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A FATAL ANAPHYLACTIC REACTION TO ORAL PENICILLIN

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NUMEROUS instances of anaphylactic reactions following the parenteral administration of penicillin have been recorded in the literature. However, there have been comparatively few such cases reported from oral penicillin therapy. Only two of the patients died. To our knowledge the following case report represents the thirtieth described case of anaphylaxis from oral penicillin and the third fatality. It includes a complete postmortem examination and an interesting family history.

In 1953, Pierce¹ reported the first anaphylactic reaction following oral penicillin therapy. About the same time, Mayer and his associates² reported six anaphylactic reactions from parenteral penicillin administration, and noted that the one fatal reaction had been preceded by a fainting episode upon the use of a penicillin troche. Welch and associates³ conducted a survey of severe antibiotic reactions and learned of one fatal reaction to oral penicillin. This case has been summarized in an article by Weiner and colleagues,⁴ who listed the autopsy diagnoses of mild pulmonary edema, cardiac dilatation, and anaphylaxis. Weiner and his group added a nonfatal anaphylactic reaction of their own, and summarized another case reported to them by Feinberg. Case reports of twenty additional nonfatal shock-like reactions to oral penicillin,⁵⁻¹⁸ and three from penicillin lozenges¹⁹⁻²¹ have been published. The second fatal shock reaction from oral penicillin therapy was reported in 1957 by Mason.²² Autopsy examination was not permitted in Mason's patient. Welch and co-workers³ and Burdick²³ have alluded to other similar nonfatal reactions and, in a recent nation-wide survey, Welch²⁴ counted forty-nine anaphylactic reactions from oral penicillin preparations out of a total of 793 such reactions from all forms of penicillin. However, no specific case information was recorded.

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CASE REPORT

M. P., a 21-year-old Negro man—an animal caretaker, complained of headache on Aug. 14, 1957, and took aspirin. He had headache the next day and complained of "catching a cold." Immediately after supper, on his own initiative, he took one oral dose of penicillin powder (1,000,000 units of penicillin G sodium) in water. Immediately afterward he developed a hacking cough, with a strangling or choking sensation. Within a minute he fell back, bumped his head on the floor, jerked his head three times, then got up on his feet only to slouch down again. He was coughing at this time. A swelling of the nose and mouth, with mucoid nasal discharge, was noted. The patient's father, who related this history, helped him up, but the patient became limp. The father removed the patient's dentures and found the pulse to be present, but observed no coughing, dyspnea, or sweating. The patient seemed unconscious. He became incontinent and developed an ashen color with circumoral pallor. En route to the hospital the face twitched to the left side and the head jerked to one side. At the hospital more twitching was noted and the patient was limp. No pulse was present. The patient was pronounced dead approximately twenty to thirty minutes following the onset of symptoms.

Prior to this illness the patient had been considered in good health. He was a nervous person, easily excited and upset and, at times, somewhat depressed. In the year before his death he had gained thirty pounds, and weighed approximately 200 pounds. There was some increase in sweating in his last week of life, although he had always noted excessive sweating. He had complained of frequent headaches since a dental extraction in March, 1957. He experienced much sneezing every morning, without other nasal symptoms.

In 1954, at age 18, the patient had been given intramuscular penicillin for an infected knee. In 1956, he had received prophylactic penicillin therapy intramuscularly when a sister was found to have rheumatic fever. In November, 1956, he was first given the penicillin powder by mouth because of a cold, but he took only one dose. No known untoward effects resulted. Tonsillectomy had been performed at the age of 12.

The patient was one of thirteen children, of whom eight survived. He was unmarried. His mother and father were living and well, but the mother had had rheumatic fever. Three of the surviving sisters had had rheumatic fever, and one of these had "bronchial trouble." Another sister had hay fever. One brother had a history of rheumatic fever and of eczema caused by milk. Another brother had hay fever and asthma, and was rejected for military service because of a "bad heart." This brother is presently confined to a mental hospital for a nervous condition.

Four sisters were dead: two died in infancy, one committed suicide at age 22, and the fourth died at age 26, allegedly from tetracycline toxicity during treatment of actinomycosis of an upper extremity. The latter sister had a history of rheumatic fever and of hives from penicillin.

Autopsy Findings.—At postmortem examination, the body was that of a well-developed 21-year-old Negro male, weighing an estimated 210 pounds and measuring 165 cm. in length. Both lungs were voluminous and together weighed 810 grams. They were soft and pillowy throughout. The posterior portions were somewhat heavy. Microscopic examination showed moderate emphysema and chronic passive congestion with "heart failure" cells in the alveoli. The heart weighed 400 grams. The left ventricle measured 1.8 cm. in thickness and the right ventricle measured 0.4 cm. in thickness. The valves appeared competent. The thymus weighed 30 grams, but was grossly and microscopically normal. The brain weighed 1,300 grams. There was an excessive amount of fluid in the subarachnoid space. The cerebellar tonsils showed moderate pressure coning. The microscopic examination of the brain revealed moderate generalized edema. There was no evidence of brain injury. The remaining organs showed no significant changes, either grossly or microscopically. It was noted that blood collected from the right heart at the time of autopsy failed to clot after 72 hours while remaining under refrigeration. Bacteriologic examinations were negative.

DISCUSSION

What was the cause of death in this patient? The history of penicillin ingestion, the immediate reaction and subsequent course, and the autopsy findings are consistent with the diagnosis of anaphylaxis due to penicillin hypersensitivity. Other causes of sudden death, such as coronary occlusion, cerebral vascular accident, embolism, hemorrhage, laryngeal edema, and tracheal obstruction were not found at postmortem examination. There was no apparent reason to consider other drug reactions or cardiac arrhythmias. Unfortunately, the blood specimen obtained at postmortem examination was inadvertently discarded before any tests for penicillin antibodies could be made.

How did sensitization occur? The history of previous penicillin administration by intramuscular and oral routes would indicate that ample opportunity for sensitization had occurred. Twenty-six of the twenty-nine patients reported with anaphylactic reactions to oral penicillin had previously received penicillin intramuscularly. In one case,²² penicillin had been given previously only by mouth. In one case,²⁰ no previous penicillin therapy was recalled, and, in one case,⁴ this information was not recorded. This would suggest that anaphylactic sensitization to penicillin occurs mainly by the parenteral route and rarely by the oral route.

Why did the reaction occur so rapidly? Obviously, the penicillin was absorbed rapidly, and in sufficient quantity to react with antibody and cause anaphylaxis. Penicillin is known to be absorbed sublingually²⁵ and by way of mucous membranes, as well as via the intestinal tract. Once antibodies are present, elicitation of symptoms can occur following contact with antigen administered by any route—parenteral, oral, or topical.

What was the role of heredity? This patient had one parent and five siblings with histories of rheumatic fever, and he had four siblings with allergic diseases of the "atopic" group. This family history is striking. It has been reported that penicillin anaphylaxis is more likely to occur in patients with other allergic disorders.²⁶ The role of other factors, such as constitutional, psychogenic, or neurologic factors is only speculative, but should be considered.

This case report again calls attention to the importance of the indiscriminate use of penicillin and the dangers of self-medication. In instances where penicillin is indicated, oral administration, where applicable and effective, would be the preferred route in order to minimize the risk of sensitization. When a patient has had previous penicillin therapy, careful inquiry into the history for any untoward reaction is essential in order to anticipate and avoid possible sensitivity reactions. Of the twenty-nine collected cases of anaphylaxis from oral penicillin, in ten of them there had been previous reactions, either local or systemic. Any patient with a history of such a reaction should not receive penicillin by any route, except under circumstances which justify the risk of an untoward reaction.

Skin testing with penicillin prior to its administration has been advocated by many authors in order to identify possible anaphylactic sensitization in those

patients previously treated with penicillin without untoward reaction.²⁷⁻³⁰ Such tests have been said by some authors to be unreliable,³¹ impractical, and, even, dangerous. However, these objections are based largely on the results of testing patients after the occurrence of penicillin reactions, in whom variable percentages exhibit positive skin tests or eye tests.^{30, 32} Testing patients with known reactions is certainly dangerous and should not be done as a general rule. Indeed, of the twenty-nine recorded cases of anaphylaxis from oral penicillin therapy, nine patients were subsequently skin-tested with penicillin and seven again developed constitutional symptoms. The use of skin and eye tests prior to administration of penicillin was described by Smith,³³ who found such testing to be simple and accurate in identifying patients susceptible to penicillin anaphylaxis. Because of the small percentage of anaphylactic reactions that would be expected in one individual's experience, many similar studies will be necessary to permit statistical evaluation of these procedures. On the basis of present information, we would agree that proper testing appears to be safer than the administration of a full therapeutic dose of penicillin without testing, and offers the possibility of minimizing the occurrence of serious or fatal immediate anaphylactic reactions. We would advise routine testing in all patients previously treated with penicillin without known allergic reaction. The most practical technique might be the scratch test using the full strength or dilutions of penicillin, depending on the individual situation. In those exhibiting positive reactions, penicillin should not be administered unless the risk of the disease is as great as the risk of an untoward reaction.

SUMMARY

A case of fatal anaphylaxis following oral administration of penicillin is reported. Autopsy data are included. The importance of the indiscriminate use of penicillin and the danger of self-medication are emphasized. Methods for the prevention of anaphylactic reactions are discussed.

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