venereol (Stockh) 1984; 64: 83.
9. Postlethwaite R. Molluscum contagiosum: a review. Arch Environ Health 1970; 21: 432.
10. Pauly OR, Artis WM, Jones HE. Atopic dermatitis, impaired cellular immunity and molluscum contagiosum. Arch Dermatol 1978; 114: 391.

11. Pinkus H, Frisch D. Inflammatory reaction to molluscum contagiosum possibly of immunologic nature. J Invest Dermatol 1949; 13: 289.
12. Spencer ES, Anderson HK. Clinically evident nonterminal infections with herpes virus and wart virus in immunosuppressed renal allograft recipients. Br J Med 1970; 3: 251.
13. Tagami H, Takigawa M, Ogino A, Inamura S, Ofugi S. Spontaneous regression of plane warts after inflammation. Arch Dermatol 1977; 113: 1209.

Remission of Sézary's Syndrome with Cyclosporin A. Mild Capillary Leak Syndrome as an Unusual Side Effect

DOLORES RAMON,[1] ISABEL BETLLOCH,[1] ANTONIO JIMENEZ,[1] RAFAEL BOTELLA,[1] ANTONIO CASTELLS[1] and VICENTE ALBEROLA[2]

[1]*Department of Dermatology and* [2]*Department of Hematology and Oncology, Hospital Clínico Universitario, Valencia, Spain*

Ramón D, Betlloch I, Jiménez A, Botella R, Castells A, Alberola V. Treatment of Sézary syndrome with cyclosporin A. Mild capillary leak syndrome as an unusual side effect. Acta Derm Venereol (Stockh) 1986; 66: 80-82.

A case of Sézary syndrome treated with cyclosporin A is reported. A dramatic cutaneous improvement was obtained within a few days after initiation of treatment. Among the side effects produced were linear purpuric lesions in skin folds and friction areas. *Key words: Drug toxicity.* (Received June 14, 1985.)

D. Ramón, Department of Dermatology, Hospital Clínico Universitario, Avda. Blasco Ibáñez 17, 46010 Valencia, Spain.

Cyclosporin A is an immunosuppressive drug which acts on T cell helper response. It inhibits the production of Interleukin-2 (1) which is needed to support the growth of this lymphocyte sub-population (2).

Its inhibitory effect on the growth of a human leukemia cell line was reported by Foa et al. (3). Totterman et al. (4) found it was selectively cytotoxic and cytostatic on the Sézary cells. Some authors have used Cyclosporin A in the Sézary syndrome treatment (6, 7).

CASE REPORT

A 49-year-old man, was first examined in August 1983. He suffered from an erythrodermia, with itching, palmoplantar keratoderma, subungual hyperkeratosis, and loss of body hair. A skin biopsy revealed the presence in dermis of an infiltrate of atypical mononuclear cells with epidermotropisme and formation of Pautrier microabscesses. White blood cells (WBC) were 20 000, with 70% lymphocytes of which 19% were Sézary cells. Lymph nodes, internal organs, and bone marrow were not affected. Sézary syndrome was diagnosed.

The patient was treated with prednisone (20 mg per day) in combination with low-dose of chlorambucil. Later, the dose of prednisone was increased and 13-*cis*-retinoic acid was introduced. Subsequently, leukapheresis sessions were performed without showing improvement. Treatment was then changed to Cyclosporin A at the dose of 17.5 mg/kg per day and within a week a dramatic cutaneous improvement was observed. Clearing of the erythrodermia and presence of leukodermic areas were noted. Disappearance of the palmoplantar hyperkeratosis and itching were also observed. Blood count remained unchanged.

During the next few weeks the following symptoms were observed: Epigastric burning, transitory increase of arterial tension, paresthesias, tremor, hypertricosis in the face, thorax and arms, gum hypertrophia, gingivitis ulcerative necrotizing, facial aedema and purpuric lesions in friction areas and small skin folds subject to pressure (Fig. 1). Coagulation tests were normal.