Medical Memorandum

Anaphylactic and Purpuric Manifestations due to Procaine Penicillin G in Aqueous Suspension

Although many millions of penicillin injections are given each year in almost every corner of the globe, the incidence of reported serious reactions is amazingly low. With its indiscriminate use, many of the drug's serious potentialities have often been overlooked, and it may be with surprise that one reads of 15 reported deaths in a period of 18 months from March, 1952 (Kern and Wimberly, 1953), and of a series of 20 unreported deaths collected by Welch and his co-workers (1953) by sending questionaries to 95 large general hospitals in the country. Other serious reactions that have been reported include anaphylactic shock (Pick and Patterson, 1953), peripheral neuritis (Kolb and Gray, 1946), convulsions (Talbott, 1948), exfoliative dermatitis (Langdon, 1950), and severe serum-sickness type of reactions (Keefer *et al.*, 1943). Mention, too, has been made of the possible relationship of penicillin reactions to the later development of periarteritis (Harkavy, 1952) and lupus erythematosus (Gold, 1951).

A case of unusual penicillin sensitivity manifested by purpura and anaphylactoid type of reaction is here reported. Purpura (Criep and Cohen, 1951) is not a particularly common complication of penicillin administration, and its association with anaphylaxis is even less common. However, there have been reports of fatal reactions involving purpuric manifestations (Welch *et al.*, 1953). Cases have been reported of purpura as the sole manifestation, of purpura associated with other skin lesions or with serum-sickness type of reactions. Anderson (1947) reports a case of purpura associated with melaena and hematuria. In all cases so far the platelet count has been reported as normal.

Case Report

A healthy white man of 28, with no past or family history of allergy, had always been in good health and to his knowledge had never received penicillin in any form. He had received procaine for dental work on several occasions without untoward reaction. His only complaint was that since serving in the second world war he had had a persistent mild recurrent epidermophytosis.

For a month before his hospital visit he had had a mild folliculitis of one buttock, which in the last two days had begun to spread so that he had developed an area of cellulitis with a fluctuant centre. There were no constitutional symptoms.

Prior to incision he was given 600,000 units of procaine penicillin G in aqueous suspension into the gluteal region. There was no immediate reaction, but four hours later he developed a generalized burning of the skin of the legs and trunk, and about an hour later, while urinating, noticed the development of a purpuric rash on his legs and in his groin. On examining himself further, he noticed that the rash was also present in his antecubital fossae and around the neck band. He was not alarmed, as he assumed that he was having a reaction to penicillin, having heard of and seen this type of thing before. He kept on working at his job as a truck helper. However, nine and a half hours after the injection he very suddenly felt quite ill and became apprehensive, pale, dizzy, and nauseated. His bowels moved and he had profuse watery stools.

On physical examination the patient was well nourished and well developed. He was pale, anxious, and sweating. His temperature was 97.6° F. (36.4° C.), pulse 120, and blood pressure 84/60 (usual blood pressure 120/75). Examination of his heart, lungs, and abdomen was unremarkable, but all over the body were scattered petechiae. These were widely scattered on the arms and upper trunk, but were marked, confluent, and ecchymotic on the legs and in the groin. There was no unusually severe reaction at the site of the injection. The rash was also confluent in the antecubital fossae and around the neck. No petechiae were noted on the mucosal surfaces. At this time the hands and feet were slightly swollen. The tourniquet test (80 mm. for five minutes) was strongly positive.

He was immediately treated with adrenaline, ephedrine, and tripelennamine, and his anaphylactic symptoms regressed rapidly, his pulse and blood pressure returning to normal. Although for the next eight hours he kept on with the ephedrine and tripelennamine, his rash continued to spread. At the end of this time the rash no longer spread and he retired to bed, spending a restless night. There was minimal itching of the affected areas. At the height of the rash he showed 10 to 15 red blood cells per high-power field in his centrifuged urine specimen.

Next day he was taken off all medications. He was kept in bed for a week, making an uninterrupted clinical recovery, the skin lesions fading, with desquamation over the affected areas. Laboratory studies 24 hours after the onset of symptoms showed:—Blood: haematocrit, 48%; red cells, 5,610,000 per c.mm.; white cells, 14,200 per c.mm.; differential count normal except for 6% eosinophilia; red cells normal on smear; platelets, 202,000 per c.mm.; bleeding-time, clotting-time, and clot retraction were all within normal limits. The tourniquet test (five minutes at 80 mm. Hg) was positive. Urinalysis showed a trace of albumin and 10 to 15 red blood cells per h.p.f. Culture of pus taken from abscess at time of incision showed *Staphylococcus albus* resistant to penicillin.

Five days after onset the laboratory findings had returned to normal with the exception of the leucocytosis, which had risen to 23,000 with a shift to the left, and 4% eosinophils. The leucocytosis gradually subsided, so that within three weeks after the onset of the illness it was 10,000, with a normal differential.

Scratch tests to penicillin G solution and to procaine were negative, but there was a slight weal when using the procaine and penicillin G in aqueous suspension. Permission to inject intradermally dilutions of this was refused. Subsequent patients were given injections from the same bottle that was used on this patient without adverse effects.

Comment

It would seem that this was a case of severe reaction to procaine penicillin G in aqueous suspension in a patient in whom there was no knowledge that he had ever received penicillin before. However, it may be that he actually had had it prescribed for a minor laceration or skin lesion in the past without his knowledge when this type of medication was used locally rather extensively, or he may have had a cross-sensitivity with one of the fungi which had caused his athlete's foot, for this cross-sensitivity has been reported (Peck *et al.*, 1948). Although prior skin testing and questioning probably would not have helped in the decision to administer the penicillin, this case emphasizes the caution necessary in giving this drug, especially in combination with another foreign substance such as procaine. As it turned out, the organism was insensitive to the drug, and the only potentialities procaine penicillin had were for harm in this case, and time alone will tell whether any more serious manifestations are likely to follow these immediate severe anaphylactoid reactions.

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