

SUDDEN DEATH FROM BRONCHIAL ASTHMA FOLLOWING INJECTION OF PYROMEN

CASE REPORT*

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THERE have been many reports of death from asthma.¹ This case is reported because of its somewhat unusual circumstances.

The patient was a white married woman, thirty-one years old at the time of her death (Sept. 14, 1951). She had been under nearly continuous observation since April 16, 1948. During her first pregnancy in September, 1945, she suffered symptoms suggestive of asthma but no record existed of such a diagnosis. At that time she was said also to have toxemia with hypertension. She remained well after that until early in her second pregnancy when in July, 1947, she developed allergic rhinitis with early polyp formation. In Sept., 1947, she had mild asthma and this recurred at intervals until her second baby was born in February, 1948. In March, 1948, she underwent a nasal polypectomy and a bilateral radical antrostomy. Following this, her asthma became very severe and intractable. There was no known family history of allergy.

The patient was depressed and anxious and there was a considerable amount of domestic discord. Her physical examination showed the usual pulmonary findings of severe asthma. The nasal mucosa was reddened and there was evidence of continued polyposis. A mucopurulent nasal discharge was noted. There was moderate arterial hypertension and her ocular fundi showed arteriolar changes, classified as grade I. She was underweight. Blood examination revealed a hemoglobin content of 11.8 Gm., 4,010,000 red blood cells, 8,350 leukocytes, and of these 16 per cent were eosinophils. Urinalysis yielded normal findings.

She was tested to the common inhalants, intradermally, but failed to react except very slightly to some fungus spores, feathers, kapok, and tobacco. The history indicated marked aspirin sensitivity. A test elimination diet was carried out. The results of this were inconclusive but the patient was certain that she did not tolerate wheat, onion, chocolate, and egg and usually left these articles out of her diet.

During the early phase of her management she was deeply disturbed psychologically. She suffered from anxiety reactions, personality conflicts, feelings of inferiority, tension, insecurity, and an inability to get along with her husband. In June, 1948, she took an overdose of bromides, accidentally, and this led to an acute psychosis necessitating her admission to the psychopathic hospital. Up to this time her asthma had been severe and nearly intractable. When she became psychotic her asthma subsided almost completely and all abnormal physical signs disappeared from her chest. She recovered from her acute psychotic episode quickly and was discharged within seventeen days. Immediately her asthma returned so severely that she required several hypodermic injections of epinephrine daily.

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For the next six months she presented a difficult therapeutic problem but was able to carry on at home. She had a remission in March and April, 1949 but during the following summer had gradually increasing asthma. During this time and the following winter she required periodic relief of intercurrent infections with antibiotics and with frequent use of symptomatic measures carried on fairly well until a very severe asthmatic state necessitated admission (her first in thirty months) to hospital in November, 1950.



Fig. 1.—Section through lung root showing mucosal thickening and mucous plugging in secondary bronchi, vesicular emphysema and enlarged bronchopulmonary nodes.

There was moderate improvement while in the hospital but she relapsed soon after discharge and readmission was necessary on February 10, 1951. Her inability to respond to any medication led to the use of ACTH. After 500 mg. given over a period of five days, she became free of all signs and symptoms. Her psychological problems went into abeyance and she seemed well in every way. Within two weeks need of medication returned. However, she managed to carry on with only minimal difficulty until late March, 1951, when symptoms again increased considerably and were almost intractable on her admission to hospital again on July 6, 1951. She received 280 mg. ACTH over a period of four days, most of it intravenously, and made another dramatic recovery, going home free of signs and symptoms on July 12, 1951. Symptoms began to recur on July 31, 1951, and increased steadily. These symptoms were aggravated by much vomiting and she was readmitted to hospital on August 31, 1951, because of vomiting and a fainting attack.

Her asthma was not especially severe. Epinephrine, rectal aminophyllin and inhaled Isuprel was required daily but she was able to be up and about the ward and she was not as severely incapacitated as on previous occasions. Signs of asthma were constantly present in her chest, but dyspnea was moderate and she slept well. Her condition did not warrant the use of ACTH.

TABLE I.

DATE	INTRAVENOUS PYROMEN	REACTION
7 Sept. 51.	1 microgram (0.1 c.c.)	Chilliness. T.99°F.
8 Sept. 51.	2 micrograms (0.2 c.c.)	Slight shivering. T.99.3°F.
9 Sept. 51.	3 micrograms (0.3 c.c.)	Slight shivering. T.99.3°F.
10 Sept. 51.	3 micrograms (0.3 c.c.)	No reaction
11 Sept. 51.	5 micrograms (0.5 c.c.)	Flushed—no elevation of temperature.
12 Sept. 51.	3 micrograms (0.3 c.c.)	No reaction
13 Sept. 51.	None used	
14 Sept. 51.	5 micrograms (0.5 c.c.)	No immediate reaction—then rapidly increasing dyspnea and death in 85 minutes.

It was decided to give her a trial on Pyromen* therapy,² and this was done as shown in Table I. No immediate reaction occurred following her last intravenous injection of Pyromen and although she still manifested asthmatic

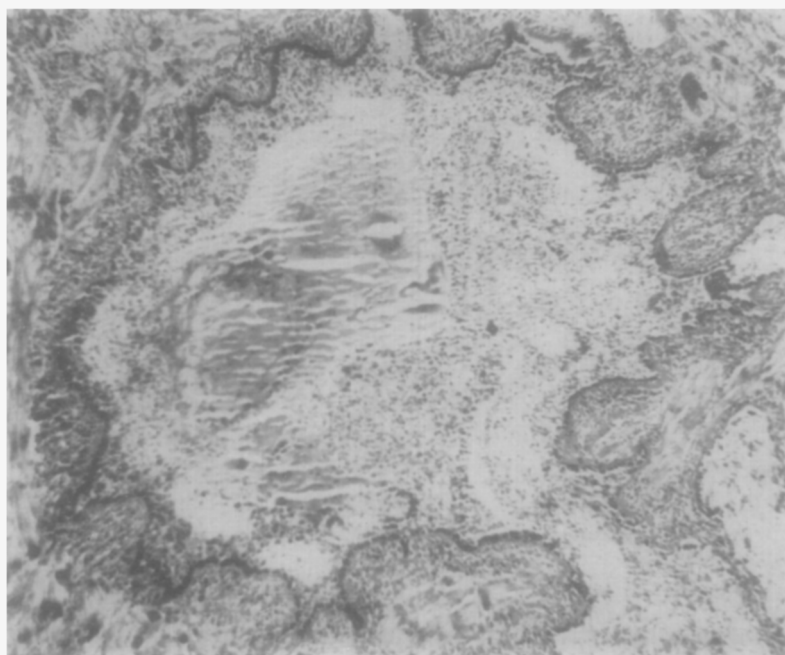


Fig. 2.—Tertiary bronchus, lumen 2 mm., occluded by mucus which contains numerous eosinophils. Dark wavy line made up of nuclei of epithelium, the free border of which is ruptured. At the lower right corner is a distended mucous gland duct.

signs throughout her chest she was not specially dyspneic nor was she cyanosed. Shortly afterwards, dyspnea increased and she asked for epinephrine. Up to this time the ward staff were not alarmed, but when epinephrine in repeated

*Pyromen is a nonprotein bacterial pyrogen, the active factor in which appears to be a complex polysaccharide. It is prepared by the Baxter Laboratories, Inc., Morton Grove, Ill. and distributed by Travenol, Inc. The material used in this case was provided by Travenol, Inc.

doses was without effect, administration of intravenous aminophyllin was requested because of rapid deterioration in her condition. Before this could be started she suddenly became deeply cyanosed, breath sounds became almost inaudible and she died suddenly one hour and twenty-five minutes after the Pyromen had been injected intravenously.

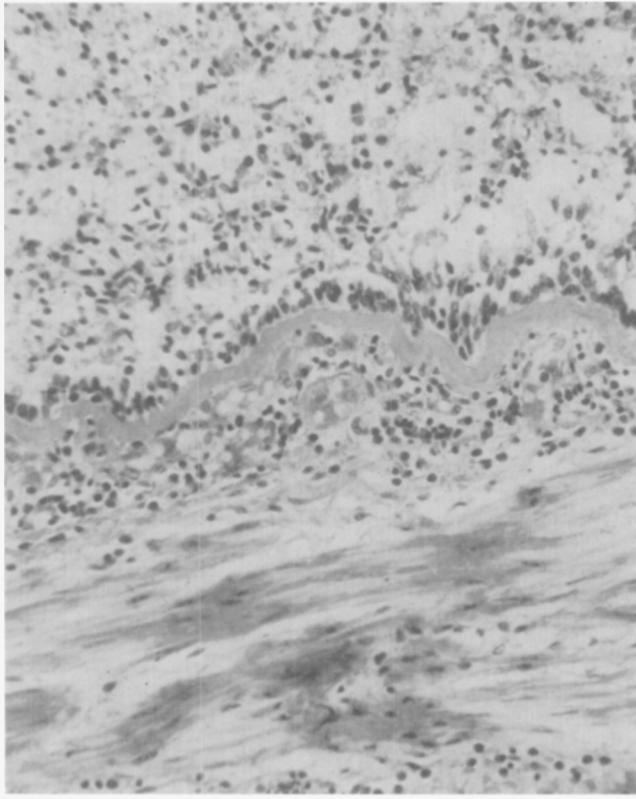


Fig. 3.—Section of wall of tertiary bronchus. From bottom to top: circular muscle and edema; lamina propria, eosinophil and lymphocyte infiltration; basement membrane markedly thickened; bronchial epithelium with cytoplasmic rupture. Lumen filled with mucus containing eosinophils, lymphocytes and shed epithelial cells. Magnification $\times 206$.

AUTOPSY

An autopsy (W. G. H. A-8363) was performed to exclude common causes of sudden death, confirm the diagnosis of bronchial asthma, and to observe any effect of Pyromen.

External examination was normal except for cyanosis of the face and nail beds, evident twenty-four hours after death. The cardiovascular system showed heart weight of 240 grams, right ventricle wall 2 mm. thick, no dilatation of either ventricle, no valvular, coronary artery, myocardial, arterial or venous abnormality. There was no thrombosis or embolism; pulmonary vessels and femoral veins contained fluid blood. The kidneys showed congested parenchyma but were otherwise normal as were the ureters, bladder, and pelvic organs.

The gastrointestinal tract, liver, pancreas, spleen, and adrenals were normal. As the patient had been in hospital for a period of two weeks no examinations for poisons were carried out.

Skull, meninges, and brain showed no lesion except for a few petechial hemorrhages over the right posterior parietal region. Microscopic examinations of all brain sections and the pituitary showed marked congestion. The thyroid weighed 15 grams and contained colloid. The thymus weighed 20 grams, was bilobed with a soft pink cut surface.

The nares and fauces were patent, and the tongue not swollen or bitten. The larynx, trachea, and main bronchi were congested and contained a little clear sticky mucus but were not obstructed. The whole lungs were voluminous and crepitant. After fixation by formalin perfusion and immersion they were sliced at 4 mm. intervals, and showed findings characteristic of bronchial asthma, namely, most secondary and tertiary bronchi completely occluded by thick tenaceous plugs, and a fine honeycomb appearance of the parenchyma characteristic of emphysema. No atelectasis, consolidation, or scars were seen. The pleura was normal. Bronchopulmonary lymph nodes were enlarged to 2 by 1.5 by 1.5 cm., in contrast to the other nodes of the body which were average.

Microscopic examination showed diffuse mucus plugging of medium and small bronchioles with rupture of lining epithelium, swollen basement membrane, prominent mucus glands with ducts greatly distended by mucus, marked bronchial wall edema and alveoli distended, and empty except for a few free mononuclear cells. Numerous eosinophils were noted in hilar lymph node sinuses, lung venules, bronchial walls, and lumen where they were most numerous near the mucosa.

Except for visceral congestion the only pathological findings of importance were those of the lungs which presented the picture characteristically seen in sudden death from asthma.¹

SUMMARY

1. A case of sudden and unexpected death from asthma following the intravenous use of Pyromen is presented. This young woman had an intrinsic type of asthma starting in pregnancy and becoming very severe after a double radical antrum operation. She was aspirin sensitive.

2. The patient had been psychologically unstable and during one acute psychotic phase became temporarily and completely free of asthma.

3. Two courses of ACTH, in February and July, 1951, respectively, produced complete remissions of asthma for a few weeks and led to temporary psychological stability.

4. Her fourth admission to hospital was characterized by less severe asthma than on previous occasions. Therapy with Pyromen produced no beneficial effects of any kind and her last treatment with this substance was followed by very rapidly increasing bronchial obstruction and death within eighty-five minutes. The fatal termination was not anticipated because although she had required daily medication her asthma was not severe at the time and she was ambulant.

5. Asthmatic patients of this type have a notoriously bad prognosis and often require very little to upset their delicately balanced respiratory state. Whether or not the use of Pyromen was causally related to her death it is impossible to say. It can be said with certainty that Pyromen had no demonstrable beneficial effect.

6. The pathological findings were limited to the respiratory tract. These showed a striking example of intense bronchial and bronchiolar obstruction due to mucus plugging and mucosal edema. The thymus was persistent. Death was due to asphyxia.

REFERENCES

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