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CORRELATIVE STUDY OF RUBELLA ANTIBODY TITRE, BASEMENT ZONE ANTIBODY TITRE, AND IgG CONTENT OF SERA OF PATIENTS WITH BULLOUS PEMPHIGOID

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Abstract. In 22 sera from 15 patients with bullous pemphigoid, basement zone antibody titres and rubella antibody titres were investigated. The mean rubella antibody titre showed a rise of 2½ titre steps in the sera as opposed to a control group of the same age. Calculations showed a correlation coefficient of 0.66 between the level of the antirubella titre and of the basement zone antibody titre. A parallel could be observed for the duration of one year between the development of the rubella antibody titre and the basement zone antibody titre in the case of one female patient. The overall IgG concentration did not appear to be a function of the titre level for rubella antibodies.

In the investigation of etiological factors in dermatoses, some groups have recently undertaken a serological approach (9, 10, 12) on the theoretical basis of some novel discoveries relating to the occurrence of persistent virus infections (5, 11) such as have been known for some time in animal pathology (8). Likewise, some diseases from which human beings suffer have been recognized as being associated with persistent infections, e.g. recurrent herpes simplex and congenital rubella infection (5, 11). The findings for such human disease have been fragmentary. Either virus-like particles could be shown, such as in the case of lupus erythematosus (6), or it could be demonstrated that antibodies to various viruses were present in cases of diseases that could not be specified etiologically (9, 10, 12). Usually only a single determination was performed in which increased antibody titres were detected, whereas investigations dealing with titre development over a period of time have seldom been undertaken.

Elevated antibody titres against measles and parainfluenza virus type 1 in the sera of patients suffering from lupus erythematosus and like diseases have been found by Phillips & Christian (9). Since the role that is played by viruses as possible eitiological factors in bullous dermatoses has recently been brought up for discussion again, particularly by Jablonska et al. (7), and inasmuch as, moreover, an elevated rubella antibody titre has been found in the serological examination of some patients suffering from bullous pemphigoid (own findings), we have determined the rubella antibody titres in sera from 15 patients showing basement zone antibodies. We looked for possible correlation among a variety of criteria.

MATERIALS AND METHODS

Twenty-two sera from 15 patients with bullous pemphigoid were studied, mostly at the inception of the disease. In a few cases, follow-up studies were also possible. The patients received no corticosteroids or cytotoxic drug therapy during the period of study.

The determination of the rubella antibody titres was performed using the hemagglutination-inhibition test (1). The investigation of basement zone antibodies was carried out using indirect immunofluorescent staining according to the procedure of Beutner et al. (2). Cryostat sections of guinea pig tongue served as antigenic substrate. Fluorescein-conjugated anti-IgG sera were furnished by the Behring Co. The findings were then assessed objectively by three researchers. Details as to the method of procedure have been described elsewhere (3).

RESULTS

The arithmetic mean rubella antibody titre from the 22 samples of sera taken from 15 patients was 1 : 102 ($^2\log M = 6.95$ with $s = \pm 1.17$). A comparison with previously determined (4) corresponding values for healthy test persons of the same age group ($^2\log M = 4.18$ with $s = \pm 1.51$) revealed that the entire group of patients suffering from pemphigoid had a rubella antibody titre of, on average, 2½ dilution steps

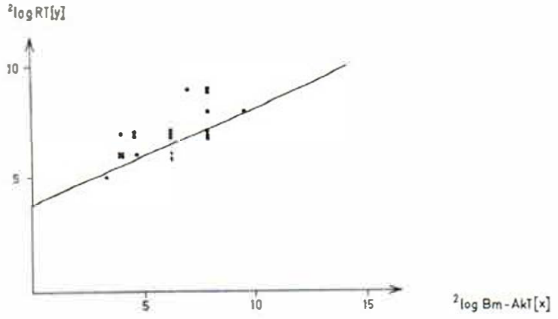

Fig. 1. Titre determination (rubella antibody titre and basement zone antibody titre) in 22 serum samples. The regression straight line derived from these two variables is illustrated. *Ordinate* (*y*): ²log rubella antibody titre (RT); *abscissa* (*x*): ²log basement zone antibody tire (Bm-AkT).

higher than the control group. This difference between the average values proved to be highly significant in the statistical calculation on the 0.3% level.

These patients were additionally examined in parallel determinations using separate serum samples with respect to the question of whether there were any indications of a direct quantitative relationship between rubella antibody titres and basement zone antibody titres. Assuming linearity, a calculated correlation coefficient of $r = 0.66$ suggests with adequate probability that there is in fact a positive correlation (Fig. 1). In assessing such findings, we make reference to Wallis (14): "An association found in a poorly statistical investigation made on an

Fig. 2. Observation of rubella antibody titre, basement zone antibody titre and the immunoglobulin G (IgG) concentration for a period of 11 months in the case of one 81-year-old female patient. *Ordinate:* ²log rubella antibody titre (RT) and basement zone antibody titre (Bm-AkT), respectively; *abscissa:* time in months. There was an approximate parallel development of both titres at almost constant IgG values.

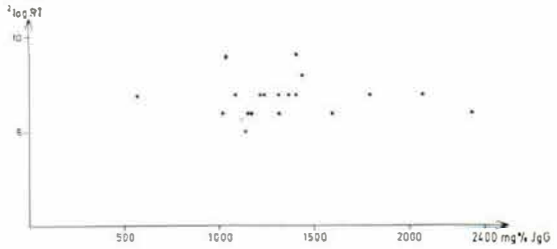

Fig. 3. Determination of the rubella antibody titre and the IgG contents in 19 serum samples. *Ordinate:* ²log of rubella antibody titre (RT); *abscissa:* IgG contents in mg%. No correlation was discernible.

existent population, by which I mean an investigation which is retrospective as regards either of the variables concerned, however, strongly it may suggest association as a presumptive conclusion, is tentative until it is corroborated fully by means of experiment."

For one case of bullous pemphigoid showing elevated rubella antibody titres (up to 1:256), four determinations performed over the period of a year indicated a rubella antibody titre variation of only two titre dilution steps while the titre of the basement zone antibodies varied over three such steps (Fig. 2).

We have also investigated the question of whether there was a correlation between titre level of the rubella antibodies and the IgG-content of the corresponding serum in patients suffering from bullous pemphigoid. Fig. 3 shows that such a relationship was not ascertainable.

Measurements of basement zone antibodies (Fig. 2) in parallel with simultaneous quantitative determinations of IgG that were performed on a patient suffering from bullous pemphigoid, also revealed unequivocally that the IgG content of the serum had remained practically constant during the entire span of the investigation, in spite of repeated titre variations in basement zone antibodies.

DISCUSSION

Although Phillips & Christian (9) as well as other investigators initially considered that the measles-antibody titre rises in the case of lupus erythematosus and similar diseases are an indication of chronic virus infections, they later concluded on the basis of a subsequent investigation (10) that significant changes in the range of antibody titres against mea-

sles could result, firstly, from changes in the entire IgG level, without the necessity of a reinfection with measles and that, secondly, patients having an elevated level of polyclonal IgG could show a rise in the measles antibody titres. In this manner these authors explain the elevated titres against measles in systemic lupus erythematosus. The interpretation of Phillips & Christian (9) could be confirmed neither by the present investigations of rubella antibody titres with a group of patients suffering from bullous pemphigoid, nor in the control studies, following titre development over a period of time, as were performed on individual patients.

An appraisal will have to be made on the basis of the rubella antibody titre constellation found by us to exist in patients suffering from bullous pemphigoid, to find out whether or not we are here concerned with cross-reacting antibodies of low specificity within the framework of an auto-immune disease (13).

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