

## The Exanthema of Acute (Primary) HIV Infection

### Identification of a Characteristic Histopathological Picture?

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**A male homosexual presented with a skin rash, pharyngitis, fever and lymphadenopathy. The clinical symptoms were suggestive of an acute primary HIV infection. The diagnosis was confirmed serologically. We describe here the clinical and histopathological picture of the exanthema. Biopsy from a papular skin lesion revealed a possibly characteristic pattern. Key words: Viral exanthema; AIDS.**

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In some cases of infection with human immunodeficiency virus (HIV), an acute illness, characterized by skin eruption, fever, sore throat and lymphadenopathy, can occur shortly after the subject has been exposed to the virus (1–7). The illness is of sudden onset and lasts from 3 days up to 3 weeks. The estimated incubation period is 1–8 weeks. A characteristic sequence of serological markers confirming the diagnosis of acute HIV infection has been described (8, 9).

We present here a patient with acute HIV infection and widespread skin lesions. A skin biopsy from a papular lesion showed a possibly characteristic histopathological pattern. This has not been described earlier.

### CASE REPORT

A male homosexual, 30 years of age, who had been examined regularly during a 3 year-period at the outpatient clinic for venereal diseases, presented with an acute exanthema. He also had fever and pharyngitis, which had preceded the appearance of the rash by a few days.

Clinical examination revealed a widespread symmetrical, erythematous and closely set maculopapular or in some areas papulovesicular, sometimes confluent, eruption over the trunk, the upper extremities and the face. There was no itching or scaling. The lymph nodes on the neck were enlarged.

All clinical symptoms, except the lymph node enlargement, cleared in 2 weeks. At a follow-up 2 months later there was generalized lymphadenopathy.

### Immunological findings

At the time the skin rash occurred, no HIV antibodies were

detectable in the serum. The presence of HIV antigen was proved. HIV antibody screening was performed with commercial enzyme immunosorbent assay kits, ELISA (Abbott Laboratories, Wellcome Diagnostics). HIV antigen was detected by an enzyme immunoassay (Abbott Laboratories). Five weeks later the patient had seroconverted and HIV antibodies were demonstrable with ELISA tests and confirmed with Western blot. At this time, HIV antigen could no longer be detected.

T lymphocyte subsets were analysed by using a fluorescent-activated cell sorter analyser and fluorescein-conjugated monoclonal antibodies to CD4 and CD8 on two occasions: 7 months before the appearance of the primary HIV infection and 2 months after the acute illness. There was a 40% reduction in the number of circulating CD4+ cells ('T helper cells') and a 58% increase in CD8+ cells ('T suppressor cells') resulting in an inversion of the CD4+:CD8+ ratio when comparing the T cell subsets before vs. after the acute HIV infection.

### Histopathology

A punch biopsy was taken from an apparently papular efflorescence located on the chest. It was fixed in 10% formalin, paraffin embedded, cut serially and stained with hematoxylin-eosin. Some sections were also stained according to van Gieson and with PAS.

The investigation showed a well circumscribed dense cell infiltrate in the dermis, situated in and around a hair follicle. The infiltrate, which partly destroyed the follicle, was made up of small lymphocytes. No blast cells could be identified. There was a slight but distinct admixture of non-segmented neutrophils. Histiocytes were not seen and plasma cells only occasionally. Above the hair follicle there was a single epidermal vesicle due to necrosis of the epithelial cells. The vesicle engaged the entire thickness of the epidermis. It contained a few lymphocytes and a few neutrophils. Fig. 1. The surrounding epidermis was normal. There was a slight subepidermal edema. In the upper dermis around small vessels and around an eccrine sweat duct, sparse cell infiltrates with the same composition as the follicular infiltrate were seen. There was no vasculitis.

### DISCUSSION

Since 1984, several reports have described the clinical picture of acute HIV infection and the subsequent seroconversion to HIV (1–7). The patients display an array of symptoms, which include fever, malaise, sore throat, lymphadenopathy, exanthema, leukopenia, thrombocytopenia, myalgia, arthralgia, nausea, diarrhea and headache. Skin rash is one of the most common symptoms. In the two largest series of pa-



*Fig. 1.* A hair follicle in the dermis is infiltrated and surrounded by small lymphocytes. Above the follicle there is an intra-epidermal vesicle due to necrosis of the epithelial cells. It contains a few lymphocytes.

tients on record, 7/11 and 15/20 had skin lesions (2, 9). In most cases the rash is described as a non-pruritic, non-scaling macular or maculopapular exanthema. In one patient papulovesicular efflorescences,

as in our case, were also observed (7). In 2 cases there were small ulcerations on the penis and scrotum (6, 7). The most common sites are the trunk, face, neck and upper part of extremities, but even the palms and soles can be involved (2, 4). In a few cases enanthema or small ulcers in the oral cavity have been noticed (4-7). The intensity of the rash varies. Vesicles, sometimes progressing to small ulcers, probably occur only in severe cases.

The establishment of HIV antigen in serum and the isolation of HIV from cell-free plasma and from blood mononuclear cells in the absence of antibodies during the acute illness and the disappearance of the antigen later on, clearly indicate that there is in HIV infection, as in other generalized virus infections, a period of viremia before the antibody response (2, 8, 9).

Many systemic viral diseases are accompanied by exanthema. It is known that this can either be due to a direct cytotoxic effect of the virus as in varicella, or can be the result of a T cell mediated immunoreaction as in rubella.

Ringler and co-workers (10) have observed that a transient erythematous maculopapular eruption occurred in rhesus monkeys shortly after infection with a T-cell tropic retrovirus, simian immunodeficiency virus (SIV). This virus is very similar to HIV. The authors investigated biopsy specimens taken from the rash in SIV inoculated rhesus monkeys with electron and immunoelectron microscopy, monoclonal antibodies and light microscopy. Histopathologically the exanthema was characterized by perivascular predominantly mononuclear inflammatory infiltrates in the upper part of the epidermis, variable epidermal injury, and endothelial cell hypertrophy and degeneration. On the basis of their immunological and electron microscopic observations, the authors suggested that the exanthema associated with early SIV-infection is caused by a T cell mediated immunoreaction, potentially directed against Langerhans' cells. Their observations may correspond to our findings of a dense lymphocyte infiltrate associated with an epidermal vesicle due to necrosis.

A more conclusive concept of the histopathology and the pathogenesis of the rash in acute HIV infection must await further investigation. However, acute HIV infection is rarely recognized. Should it be identified, it is essential to take the biopsy specimens when the rash is in its prime. Therefore the opportunities to obtain significant skin samples are few. This is why we have judged it worthwhile to present this

single case with what we consider to be a histopathologically characteristic skin lesion.

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