

CASE REPORTS

An Anaphylactoid Reaction to Penicillin during Anesthesia

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Since the first report of an anaphylactic reaction to penicillin appeared in 1949,¹ many cases have been reported and some excellent reviews have been published.²⁻⁶ Anaphylactoid reactions in patients during anesthesia have occurred with a variety of drugs, including thiopental,⁷⁻⁹ Dextran,¹⁰⁻¹¹ propanidid,¹² hexylcaine,¹³ and succinylcholine.¹⁴ A search of the literature failed to reveal any reports of anaphylactoid reactions to penicillin while the patient was receiving general anesthesia. In view of this, the following case history is reported.

CASE REPORT

The patient was a 34-year-old woman with a history of emotional instability and grand mal and petit mal epilepsy. Her seizures were controlled with primidone, diphenylhydantoin, and phenobarbital. The patient had a history of "hay fever" and was allergic to chocolate and eggs. There was no history of eczema or asthma.

On July 17, 1968, she underwent emergency surgery for perforation of both antral and duodenal ulcers. Anesthesia was induced rapidly with thiomytal, followed by succinylcholine to facilitate endotracheal intubation. Anesthesia was maintained with nitrous oxide, oxygen, *d*-tubocurarine, and meperidine. Anesthesia and recovery were uneventful. During and after surgery the patient received crystalline penicillin and chloramphenicol intravenously over a period of seven days. The postoperative course was uncomplicated.

On September 5, 1968, seven weeks after her original surgery, the patient underwent elective vagotomy and partial gastrectomy. There were no abnormal findings on physical examination. Preoperative laboratory studies revealed a hematocrit of 40 per cent; leukocyte count 6,550 with

a normal differential; normal urine and chest x-ray.

The patient received atropine, 0.5 mg, morphine, 4 mg, and diphenylhydantoin, 100 mg intramuscularly 75 minutes before induction of anesthesia. The preoperative blood pressure was 110/70 mm Hg, pulse rate 66 beats/min. Anesthesia was induced with thiomytal, 200 mg, intravenously. After 80 mg of succinylcholine, injected intravenously, the trachea was sprayed with 2 ml of 4 per cent cocaine and intubated with a cuffed endotracheal tube. Anesthesia was maintained with nitrous oxide, oxygen, *d*-tubocurarine and morphine, with control of ventilation. The blood pressure stabilized at 140-160/100 mm Hg with a pulse rate ranging between 60 and 80 beats/min. Three hours and 15 minutes after induction, aqueous penicillin, 500,000 units, and streptomycin, 0.5 gm, were injected intramuscularly into the left deltoid region. Thirty-five minutes later the blood pressure suddenly fell to 80, then to 60, mm Hg systolic, with a simultaneous rise in the pulse rate to 120 beats/min. At that time blood loss was estimated at about 500-700 ml. The first unit (450 ml) of A.C.D. blood, which had been running 50 minutes, was quickly infused, and a second unit rapidly administered. The pulse rate continued to rise to 156 beats/min. All packs were removed from the abdomen without any effect on the vital signs. A deep erythematous blush was noted on the face, chest, and arms. Periorbital and facial edema and marked swelling of both pinnae developed. There was marked swelling of the left arm. A maculopapular rash appeared over the face and chest.

Ephedrine, 25 mg, was given intravenously with no effect on peripheral blood pressure or pulse rate. A central venous pressure catheter was inserted and the central venous pressure was found to be 8 cm water. An electrocardiograph demonstrated a regular sinus tachycardia.

During the next hour, without specific therapy, the blood pressure rose to 110/90 mm Hg and the pulse rate fell to 90 beats/min. The patient received no intraoperative steroids or antihistamines, and the operation was completed uneventfully. The facial swelling resolved over the next few hours, and the rash slowly faded and disappeared within 24 hours. Samples of the transfused blood were sent to the blood bank for further study. No evidence of transfusion incompatibility was found.

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DISCUSSION

The patient had many of the signs seen in anaphylactic shock, namely, generalized erythema, facial and other localized edema, tachycardia, and hypotension. Bronchospasm was notably absent.

It might be conjectured that an agent other than penicillin caused this reaction, or that it was a delayed response to the blood transfusion. No other agent administered during the second operation is consistent with the first premise. A transfusion reaction was excluded by recrossmatching of both pre- and posttransfusion samples and by direct and indirect Coombs testing. The exposure to penicillin seven weeks before and the onset of signs shortly after the penicillin injection focuses attention on this drug. The time of onset and the severity of the reaction seem to place this allergic response into that group of allergic manifestations known as "anaphylactoid."

When a diagnosis of an allergic reaction had been made, the patient's condition had begun to improve. It was decided to withhold all drug therapy and observe her condition.

The effect of anesthesia on anaphylaxis is unclear. Katz¹⁵ has demonstrated in guinea pigs a protective effect of ether and urethane on *in-vitro* preparations. The protection was thought to be secondary to inhibition of histamine release. Later work by Parish¹⁶ demonstrated an *in-vivo* protective effect of ether and oxygen against inhaled anaphylactic challenge in guinea pigs. However, he found that several other anesthetics (halothane, nitrous oxide, trichlorethylene and pentobarbitone) did not protect these animals. Of interest is that carbon dioxide in some way protected sensitized animals from the immediate fatal effects.

The infrequency of reports of anaphylaxis under anesthesia suggests that general anesthesia does provide protection against anaphylactic shock. The wide variety and quantity of drugs used by anesthetists provide fertile ground for these reactions. We know of no reported case in which a patient died of anaphylactic shock occurring during anesthesia. There are four possible reasons why

anaphylaxis occurs so rarely during anesthesia. First, "anaphylaxis" may be manifested by a group of signs and symptoms, some of which may go unrecognized when the patient is anesthetized. Second, general anesthetics may suppress the signs of anaphylaxis, diminishing its catastrophic proportions to levels that lead to misinterpretation. Third, general anesthesia may simply delay the onset and severity of anaphylaxis. Finally, anesthetics, or agents they cause to be released, may interrupt the initiating mechanism of anaphylaxis.

In the case reported here, several of these possibilities were present. First, the reaction to penicillin was delayed until 35 minutes following the injection. With this time interval, the peak of circulation levels presumably is being approached. In typical anaphylactic reactions very high blood levels of the antigen are not necessary for the reaction to occur. Second, although there was a fall in blood pressure to low levels, it was not complete cardiovascular collapse. Third, the bronchospasm and difficult ventilation seen with anaphylaxis were totally absent. Thus, there appears to have been a modification of the classical signs of anaphylaxis. It is our belief that a significant number of inexplicable reactions of patients during anesthesia may fall into this category.

ADDENDUM

Since this manuscript was submitted for publication an excellent review article has been found, *i.e.*, Carron, H.: Anaphylaxis and anesthesia, *ANESTHESIOLOGY* 8: 625, 1947.

The author cites a report of a death following injection of tetanus toxoid temporally related to ether anesthesia (Quill, L. M.: Anaphylaxis during ether anesthesia, *J.A.M.A.* 109: 854, 1937).

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Obstetrics and Pediatrics

OPIATES FOR DELIVERY The effect on the newborn of a heavy opiate-opiate-antagonist regimen for labor and delivery, popular in some parts of the country, was evaluated in 30 normal parturients. All mothers received chlorpromazine, 25 mg, and divided doses of meperidine-scopolamine during labor. This produced complete unconsciousness, and in most instances, no further anesthesia was needed for episiotomy, forceps application, and delivery. The total dose of meperidine ranged from 200 to 1,000 mg (average 356 mg). Nalorphine, 10 mg, was given intravenously to the mother ten minutes before delivery. Infants were evaluated by Apgar score at one minute, and acid-base studies were made at birth and at one hour of age. Compared with infants born under regional anesthesia, these infants had lower Apgar scores and were more acidotic at birth and at one hour of age. (Clark, R. B., and others: *Neonatal Acid Base Studies II: Effect of a Heavy Medication-Narcotic Antagonist Regimen for Labor and Delivery*, *Obstet. Gynec.* 33: 30 (Jan.) 1969.)

UMBILICAL ARTERY CATHETERIZATION Umbilical artery catheterization was performed in each of 387 infants over a five-year period, for a variety of reasons, by research pediatricians, practicing pediatricians and residents in pediatrics. In 232 instances, the catheter was used for withdrawal of blood only. In 104 it was used for withdrawal of blood and administration of fluids. In 51, it was used for administration of fluids. Thirty-one infants, or 8 per cent, developed complications noted either clinically or at autopsy. No deaths were directly attributable to the technique. Umbilical artery catheterization should be limited to those infants with moderate or severe respiratory distress, the very small premature infant with tiny fragile veins, and the occasional infant who is critically ill from other causes. (Cochran, W. D., Davis, H. T., and Smith, C. A.: *Advantages and Complications of Umbilical Artery Catheterization in the Newborn*, *Pediatrics* 42: 769 (Nov.) 1968.) **ABSTRACTER'S COMMENT:** While documenting complications, the authors have also emphasized the value of the technique in the management of certain neonatal conditions. In our experience in 183 cases, two deaths were directly attributed to the technique. Improvements in technique, especially continuous infusion of saline solution by an infusion pump, should significantly decrease the incidence and severity of complications.