Anaphylactic Death from Erythromycin

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IT HAS BECOME INCREASINGLY apparent that the use of antibiotic drugs may entail some danger to the patient. Many of the reactions noted are those that physicians had become accustomed to seeing in past years in connection with the treatment of disease with serums and antitoxins. A condition analogous to serum sickness after the use of various members of the antibiotic group has become very common and usually occurs from the sixth to the tenth day after the beginning of antibiotic therapy. Death from acute shock due to use of antibiotic agents also has occurred, clinically typical of anaphylaxis as observed in the past in serum or antitoxin therapy. It would seem wise to make such cases a matter of record, the better to evaluate the safety or danger of the various individual members of the antibiotic group. The case reported here was one of acute anaphylaxis due to erythromycin.

CASE REPORT

A two-year-old Negro girl came to the admitting room of the Communicable Disease Unit of the Los Angeles County General Hospital on 27 January, 1958, with complaint of anorexia and fever for two days and generalized diffuse exanthem over the entire body for one day.

In taking the history it was learned that one year previously the child had had an allergic urticarial rash after the administration of penicillin.

Upon physical examination, an erythematous papular rash over the body and face was noted. The rectal temperature was 100.6° F. Some circumoral pallor was present and the vessels of the pharynx were engorged. Cervical nodes were palpated on both sides. Leukocytes numbered 6,000 per cu. mm. of blood (the differential was not obtained). The urine was clear. A diagnosis of scarlet fever was made (although in retrospect this seems highly improbable in view of the leukocyte count). Because of the pharyngeal redness and the bilateral cervical node enlargement, a dose of 500 mg. of erythromycin was given and it was intended to send the patient home. However, five or ten minutes later, while the child was getting dressed to leave, she was seized with a generalized convulsion, for which 0.12 gm. of phenobarbital was given intramuscularly at once, even though she already was apneic and pulseless. Then 1 cc. of 1:1,000 epinephrine was given into the heart and a slowing of the heartbeat resulted. Oxygen was administered by positive pressure immediately. Spinal fluid aspirated at this time was clear. Tracheotomy was performed to facilitate breathing but before it was completed the patient died, less than twenty minutes after the injection of erythromycin.

Complete autopsy was carried out. The brain was removed and sent to the Ramon E. Cajal Laboratory for examination, a procedure customary in this hospital. The anatomical observations were as follows: Atrophy of the adrenal glands, hypertrophy and hyperplasia of lymphoid tissue throughout the body, hemorrhage into the right lung, bronchopneumonia of both lungs, subacute bronchitis, extramedullary hematopoiesis of the liver, high tracheotomy, exanthem of unknown cause.

There was no growth on cultures from the lungs or the blood, but a culture of material from the spleen showed *K. aerobacter*, and one from the larynx produced the same *K. aerobacter*, *Staphylococcus aureus*, coagulase-positive, and a nonhemolytic streptococcus. Microscopic examination of tissues removed from the various organs was consistent with the macroscopic conditions already described.

The Cajal Laboratory reported meningocerebral congestion. Microscopically observed were: Acute changes in nerve cells (nonspecific), meningocerebral congestion and ependymal granulation of the floor of the fourth ventricle. No focal softening or perivascular inflammatory cells were found in the central nervous system.

DISCUSSION

The sequence of cause and effect seem obvious in this case, and erythromycin must be added to the growing list of antibiotics for which sensitivity tests had better be applied before the drug is given hypodermically. This would appear to have been

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particularly indicated in this case owing to the history of sensitivity when penicillin was given one year previously.

SUMMARY

A child with apparently minor illness when examined on admittance to hospital was given 500 mg. of erythromycin intramuscularly because of laryngeal redness and enlargement of cervical nodes. Within a few minutes, generalized convulsion occurred, and 20 minutes after the antibiotic was given the patient was dead. At autopsy, conditions typical of anaphylactic shock were observed.

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Fibrocystic Disease of the Pancreas and Diabetes in an Adult with Unusual Pulmonary Manifestations

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CYSTIC FIBROSIS OF THE PANCREAS is predominantly a disease of infancy. Although the cause is still unknown, much progress has been made toward a better understanding of the disease since the first complete description in this country by Anderson[1] in 1938. Several years later, when the widespread involvement of all the mucus-producing exocrine glands in the disease was described, the term *mucoviscidosis* was suggested because of the thickening of the mucus which occurs. More recently di Sant 'Agnese[5] pointed out that both names are improper because the pancreas is usually but not always involved and the disease is not confined to the mucus-producing exocrine glands. In the light of present knowledge, he suggested the term generalized *exocrinopathy* as being more accurate from a descriptive point of view.

In the American and English literature there are few references to cystic fibrosis of the pancreas in adults. In 1955 di Sant 'Agnese[5] reported his findings in 325 patients he observed over a 15-year period in Babies Hospital, Columbia University. The oldest patient in the series was 19 years of age. In 1946, Hellerstein[8] reported a case in a 35-year-old Negro male who died 12 hours after admission to a hospital with Friedlander's pneumonia; there was no antecedent history and the diagnosis of cystic fibrosis of the pancreas was based upon the incidental observation at necropsy of numerous cysts and diffuse fibrosis in the pancreas. Hellerstein[9] recently called attention to the fact that many cases of cystic fibrosis of the pancreas in adults were reported in the German literature and cited a reference to the adult cases in *The System of Pathology* by Henke-Lubaesch. In 1954 Baxter[2] reported experience with the disease at Ohio State University and stated that before antibiotics the life span of patients was measured in months or a very few years, perhaps only one or two. He indicated that with proper management some patients may live until they are 18 to 22 years of age. This obvious disparity in survival ages reported by previous German and present-day observers leads one to wonder whether the German adult cases reported might not be attributable to cystic fibrosis following pancreatitis.

Di Sant 'Agnese[5] has proposed the following four criteria for present-day clinical diagnosis of cystic fibrosis of the pancreas:

1. Pancreatic deficiency.
2. Pulmonary pathologic changes
3. Excess chlorides in sweat.
4. Family history (assists only).

These criteria are based on his observations that there is complete absence of pancreatic exocrine function in 90 per cent of the patients; pulmonary pathologic change occurs in all patients at some time in the disease; and finally, abnormal sweat with increased chloride and/or sodium content occurs in 99 per cent of patients. Absence of the disease in siblings does not rule out the disease in the patient.

In reviewing the literature, we were unable to find a single reference to cystic fibrosis of the pancreas and associated or co-existing disease since 1938. In 1950 Molnar[11] reviewed the literature up to that time in a case report and made no reference to associated diabetes.

In 1955 di Sant 'Agnese[6] presented an excellent and comprehensive review of the pulmonary manifestations of fibrocystic disease of the pancreas, one of the unusual aspects of the case herein presented. He said that respiratory involvement has a variable onset from the age of a few weeks to several years, occurring between six months and two years of age in the great majority of cases. It must be recognized, he pointed out, that this is in reality a generalized disease of which the pancreatic and pulmonary lesions are only one expression. The 292 patients reported upon had, at some time during their illness, pulmonary disease of variable degree —severe in most instances and accounting for 90 per cent of the deaths. He made the observation that if patients reached late childhood without irreversible damage being done to their lungs, they seemed to improve and the degree of clearing in the roentgen picture was surprising. With regard to prognosis in this group, he suspected that at least many would go on to chronic pulmonary disease as adults. The oldest in the reported group was 18 years of age.

The following unusual case of cystic fibrosis of the pancreas is presented because the patient is an adult who has associated diabetes and the pulmon-

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