ACUTE SCARLATINIFORM DERMATITIS FOLLOWING INJECTION OF TOXOID-ANTITOXIN

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As I am not aware of any report of a similar reaction following the use of toxoid-antitoxin in diphtheria prophylaxis, the following record of a troublesome allergic dermatitis may be of interest to those engaged in active immunization against diphtheria.

A healthy girl, aged 16, whose work brought her constantly into contact with diphtheritic infection, wished to be immunized. She was Schick-tested on July 14th, 1932, and gave a positive and pseudo reaction. On July 21st a 1 c.cm. dose of toxoid-antitoxin was injected into the region of the deltoid insertion, and next day a reaction about 1½ inches in diameter resulted at the site of inoculation, and she had a feeling of lassitude and malaise. On July 24th a slight itching erythema (somewhat like "prickly heat") appeared on the neck and chest, but its connexion with the injection was not realized. On July 28th a second injection of 1 c.cm. T.A.M. was given, a well-marked local reaction again occurring at the site of inoculation. Two days later the skin erythema flared up in an acute dermatitis, spreading from the neck and chest to the back, the abdomen, then to the arms, legs, and head, until the whole body was involved, with the exception of the hands and feet.

The eruption was bright red in colour, the skin hot, dry, and rather itchy, though not markedly so. Peeling in moderately large flakes began about August 2nd (nine days after the onset), the skin feeling dried up and rendering movement uncomfortable, and in fact painful.

On August 9th, as the condition showed no sign of improvement, and there was marked inflammation of the skin with coarse, flaky desquamation, I sent the patient to see a dermatologist, who regarded the condition as a "sensitization" eruption, arising as an erythema scarlatiniforme.

After about a week's treatment the acute stage of the skin eruption settled down, but the coarse desquamation continued for another week. In view of the disturbance following the injections I decided it would be extremely risky to complete the immunization course by giving the third 1 c.cm. dose of T.A.M. On October 4th I again Schick-tested the patient, the result being pseudo and doubtful positive. Having given several thousand injections of toxoid-antitoxin without any more notable sequelae than in a few cases a localized reaction, and rarely a slight transient constitutional disturbance, I was interested to confirm as far as possible my opinion that the dermatitis was the direct result of the toxoid-antitoxin, and was not purely fortuitous. It was clear that the only positive way by which to confirm the T.A.M. as the exciting cause was to repeat the 1 c.cm. doses, and obviously this course was out of the question. Early in December I again Schick-tested, and, obtaining a pseudo and negative result, I decided to observe carefully the effect of a small dose of T.A.M.; 0.1 c.cm. was given subcutaneously on December 6th, and that evening the temperature rose to 101.1° F., and on the following day the site of the injection was very tender, the surrounding skin red and indurated, and there was general malaise. On December 8th the area was still well defined, about 1½ inches in diameter, the arm being stiff and tender on movement. The morning and evening temperatures were just under 100°. The temperature readings on December 9th were 99.4° (a.m.) and 100° (p.m.), and the reaction was subsiding. On December 10th the temperature remained normal, the patient felt well, and the site of injection was no longer tender or inflamed. In view of the apparent marked intolerance of the patient to the toxoid-antitoxin mixture, I decided to try the effect of a skin test, using a dilution of 1 in 100 of T.A.M. A 0.2 c.cm. intradermal injection was given in the forearm. In twenty-four hours there was a well-defined inflammatory area about 20 mm. in diameter. This persisted for about forty-eight hours, and was somewhat

indurated and tender. As I had previously had injections of T.A.M., and was also a pseudo and negative reactor, I injected a similar dose of the dilute T.A.M. intradermally in my forearm as a control, and in twenty-four hours there was a faint flush, without induration or tenderness, which faded by the following day. The result of this test added further confirmation that the patient was very sensitive to even small doses of toxoid-antitoxin. A 0.2 c.cm. intradermal injection of a 1 in 100 dilution of toxoid (M.T.) gave rise in the patient, and in myself as control, to a faint 10 mm. flush, which disappeared within twenty-four hours.

After consultation with Dr. R. A. O'Brien, I carried out skin tests with dilutions of the constituents of the toxoid-antitoxin mixture in an endeavour to ascertain which of the constituents was responsible for the peculiar allergic reaction. On February 28th I made three intradermal tests, using 0.2 c.cm. of a 1 in 100 dilution of the antitoxin serum, 0.2 c.cm. of a 1 in 100 dilution of peptone, and 0.2 c.cm. of a 1 in 100 dilution of veal infusion. That evening there was a well-marked and painful reaction, 5 cm. by 3 cm., at the site of the injection of antitoxin. The following day this area was tender, with a definite palpable raised margin, similar to an urticarial wheal. By March 3rd this reaction was practically gone. There was no reaction to the injections of peptone and veal infusion. Three similar injections in my own case as a control gave rise to no local reaction whatsoever.

REMARKS

There are three methods of explaining the disturbance which commenced toward the end of July: (a) that it had no relation to the injection on July 21st or 28th; (b) that the patient showed the uncommon type of very acute sensitivity to serum; (c) that she was acutely sensitive to the products of metabolism of diphtheria bacillus, which are found in toxoid, and which, in very rare highly sensitive people, may cause unusually troublesome local or general reactions.

The only argument in favour of (a) is the extreme rarity of a dermatitis of the kind after the use of the English toxoid-antitoxin mixture or the American toxin-antitoxin mixture. Since the patient in December reacted acutely to 0.1 c.cm. injected subcutaneously, and in February showed an unusual reaction after 0.002 c.cm. of T.A.M. intradermally, it is probable that the dermatitis was due to the injection of T.A.M. In order to find out with certainty which constituent was responsible it would have been necessary to inject subcutaneously, on separate occasions, into the patient, the constituents of the T.A.M., and see whether the fraction of serum, of toxoid, of peptone, or of veal infusion would produce another attack of dermatitis. Although the patient was very helpful, it appeared quite unjustifiable to do an experiment scale, and the most that could be done was to carry on the intradermal tests with serum, peptone, and veal infusion in February. All that we can be sure of is that the patient was, at this date, unusually sensitive to serum, and we must rest satisfied with the possible explanation that the minute amount of serum in the original injection of 1 c.cm. of T.A.M. had caused the dermatitis. There was no trace of asthma or any other "allergy" in the previous history of the patient or of her family.

SUMMARY

A troublesome exfoliating dermatitis occurred in a girl of 16, following the injection of two doses of 1 c.cm. of T.A.M. given within a period of seven days. The dermatitis was possibly due to an acute sensitivity to serum.

I am indebted to the patient for her willing co-operation in submitting to the tests, to Dr. S. Watson Smith of Bourne-mouth for his clinical report on the skin condition, and to Dr. R. A. O'Brien for supplying the test constituents of the T.A.M., and for his valuable critical suggestions.