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PULMONARY OEDEMA DUE TO ANGIOCARDIOGRAPHY

TREATMENT WITH INTRAVENOUS HYDROCORTISONE

BY

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Serious reactions to contrast media containing iodine are a not uncommon sequel to angiocardiology. Dotter and Jackson (1950) reported 26 deaths out of a total of 6,824 investigations, an incidence of 0.38%. Respiratory difficulty, respiratory arrest, or pulmonary oedema occurred in 12 of the fatal cases. McAfee (1955) reported eight deaths in a series of 732 angiocardiology. He found that patients with primary pulmonary hypertension and pulmonary stenosis appeared to be especially liable to develop serious reaction. Two deaths were reported following selective angiocardiology: in one patient, with multiple pulmonary arteriovenous aneurysms, 35 ml. of a 70% solution of diodone was injected through a catheter in the right atrium; the patient died from acute pulmonary oedema after twenty-five minutes.

We report below the case-history of a patient who developed fulminating pulmonary oedema after the injection of sodium acetrizoate into the pulmonary arteries.

Case Report

A man aged 39 had been well until a brief attack of unconsciousness during a strenuous game of football thirteen years previously. After this episode he became slightly breathless on exertion. He had a further syncopal attack, again precipitated by exertion, seven years ago. After a herniorrhaphy in January, 1955, he developed pulmonary infarction. There had been no other history of chest illness. He was admitted for investigation in November, 1955. On examination there were signs of pulmonary hypertension: a dominant "a" wave in the jugular pulse, an early ejection sound at the pulmonary area, and an accentuated pulmonary component of the second heart sound. The electrocardiogram showed right bundle-branch block. The chest x-ray picture showed moderate dilatation of the main branches of the pulmonary artery, with narrowing of the peripheral vessels.

The differential diagnosis included primary pulmonary hypertension, chronic thrombo-embolic pulmonary hypertension, and Eisenmenger's syndrome. Cardiac catheterization confirmed the presence of pulmonary hypertension. The pulmonary artery pressure was 90/20 mm. Hg, and the pulmonary vascular resistance was 10 units. The brachial arterial oxygen saturation was 91%. There was no direct or reversed shunt at any level. Selective angiocardiology was then performed to see whether any large pulmonary vessels were occluded. Promethazine hydrochloride, 25 mg., had been given one hour previously. A test dose of 1 ml. of sodium acetrizoate was injected through the catheter into the pulmonary artery. As there was no reaction, 15 ml. was injected into the left pulmonary artery, and a film taken. Then 20 ml. was injected into the right pulmonary artery and a further film taken.

At 11.15 a.m., forty-five minutes after the injection, the patient complained of nausea, and became dyspnoeic and slightly cyanosed. He also coughed up small amounts of frothy blood-stained sputum. He was given 50 mg. of diphenhydramine hydrochloride by mouth, but his condition became steadily worse. By 12.30 p.m. he was very distressed and breathless, and fine crepitations due to acute pulmonary oedema were widespread. He was transferred to a "cardiac" bed, venous cuffs were applied to the thighs, and he was treated with morphine, adrenaline, aminophylline, and oxygen without benefit. At 2 p.m. 25 mg. of promethazine hydrochloride and 200 mg. of cortisone were given intramuscularly. Oxygen was bubbled through 45% ethyl alcohol in a fruitless attempt to reduce the frothiness of the sputum. His condition progressively deteriorated, and he developed signs of extreme peripheral vasoconstriction, with an unrecordable blood pressure. He became increasingly drowsy, and by 4 p.m. he was unrousable; his upper respiratory tract was choked with profuse frothy sputum which he was unable to expectorate. Death appeared to be imminent.

At this stage, laryngoscopy was performed by direct vision and a considerable amount of sputum aspirated; this brought slight improvement. An intravenous injection of 5 ml. of nikethamide caused the patient to recover consciousness and expectorate a large amount of frothy sputum. He then gradually relapsed into coma. Thirty minutes later, at 4.45 p.m., a further dose of nikethamide produced a similar result. Then from 5 to 6.30 p.m. he was given an intravenous infusion of 100 mg. of hydrocortisone (free alcohol) in 500 ml. of isotonic saline. During this time his condition steadily improved, his breathing became less distressed, and he recovered consciousness. There were fewer rales in his chest. When 5 ml. of nikethamide was given intravenously at 5.45 p.m. he produced much less sputum than after the previous doses. At 6.30 p.m. the hydrocortisone was stopped, and a slow drip infusion was continued with isotonic saline alone; 25 mg. of promethazine hydrochloride was given intramuscularly. At 10 p.m. pulmonary oedema recurred and responded again to an infusion of hydrocortisone, which was continued until 1.30 a.m. At 3 a.m. a second relapse occurred, and the signs of pulmonary oedema diminished within five minutes of starting the third hydrocortisone infusion. This was maintained for three hours, and thereafter his condition remained satisfactory.

Oral cortisone was subsequently given in gradually decreasing doses for nine days. During this time he was pyrexial, and developed signs of consolidation of the apical segment of the right lower lobe; this was confirmed by radiography, and attributed to pulmonary infarction.

Discussion

Of the 26 deaths reported by Dotter and Jackson (1950), sensitivity tests were performed in 19 cases and were negative. Yet the intravenous injection of 1 ml. of solution of diodone has itself caused death in four instances (Morgan, 1950; McAfee, 1955). In the present case, generalized pulmonary oedema must be attributed to a hypersensitivity reaction of

which no warning had been given from a preliminary test dose injected into the pulmonary artery. It is concluded that the administration of a test dose of contrast medium is an unreliable method of detecting hypersensitivity, and may in fact induce a false sense of security.

The treatment of the condition presented a difficult problem. As might have been expected, the methods of treatment applicable to pulmonary oedema occurring in left ventricular failure were ineffective here. Intravenous hydrocortisone, on the other hand, appeared to exert a specific and prolonged anti-allergic action in reducing pulmonary oedema. The antihistamine drugs proved of little value. Nikethamide was useful in reviving consciousness and the cough reflex so that fluid could be expectorated.

Intravenous hydrocortisone induced immediate improvement on three separate occasions, and undoubtedly saved this patient's life. Intramuscular cortisone, which was given initially, was presumably ineffective owing to poor absorption in the presence of severe peripheral vasoconstriction. The use of intravenous hydrocortisone in overwhelming allergic reactions is a rational therapeutic measure, and the present case history confirms its usefulness. Our experience indicates that the drug should be immediately at hand in all centres employing the intravenous injection of contrast media.

Summary

A case of gross pulmonary oedema following selective angiocardiology in a patient with primary or chronic thrombo-embolic pulmonary hypertension is reported. Recovery was clearly attributable to prolonged intravenous infusion of hydrocortisone. A test dose of sodium acetrizate failed to provide warning of hypersensitivity.

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FREQUENCY IN THE FEMALE DUE TO URETHRO-TRIGONITIS CAUSED BY INTESTINAL INFECTION

BY

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In his Hunterian Lecture of 1933 Winsbury-White proved by means of injected animal specimens that infection of the genital organs in the female caused marked pathological changes in the urethra and trigone of the bladder. This fact had been readily accepted as occurring in the male as a result of the anatomical relation of the prostate to the bladder neck, but it was not recognized as occurring so readily in the female. By the routine use of a urethroscope, characteristic changes at the bladder neck were found to be invariably associated with disturbances of micturition.

This is the original work which established urethro-trigonitis as a clinical entity and the commonest condition found in female patients attending a urological clinic, but, as Winsbury-White (1947) states, chronic urethro-trigonal changes are not uncommon in women with healthy cervixes. And it is not uncommon even in patients who had had the genital organs removed some time prior to the onset of the urethro-trigonitis.

General Review of Urethro-trigonitis in the Female

In a review of female patients suffering from urethro-trigonitis and attending a urological clinic over the last seven

years it was found that the incidence of this condition was remarkably constant from year to year, varying only between 25 and 30% of the total female attendances of 453. The majority of cases occurred between the ages of 30 and 50, but it might occur in any of the age groups. The most common symptom was frequency of micturition, which was pronounced in 80% of the patients. Dysuria was present in 50%, as was urgency of micturition. In spite of the old teaching that residual urine is rare in the female, an intravenous pyelogram in all cases revealed that 66% of these cases had a definite volume of residual urine left after micturition. The laboratory reported that 16% of the catheter specimens taken as a routine contained pus cells and that organisms were present in only 12%, the predominant organism being *Bact. coli*. Winsbury-White states that urethro-trigonitis is a predisposing cause of *Bact. coli* infection of the urinary tract, and that it does not produce such an infection by itself but only by causing conditions which favour the onset of infection by reason of obstruction of the bladder neck. The diagnosis was made by routine examination with a urethroscope, and characteristic changes in the urethra and bladder neck were noted in every case. The cervix was examined as a routine, and an erosion or evidence of cervicitis was present in 66% of cases; of the remainder there was no evidence of genital infection.

In each case the internal sphincter was dilated as a result of the urethroscopic examination, and dilatation was repeated in accordance with Winsbury-White's method at not less than six-weekly intervals and to a dilatation not greater than F.28. In 25% treatment was speeded up by fulguration of the polypi and granulations and hillocks: 66% were cured and 28% much improved.

Urethro-trigonitis Not due to Infection of Genital Tract

There remain, therefore, 34% of cases in which no infection of the cervix or genital organs can be found to account for the pathological changes in the urethra and trigone.

In a number of patients an association between the large intestine and the neck of the bladder had been noticed: the first instance was that of a patient in whom an acute attack of diverticulitis of the sigmoid colon followed each dilatation of the urethra and in whom marked urethro-trigonal changes had been found on urethroscopy. On further inquiry the patient stated that when she had an attack of diverticulitis the symptoms of urethro-trigonitis were very much worse.

A frequent complaint in these patients is of discomfort and even pain in the left iliac fossa, which may be associated with some irregularity of the bowels. On abdominal palpation there is not infrequently definite tenderness over the sigmoid and pelvic colon, which may in some patients be palpable.

Out of 43 cases examined radiologically by means of a barium enema, 11 showed lesions of the large intestine which were closely related to symptoms of urethro-trigonitis verified by urethroscopy. Of the 11 cases, 8 showed numerous diverticula of the lower colon with radiographic appearances strongly suggesting inflammatory changes in the surrounding bowel. Two patients had been previously diagnosed as having diverticulitis with rigidity and thickening of the sigmoid colon. In one case a barium enema showed a carcinoma of the recto-sigmoid junction though there had been no initial symptoms suggesting a neoplasm of the bowel but only those of urethro-trigonitis.

Chronic constipation was not accepted as a likely cause of urethro-trigonitis, as it does not of itself produce inflammatory changes in the wall of the bowel; nor were lesions of the anal canal included as a cause, although on anatomical grounds there would seem to be no reason why they might not form a source of infection.

In the absence of animal experiments, which made Winsbury-White's work so conclusive, a study of the relationship of the lymphatics of the lower part of the large intestine with those surrounding the bladder neck, although