PRIMARY PULMONARY HYPERTENSION WITH OBSTRUCTIVE VENOUS LESIONS

BY

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There are very few recorded examples of disease of the pulmonary veins in primary pulmonary hypertension. In 1941 Brill and Krygier described a single case of primary pulmonary hypertension and collected a further 19 that had been previously published: in only one of these were abnormalities described in the veins—an instance reported by Mallory (1937).

Since then many additional cases of primary pulmonary hypertension have been described. Gilmour and Evans (1946), Cross and Kobayshi (1947), Dresdale et al. (1951), Cutler et al. (1954), Evans et al. (1957), Heath et al. (1957), Kuida et al. (1957), Shepherd et al. (1957), and Wade and Ball (1957) reported the histological findings in a further 31 patients. In only two of these (Cases 8 and 11 of Evans et al.) were any abnormalities described in veins; and they did not appear to be the same as those found in the present case, in which there were very severe intimal thickenings in the small veins. Nearly all small veins were affected, many being almost completely occluded. It seemed likely that this condition in the veins was the cause of the widespread capillary dilatation and might have played an important part in causing the pulmonary hypertension.

Case Report

A youth of 16 was admitted to the General Hospital, Birmingham, in September, 1956. He had been well until May, 1956, when he had a pyrexial illness, thought to be influenza. He became breathless and had some pain in the right side of the chest and a cough with greenish sputum. X-rays at that time showed prominence of the pulmonary artery and some shadowing in the left lower lobe, which decreased in extent over the following two months.

During the nine months before admission he had seven or eight attacks of unconsciousness, which were brought on by exertion and accompanied by dyspnoea. He remained short of breath, and two weeks before admission the breathlessness became worse, and he developed pain below the right costal margin and began to vomit. He had a very poor appetite and complained of considerable thirst.

Clinical Examination. The patient was afebrile, dyspnoeic, slightly flushed, and with peripheral cyanosis. The pulse was regular at 110 a minute and blood pressure was 110/80. Clinical signs of cardiac enlargement were not found, but there was a heaving cardiac impulse. Although the heart sounds were normal, there was a left parasternal systolic murmur and a mid-diastolic sound at the mitral area. No abnormal clinical signs were present in the lungs.

Radiological examination showed prominence of the vascular pattern in the lungs, particularly in the central areas, suggestive of congestion and œdema. The heart had enlarged since the earlier X-ray, and on screening the enlargement appeared to be due mainly to a large right ventricle. No enlargement of either atrium was seen, but the pulmonary artery segment was very prominent and the aorta comparatively small.

Other Investigations. A blood count showed 5-7 million red cells per cu. mm. with 17-5 g. per 100 ml. haemoglobin, white cells 16,400 per cu. mm. of which 77 per cent were polymorphonuclear, and E.S.R. (Westergren) 2 mm. in one hour. The sputum showed occasional pus cells, and gave a
growth of pneumococcus and streptococcus viridans. In the urine there were occasional red cells and granular and hyaline casts. No L.E. cells were found in the peripheral blood.

The patient was given digitalis and penicillin. Despite these measures and treatment in an oxygen tent his condition deteriorated and he died six days after admission.

**Findings at Necropsy**

The heart (440 g.) showed no congenital abnormality. There was conspicuous right ventricular hypertrophy. The ventricular wall was 9 mm. thick. The other chambers of the heart were normal and the walls not thickened. No abnormality was seen in the large pulmonary veins though no special search was made. The main pulmonary artery and its large branches were macroscopically normal. Scattered throughout the lung were numerous closely set small, reddish-brown areas. The rest of the organs showed much congestion. Apart from a Meckel's diverticulum there was no other abnormality.

**Histological Examination.** The organs other than the lungs showed only severe chronic venous congestion. Several blocks of tissue were examined from each of the lobes of the lungs. All showed similar and very striking lesions. In view of these it was obviously necessary to identify with certainty the structures involved. In order to do this one block was cut serially to provide 690 sections. These were stained by Verhoeff's elastic method and van Gieson's stain. Examination of them showed again that the only certain way to identify abnormal vessels was by demonstrating their connections either with arteries or veins (Brenner, 1935).

The elastic pulmonary arteries showed little change. The muscular pulmonary arteries showed striking abnormalities of the type usually associated with severe pulmonary hypertension. There was much medial thickening and also a striking development of additional longitudinally arranged muscle bundles external to the external elastic lamina (Fig. 1). There was conspicuous cellular intimal thickening containing fine strands of collagen and little or no elastica. This cellular intimal thickening extended from the arteries into arterioles and there the cells were arranged circumferentially inside a single elastic lamina.

The capillaries showed striking dilatation in sharply demarcated areas (Fig. 2). In many of these areas of capillary dilatation the alveoli contained numerous macrophages, but there was no significant fluid and, surprisingly, only very small amounts of hæmosiderosis (Fig. 3).
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There was very severe intimal thickening of veins: this was much more fibrous than the intimal thickening of the arteries and much less cellular, and it was also much more severe so that the lumen of the veins was in many cases almost obliterated (Fig. 4).

These pathological conditions were confined to small veins, the larger vessels being normal. In addition to the intimal changes, the media in many instances was strikingly altered, being much more defined than normal, and in many cases internal and external elastic laminae were better defined than was to be expected (Fig. 4). On this account these veins might have been mistaken for arteries, but in all cases doubtful vessels were identified by following them in serial sections. Arteries and veins identified in this way showed other differences. There was a conspicuous difference in the thickness of the media of the veins and hypertrophied arteries (Fig. 1 and 4). The character of the intimal thickening was also quite different, being less cellular and more collagenous (i.e. pink staining with van Gieson's stain) in the veins. These appearances, although very striking, were not used in the definitive identification of vessels.

Discussion

The anatomical changes in the lungs consisted of severe venous intimal fibrosis combined with areas of great capillary dilatation. The changes in the muscular arteries were those commonly found in primary pulmonary hypertension. It was impossible from histological study to decide whether or not the venous abnormalities preceded the arterial. The venous intimal thickenings contained more mature collagen and were less cellular than the arterial intimal thickenings, but this could not be accepted as being more than suggestive.

In this respect the patient reported by Edwards and Burchell (1951) is of interest. A woman of 26 had obstruction of the veins of all but one of the lobes of her lungs, due to a fibrous mass in the mediastinum. In all the lobes affected there were "severe occlusive vascular changes similar to those seen in some cases of mitral stenosis". They postulate that the occlusive arterial and arteriolar lesions in the lobes with severe venous obstruction protect the pulmonary capillaries from excessive passive congestion and from elevation of pressure. Whatever is postulated about the effect of the vascular changes in this particular patient, it is clear that the venous occlusion was acquired and was primary, while the arterial changes followed and occurred only in the lobes affected by the venous obstruction.
Ferencz and Damman (1957) examined the pulmonary vessels in 18 patients with congenital lesions of the heart that caused obstruction of the pulmonary venous drainage. There was much medial thickening of the muscular arteries with dilatation, tortuosity, and engorgement of the capillaries and veins. They remarked that “the reduction in the lumen-wall ratios of the small muscular pulmonary arteries was greater than in any other group of congenital malformations of the heart. This finding suggests that pulmonary venous obstruction is an important factor in the pathogenesis of pulmonary arterial narrowing”. This obviously applies to the changes in the pulmonary vessels in mitral stenosis. It also provides support for the idea that in our case the venous lesions might be primary and might have caused the arterial lesions. There is nothing to indicate the cause of the abnormalities in the veins. The history would not suggest a congenital origin but rather that they had developed in the last year or so of life.

The congestion and œdema seen on X-ray examination resulted from capillary dilatation. Morbid conditions of this kind are unusual in primary pulmonary hypertension. It might be possible from the radiographic appearance to suspect this condition during life. Cardiac lesions, congenital or otherwise, that might cause pulmonary congestion and hypertension would have to be excluded. Additional help might be gained from measurement of the pulmonary wedge pressure which is normal in most cases of primary pulmonary hypertension but would probably have been raised in the present case.

Summary

A case of primary pulmonary hypertension with widespread obstructive venous lesions is described in a boy of 16 years. These lesions caused widespread capillary dilatation in the lungs and probably contributed to the pulmonary hypertension. The significance of the lesions and their possible diagnosis is discussed.

References