

ANAPHYLACTIC PNEUMONIA

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In animals which survive anaphylactic shock following an injection of antigen, so-called "protracted shock", has been described (Ishioka 1, Busson 2, Friedberger 3). Its principal feature is a "sterile anaphylactic pneumonia". This is either a lobar or an interstitial process with hemorrhagic infarctions of various sizes, alveolar edema and inflammatory lesions. It can be produced in guinea pigs sensitized to horse serum upon insufflation of horse serum into the trachea (Fried 4).

The equivalent of this condition in men was first described by Waldbott (5) in 1934, in connection with studies on what was then called "thymic death". It was demonstrated that this latter condition actually represented human anaphylactic shock. In 7 out of 34 autopsied cases a pneumonitis developed several hours after the onset of shock. At that time it was difficult to present conclusive evidence of what is now generally accepted, namely, that human anaphylaxis can occur by modes other than injection and by antigens other than protein. In the cases described, the antigen had obviously entered the system through inhalation, through the intestinal tract; furthermore, thermic stimuli and anesthetics were held responsible. The majority of the individuals were children. Some presented an allergic family history, whereas others had no family background of allergy whatsoever. Most patients had been in perfect health previous to the onset.

In 1940 Rich and Gregory (6) described in patients who died from sensitivity to sulfapyridene, a condition which they termed "anaphylactic pneumonia". Their observations appear to be identical with the autopsy findings noted by Waldbott in 1934 in connection with so-called "thymic death".

MANIFESTATIONS

I have had occasion to observe many additional cases with pneumonitis which evidently originated on the basis of anaphylactic shock (7). Clinically, this condition is distinct from any other type of pulmonary infiltration; it occurs in individuals who have not had asthma before. It is characterized by a prodromal stage of shock without fever lasting from two to ten hours; the subsequent febrile stage is mild, its duration less than five days; the temperature rarely exceeds 103 degrees.

The climax of "anaphylactic pneumonia" occurs at the onset. The patient is seized suddenly with marked dyspnea, cyanosis and collapse. This is accompanied by a suffocating cough and sometimes by laryngeal spasm. The pulse is fast, the blood pressure low. Some individuals have severe vomiting and diarrhea; in a few, urticaria is present. The outbreak cannot always be identified with a certain cause. A 47 year old man collapsed suddenly while entering a pigeon coop to feed his pigeons (Fig. 1); a year old infant while drinking a bottle of milk; a six year old boy while taking his first pony ride. One patient sensitive to cold temperature was seized while entering the cold water of a shallow lake in mid-summer.

Needless to say, this condition is often fatal. If the patient survives, examination reveals evidence of pulmonary edema, such as bronchial breathing and rales; consolidation soon ensues which can be visualized by x-ray. The leucocyte count is increased, but rarely exceeds 12000. There is no eosinophilia. Skin tests for the suspected antigens at this state of the disease are negative. If repeated several weeks later, they exhibit strongly positive reactions.

Once this condition has subsided, similar, less severe episodes develop on subsequent occasions. A three year old child was hospitalized 16 times within two years before true asthmatic attacks developed. The clinical picture was dominated at first by shock, moisture in the lungs, and then the pneu-

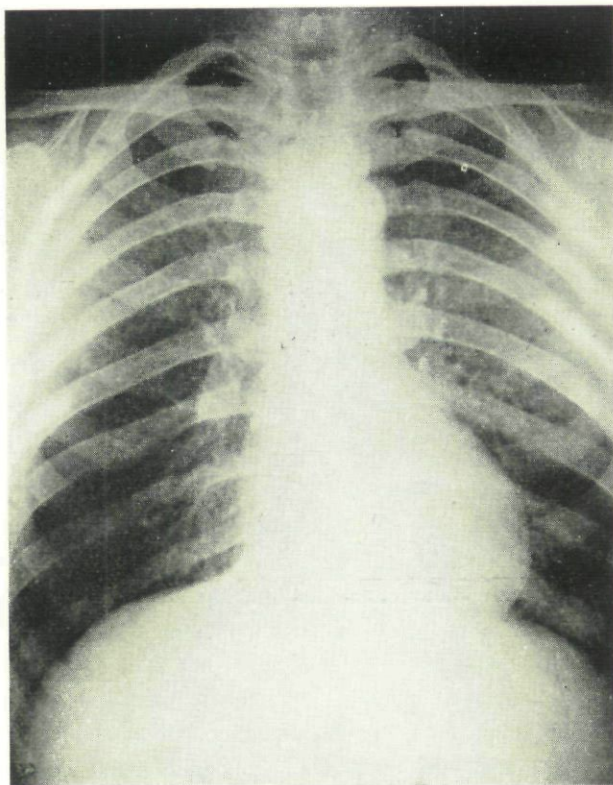


Fig. 1.

Radiograph of chest showing pneumonitis following shock due to inhalation of pigeon feathers. Skin tests for pigeon feathers because at first negative, strongly positive six weeks later.

monic process followed. In future episodes this gradually became displaced by wheezing, emphysema, and other signs of bronchial asthma such as allergic nasal disease, strongly positive intradermal skin reactions, and eosinophilia.

PATHOLOGY

The characteristic pathological changes of this condition are those which were first identified by me in human anaphylaxis, namely, engorgement of pulmonary capillaries, ex-

travasation of edema fluid through the capillary walls into the alveolar spaces and petechial hemorrhages in various parts of the lungs. In some areas there is tissue necrosis, in others traumatic emphysema alternating with atelectasis. Leucocytes can be seen immigrating into the edematous areas in an apparent attempt to organize the lesions. The sections are sterile and contain no micro-organisms. Petechial hemorrhages and edema are also found in organs other than the lungs such as the pleura, pericardium, and the bowels. The adrenal glands are usually very small.

DISCUSSION

It is difficult to estimate the incidence of "anaphylactic pneumonia" because the diagnosis often depends on the history which may not be sufficiently adequate for a statistical survey. Of 100 consecutive children with asthma below six years of age a pneumonic process preceded the onset of asthma in 52. While a true infection probably prevailed in some of these cases, in a good proportion the history clearly pointed to a prodromal period of shock. There is a tendency among the profession to term these cases mistakenly "virus pneumonia".

There is no doubt that we are dealing with a clinical entity distinct from other types of pneumonitis and certainly distinct from pneumonitis which follows asthmatic attacks¹. It has been produced experimentally in animals; it has been observed following antigenic injections in men (Dean and Webb, 8) and it was noted by Rich and Gregory (6) in death from sensitization to sulfapyridin. Furthermore, it is distinct from an allergic or so-called constitutional reaction which occurs in patients with an existing allergic disease following injection, inhalation, or ingestion of antigens to which extreme sensitivity exists (Fig. 2). Here the "shock organ" is already in an altered state and has obviously already undergone changes which are evidently designed as a defense mechanism.

¹ The latter is usually due to infection of small atelectatic areas.

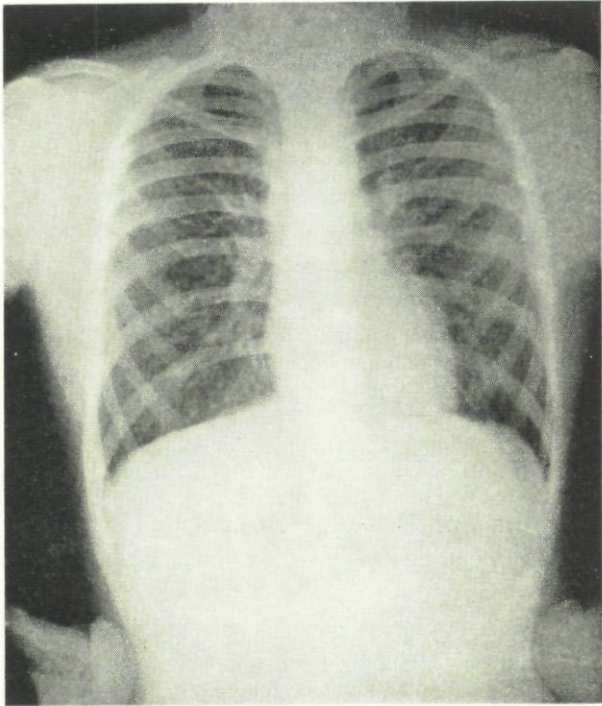


Fig. 2.

Radiograph of chest following a severe allergic reaction from an ingestion of peanut extract for skin test with a low grade pulmonary edema. In contrast with true anaphylactic pneumonia, this patient had been an asthmatic previous to this episode.

In my original description, the autopsy findings in the seven cases of pneumonitis were interpreted as a pre-allergic state or as protracted anaphylaxis. These patients had no previous allergic disease. If the individual survives he becomes, at first, subject to recurrent pneumonitis and later, to true asthmatic attacks. Therefore, the theory was advanced that, like in animal anaphylaxis, a patient sensitive to a certain antigen has not yet acquired the ability to localize and dispose of, the invading antigen like an asthmatic patient does. For instance, the mucous glands lining the bronchial wall are not yet hyperplastic as they are in advanced asthma; therefore,

insufficient mucus is created to eliminate invading antigen. The bronchial musculature has not yet hypertrophied and bronchial contractions are not yet as intense as they are likely to be in asthma. The mucus, therefore, cannot be ejected from the bronchi as effectively as in the asthmatic. Furthermore, the patient cannot yet retain an injected antigen at the site of its injection by formation of a wheal as an asthmatic does when he exhibits a positive skin reaction. He cannot yet produce leucocytes and eosinophiles. Instead, there is hyperplasia of lymphoid tissue and necrosis in lymphoid organs. Waldbott and Anthony (9) demonstrated that enlargement of the thymus gland and of other lymphoid organs precedes the development of asthma; the adrenal glands are hypoplastic at autopsy. The relationship of lymphoid hyperplasia to insufficient production of adrenal cortical hormones is now well established.

Thus, the development of pneumonitis can be interpreted as a pre-allergic condition. Like in an anaphylactic animal, it is designed to repair the morbid changes of what is human anaphylaxis in the true sense of the word. It is not of infectious origin. It plays a part in the development of bronchial asthma and differs considerably from other types of pneumonia complicating allergic asthma.

TREATMENT

In view of this interpretation, the treatment of choice is the immediate administration of ACTH and Cortisone. Indeed, there is probably no more urgent need for the employment of these medications than in this disease. Small doses of epinephrine and other measures usually advocated to combat allergic edema, such as administration of potassium chloride and antihistaminics may be resorted to. Systematic desensitization with very small doses of a suspected antigen may be considered. Antibiotics are of little avail especially in the early state.

SUMMARY

On the basis of autopsy studies reported previously, and of subsequent clinical observations a type of pneumonitis is described which develops following human anaphylactic shock. It has been termed "anaphylactic pneumonia". Pathologically it represents pulmonary edema, petechial hemorrhages and necrotic areas in the lungs which become organized by infiltration with leucocytes.

This condition not infrequently precedes the development of bronchial asthma. It is characterized by sudden onset with marked dyspnea, cyanosis, and collapse, after which a low grade pneumonia ensues. Cortisone and Corticotropin hormones are indicated in the treatment of this condition, whereas antibiotics are not effective.

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