PULMONARY ARTERIO-SCLEROSIS

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(With Special Plate)

The term pulmonary arterio-sclerosis implies a disease or syndrome the outstanding features of which are referable to arterio-sclerosis of the lesser circulation, this lesion being the predominant pathological finding. Whether or not the involvement of the pulmonary arteries is secondary to pre-existing disease—syphilitic or non-syphilitic—of the lungs themselves, if the results of such involvement alter the entire course of the disease and produce a recognizable clinical picture of their own, the term will still have its significance in diagnosis. The word "arterio-sclerosis" we retain as being clinical rather than pathological, and implying any change leading to thickening of the vessel wall. The syndrome of pulmonary arterio-sclerosis has also been described under the name of Ayerza's disease, or Ayerza-Arrillaga's disease, but as some writers have restricted the use of these terms to cases of syphilitic origin, and as neither Ayerza nor Arrillaga has an undisputed claim to being the first to recognize the syndrome, it appears preferable to adhere to a more descriptive terminology.

Vieussens in 1706 was probably the first to describe the pathological condition of pulmonary arterio-sclerosis. Ayerza in 1901 described in clinical lectures the syndrome of right ventricular hypertrophy, cyanosis, and polycythaemia (cardiacos negros) in patients with certain chronic pulmonary disorders, which his pupil Arrillaga, in a thesis published in 1913, correlated with the anatomical finding of sclerosis of the pulmonary artery. Posselt¹ (1908) had, however, already published his paper describing the clinical and pathological features. Cheney² in 1927 described two cases, and gives in his paper a complete bibliography (forty cases in all) up to that date. About twenty-five more have since been described. In the majority of the reports the diagnosis has been made only after the patient's death, and it therefore seems to be of sufficient interest to record here three cases, in which a clinical diagnosis of pulmonary arterio-sclerosis was made, together with details of the post-mortem findings.

CASE I

Female, aged 52, married. First seen by one of us on February 5th, 1928. She had suffered from bronchitis, especially in the winter, for many years, and had noticed gradually increasing dyspnoea on exertion. About four months previously there had been a rather rapid change for the worse; since then she had been confined to bed, the chief symptoms of this latter period being swelling of the legs, abdomen, and arms, more severe dyspnoea, and cyanosis of the face, mucous membranes, and extremities. The patient was propped up in bed, but lying over towards her right side, in which position breathing was not obviously distressed so long as she remained still. Cyanosis was extreme, and of a deep blue-purple shade. There was pronounced oedema of the legs, back, and arms (especially the right arm), and extreme ascites, so that the abdominal organs could not be examined. There was considerable emphysema, bronchitis, and congestion of the bases of the lungs. The apex beat of the heart could not be made out, but the right border appeared to be at least one and a half inches to the right of the sternum. The heart sounds were normal. There was no pronounced arterio-sclerosis of the brachial, radial, or retinal arteries; the blood pressure was 130/70. A provisional diagnosis of pulmonary arterio-sclerosis was made, and she was admitted to the Royal Infirmary under Professor Mellanby on February 6th, remaining in about the same

condition until midnight of March 23rd, when she vomited a large quantity of blood, and died. During the time she was in hospital the urine was scanty, of fairly high concentration (specific gravity 1020 to 1026), and contained a trace of albumin. The blood count on February 8th showed 6,480,000 red cells per c.mm., haemoglobin 100 per cent., white cells 8,400 per c.mm. A paracentesis of the abdomen was performed, 13½ pints of clear fluid being removed. Owing to the oedema, four attempts to remove blood from a vein (for Wassermann test) were unsuccessful.

At the post-mortem examination a generalized oedema, most marked in hands and feet, was found. There was marked oedema of all tissues internally. The pericardium showed increase of clear, straw-coloured fluid; "milk-spots" on right ventricular wall. There was a marked dilatation and hypertrophy of right ventricle; right auricle dilated; valves normal. Very little atheroma of the aorta present. Trachea normal; extensive oedema of lungs, resistant on section; marked atheroma of pulmonary artery, especially in the smaller branches; emphysema of anterior borders of the lung. Excess of clear fluid in pleurae. Apical adhesions on both sides. Other organs showed changes of passive congestion, and do not warrant special description. Histological examination demonstrated atheroma of pulmonary artery and its branches. There was an apparent increase in fibrous tissue round the smaller vessels, but there was no sign of any change in the muscle or intimal coats. Elastic tissue of vessels normal. Oedema, slight anthracosis, catarrhal bronchiolitis, and emphysema were also present.

CASE II

Female, aged 63, married. She was admitted to the Royal Infirmary under Dr. Yates on the evening of November 11th, 1929. She had always had good health until two years before, when she first noticed shortness of breath on exertion. Some months later she noticed swelling of the ankles, which was more pronounced towards evening. In the previous seven weeks she had become very much worse, the swelling having spread to the abdomen. According to her husband, she had some "winter bronchitis" for a few years, and had been cyanosed for some weeks. On examination extreme plum-coloured cyanosis was present, but the patient at rest in bed, with the head and shoulders supported, was not markedly dyspnoeic. There was considerable oedema of the legs, and a large ascites. The left border of the heart was 4 inches, the right 2½ inches, from the mid-line. The heart sounds were normal. The liver dullness extended 4 inches below the right costal margin. The blood pressure was 130/62. There was no pronounced general arterio-sclerosis. The lungs showed no great degree of emphysema, but adventitious sounds were present throughout. The patient was too ill for a very thorough examination to be made, and died three days after admission. The diagnosis of pulmonary arterio-sclerosis was made by exclusion of other conditions which could account for such a degree of cyanosis and failure of the right ventricle. Unfortunately a blood count and Wassermann test were not performed before the death of the patient.

Post-mortem Examination.—Pericardium: excess of clear fluid. Heart: dilatation and hypertrophy of right side; myocardium dark and firm; fibrosis in tips of papillary muscles on the right side; atheromatous plaques at bases of mitral and tricuspid valves; no stenosis. Aorta: atheroma at efflux of great vessels; atheromatous ulceration and calcification in abdominal aorta. Pulmonary artery and branches: marked atheroma. Trachea normal. Lungs: marked congestion at both bases; emphysema of both anterior borders; vessels showed numerous atheromatous plaques, most marked in areas midway between hilum and pleura; in places the lumen of the vessels was almost occluded. Pleurae: excess of clear fluid. The remainder of the organs showed no abnormality except passive congestion. Material from lung near hilum on histological examination showed atheroma, with slight medial hypertrophy; material from half-way between hilum and pleura showed most pronounced changes. There was a slight degree of emphysema, with oedema, congestion, and areas of haemorrhage. The smaller vessels of the pulmonary circulation were greatly thickened owing to medial hypertrophy. No intimal changes were noted. The bronchial vessels were in all areas quite normal. (See Figs. 1 and 2, Special Plate.) Some anthracosis and catarrhal bronchiolitis were present.

CASE III

Female, aged 46, married. Admitted to the Royal Infirmary under Dr. Yates, January 27th, 1931. For thirty years she had suffered from bronchitis and shortness of breath. In October, 1930, she had a severe headache and "turned dizzy," after which she was unconscious for two days. Since then she had been confined to bed, the legs having become swollen; she had been very short of breath on moving about in bed. On examination there was orthopnoea and extreme plum-coloured cyanosis. There was marked clubbing of the fingers. The legs and back were oedematous, and there was moderate ascites. The movements of the chest were symmetrical, but very restricted. Air entry poor. The percussion note was resonant throughout, breath sounds vesicular, with generalized rales and rhonchi. The apex beat of the heart was in the sixth interspace, and somewhat diffuse; the left border was $5\frac{1}{2}$ inches, the right $1\frac{1}{2}$ inches, from the mid-line. A systolic murmur was heard in the mitral area, conducted towards the axilla. The liver was enlarged to a level 3 inches below the costal margin. The sputum was mucopurulent, and contained no tubercle bacilli. The red blood count was 5,200,000 per c.mm., haemoglobin 85 per cent. Albumin was present in the urine, which was scanty and of normal concentration (specific gravity 1012 to 1020). The non-protein nitrogen of the blood was 43 mg. per 100 c.cm. The Wassermann reaction was negative. The combination of right-heart failure, with extreme cyanosis and the history of chronic bronchitis, suggested the possibility of pulmonary arterio-sclerosis, especially as there was no pronounced emphysema. There was no marked change in the patient's condition during her stay in hospital, and she died on February 19th, apparently from heart failure.

At the post-mortem examination the pericardium was found to contain excess of clear fluid. Gross dilatation of heart and hypertrophy of right side; left side normal. Muscle pale, but firm; no fibrosis or fatty degeneration. Valves: slight atheromatous change at base of mitral and aortic cusps; marked atheroma at base of tricuspid flaps. Aorta: very little atheroma. Pulmonary arteries showed marked atheromatous change. Pleurae: excess of clear fluid. Lungs: dark in colour; bronchi very firm and stood out above the cut surface, filled with thick tenacious mucus; marked oedema at both bases; very small vessels just beneath pleura remained patent, and stood out above the cut surface; slight anterior border emphysema, of compensatory type. Mediastinal glands: marked carbon pigmentation. Other organs showed evidence of passive congestion only. On histological examination the lungs showed marked passive congestion. Bronchi and bronchioles gave evidence of long-standing inflammation; there was pronounced muscular hypertrophy, submucous fibrosis, and formation of granulation tissue. The contents of the lumen demonstrated a catarrhal bronchitis, and in places there was a squamous metaplasia. The bronchial arteries were normal throughout. The pulmonary artery and its main branches showed marked atheroma. Some of the smaller pulmonary arteries were normal; others showed extreme degrees of arterio-sclerotic change. There was a well-marked muscular hypertrophy; whereas the bronchial arteries in cross-section were flattened, these remained circular. This was accompanied by hypertrophy and reduplication of the internal elastic lamina. Internal to this was a very exuberant proliferation of the subintimal connective tissue. (See Figs. 3 and 4, Special Plate.) Within this subintimal fibrous hyperplasia were found small vascular channels, giving the appearance of recanalization after thrombosis, but the muscular hypertrophy and elastic reduplication denoted that the change was an arterio-sclerotic and not a thrombotic one.

DISCUSSION

The cases described have occurred in a series of 700 post-mortem examinations, and are therefore of some rarity. The three examples have one feature of their morbid anatomy in common—namely, extensive atheroma of the pulmonary artery and of its branches. Pulmonary atheroma is a concomitant of pulmonary arterial hypertension. Hypertension may be due to theoretical pressor substances, or to mechanical obstruction, which may act in the venous, capillary, or arterial parts of the circula-

tion. Mitral stenosis is the commonest cause of pulmonary atheroma, and is an example of venous obstruction. Capillary obstruction is exemplified by emphysema, wherein there is a marked reduction in the total capillary bed. Pulmonary arterio-sclerosis is the example of obstruction to the arterial portion of the lesser circulation, and the arterial changes bear a striking resemblance to those found in chronic interstitial nephritis.

At post-mortem examination none of the three cases showed any valvular lesion. All three showed varying degrees of emphysema, together with signs of passive congestive heart failure. Microscopically, two of the cases disclosed hypertrophy of the muscular coat of the pulmonary arteries, and one of these had a secondary subintimal hyperplasia in the small vessels of the lung tissue adjacent to the pleural surface. A striking feature was that the bronchial arteries, being members of the systemic circulation, showed no change in the muscle coats, the sclerosis being confined entirely to the pulmonary vessels. Other features worthy of mention were an absence of microscopical evidence of syphilis and the presence of chronic bronchitis and bronchiolitis. Thus, right-heart failure, the cause of death in all three cases, was due in the first case to emphysema, and in the others to pulmonary arterio-sclerosis, all three being complicated by inflammatory disease of the bronchi and bronchioles.

The clinical features of the three cases were very similar, and fit in well with the descriptions in the literature, yet in the first case histological examination failed to reveal evidence of pulmonary arterio-sclerosis (other than atheroma) sufficient to warrant the case being recorded as an example of this syndrome. It appears, therefore, that with the clinical methods at present available only a provisional diagnosis can be made, microscopical examination of the lung being necessary before final proof is established. Pulmonary arterio-sclerosis is not the only syndrome, however, in which clinical diagnosis is somewhat uncertain, and a summary of the outstanding features which suggest the diagnosis is therefore not without importance.

The disease, whether syphilitic or otherwise, is preceded by a bronchitic stage, which may last for many years, and takes the form of chronic bronchitis with mucoid or mucopurulent sputum, and occasionally haemoptysis. The cardiac stage, which succeeds this, is divided by Nathan³ into a period of compensation, in which the colour is reddish-purple, the right heart enlarged, the pulmonary second sound loud, and polycythaemia present, and a final stage of right-heart failure (cardiopathie noire, cardiacos negros) in which the patient develops the typical extremely deep blue-violet, or almost black, cyanosis, with generalized oedema, congestion of the lungs, haemorrhages, somnolence, and sometimes anginal pain. Clubbing of the fingers has been noted, but is not a constant finding. It was present in only one of our cases. According to Yater and Constam,⁴ radiograms reveal a widening of the pulmonary artery with enlargement of the right auricle and ventricle, but no increase of the pulmonary veins or left auricle. Points which seem to us most suggestive of the diagnosis are: (1) a history of chronic pulmonary disease (bronchitis); (2) the presence of extreme cyanosis out of all proportion to the degree of dyspnoea, accompanied by polycythaemia, and enlargement of the right heart without valvular disease; (3) rapid development of oedema, which often affects the arms as well as the legs and abdomen. The diagnosis is more certain in the absence of pronounced emphysema.

REFERENCES

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FIG. 1.—Section of lung midway between hilum and pleura showing medial hypertrophy of pulmonary artery without intimal change. Haemorrhage adjacent.

FIG. 2.—Section of lung adjacent to portion illustrated in Fig. 1, showing bronchiole and accompanying vessels. Peribronchiolar lymphocytic and polymorphonuclear infiltration. Vessels show no hypertrophic change in intima or media.

FIG. 3.—Vessel midway between hilum and pleura showing medial hypertrophy and subintimal fibrous hyperplasia.

FIG. 4.—Vessel similar to that in Fig. 3 stained to show hypertrophic elastic tissue.