

An immunofluorescent study of the ampicillin rash

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Summary

The aetiology of the ampicillin rash is uncertain although numerous theories have been proposed—mainly immunological. One such concerns the presence of anti-epithelial antibodies which have received conflicting reports in the literature. In this study, skin biopsies from three patients with a maculopapular ampicillin-rash were studied by immunofluorescence to investigate the presence of anti-epithelial antibodies. However immunofluorescence for IgG, IgM, IgA and C₃ was completely negative so that we were unable to provide any support for this particular hypothesis.

Introduction

The aetiology of the maculopapular rash commonly induced by ampicillin remains unknown. One possibility is that it has an immunological basis. In this context one study (Fellner *et al.*, 1973) showed the presence of IgG anti-epithelial antibodies in the serum of thirteen patients with a penicillin-induced rash. Of particular interest was the demonstration, in two of three skin biopsies, of epithelial intercellular-staining specific for IgG by direct immunofluorescence. One of these rashes was due to ampicillin, the other being unspecified. However another study (Webster & Thompson, 1974) in which a single biopsy from an ampicillin-induced rash was examined by immunofluorescence showed no staining for IgG or any other immunoglobulin or complement. In view of these conflicting results we set out to collect skin biopsies from patients with ampicillin rashes for immunofluorescent analysis.

Materials and methods

Skin punch biopsies of 4 mm were taken from three patients who had developed a clearly defined maculopapular rash after treatment with ampicillin. Care was taken to exclude any rashes in which another drug or the underlying condition could be implicated.

The biopsies were snap frozen in liquid nitrogen and sectioned at 4 μ m in a cryostat.

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Sections were air-dried and overlain with commercially available fluorescein labelled anti-human IgG, IgM, IgA and C₃ (DAKO, Mercia-Brocades, U.K.) which are extensively used in routine diagnosis. After washing in PBS the sections were mounted in glycerine and examined with a Leitz ortholux microscope equipped for fluorescence microscopy. Additional sections were stained with haematoxylin and eosin for histological examination. Controls were prepared by treatment with unlabelled antisera followed by fluorescent antibodies.

Results

Sections stained with haematoxylin and eosin confirmed the non-specific microscopic appearance of the ampicillin rash in all three cases. The epidermis showed mild intercellular-oedema with a mild perivascular infiltrate of lymphocytes and histiocytes in the upper dermis. However, in all three cases, immunofluorescence for IgG, IgM, IgA and C₃ was completely negative.

Discussion

The results achieved do not provide any direct evidence of an immunological basis for the ampicillin rash. In addition they would suggest that the anti-epithelial antibodies which have been described (Fellner *et al.*, 1973) are a sporadic occurrence rather than a constant finding as in *Pemphigus vulgaris* (Beutner & Jordan, 1964).

Numerous studies of the ampicillin rash have all failed to uncover an aetiological basis. It is clear, however, that it differs from the classical penicillin-rash in having no involvement of IgE or skin hypersensitivity to benzylpenicillin (Kraft & Wide, 1976). Levels of specific penicilloyl-antibodies of both IgG and IgM classes are similar in patients receiving ampicillin whether or not they develop a rash (Collaborative Study Group, 1973).

The most important clinical implication of the study reported above (and of the other investigations showing little or no evidence of an immunological basis for the ampicillin rash) is that they should be distinguished from the classical rashes of penicillin hypersensitivity so that the patient is not denied penicillin later, should it be needed. In fact, several authors have reported that even continuing ampicillin therapy in spite of the rash is not followed by any worsening of symptoms (Patel, 1967; Crow, 1970; Collaborative Study Group, 1973).

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