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IDIOPATHIC COR PULMONALE IN AFRICAN CHILDREN

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Cor pulmonale in children is comparatively rare and there are not many conditions that enter into the differential diagnosis. The most important causes are chronic lung disease (unresolved pneumonia, emphysema, etc.), and pulmonary hypertension, which may be primary or secondary to congenital heart disease. In addition, in recent years reports have appeared of the Hamman-Rich syndrome in infants and children.[1-5]

We report 5 cases of a cardio-respiratory syndrome in children whose clinico-pathological features did not fall into the usual categories of cor pulmonale.

CASE 1

V.M., an African male aged 25 months, weighing 26 lb., was admitted on 9 September 1958 to Baragwanath Hospital with a history of cough and swelling of the whole body of 2 days' duration. He had been admitted to another hospital for the same complaint on 2 occasions in the previous 6 months. He was extremely dyspnoeic, cyanosed, and oedematous with a raised jugular venous pressure. There was gross cardiomegaly, hepatomegaly and ascites, with coarse crepitations in both lung bases. The cardiac impulse was strongest over the lower end of the sternum, and there was a grade I apical systolic murmur. The peripheral pulses were good and the extremities warm. No finger clubbing was present. The heart rate was 114 with regular rhythm and the blood pressure was 80/40 mm.Hg. The

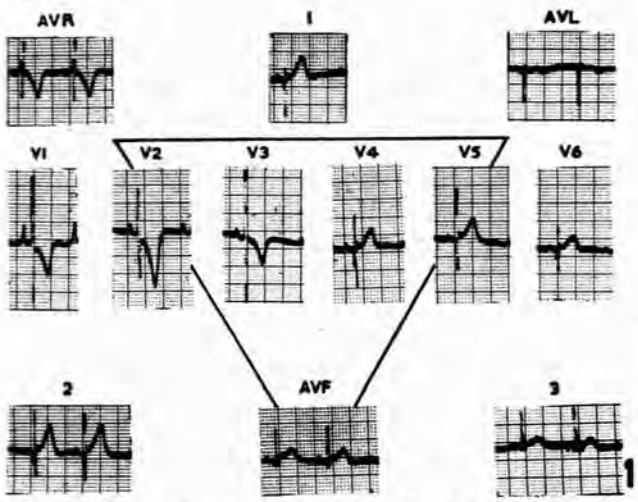

Fig. 1. Electrocardiogram showing right axis deviation — + 120°; right atrial enlargement — tall peaked P waves V_1 - V_2; marked right ventricular hypertrophy and strain — systolic overload (tall R waves with depressed ST segments and inverted T waves V_1 - V_4).

ECG pattern showed a large right ventricle (Fig. 1) which was confirmed radiologically (Fig. 2). He was given oxygen and digitalis and after 48 hours had responded very well, with disappearance of the cyanosis and the systolic murmur. The 2nd pulmonary sound was accentuated, but unsplit. At this time a loud early diastolic murmur was audible in the 2nd left interspace, but disappeared after 24 hours. During convalescence an attempt at cardiac catheterization was made, but had to be abandoned because the child developed a cardiac arrhythmia. Over the next 2 or 3 weeks the systolic murmur over the praecordium and the diastolic murmur in the 2nd

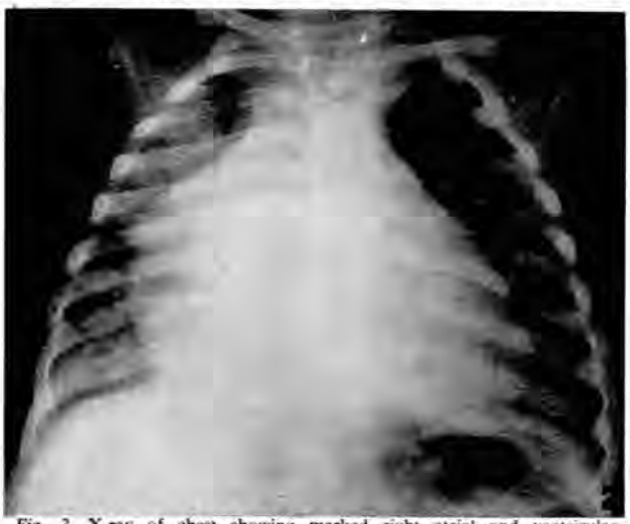

Fig. 2. X-ray of chest showing marked right atrial and ventricular enlargement.

left interspace came and went without explanation. He recovered completely from the congestive cardiac failure and left hospital 32 days after admission.

He was re-admitted 6 weeks later with signs of cor pulmonale and with bronchopneumonia. He responded fairly well to treatment and was sent home on the 23rd hospital day. A month after leaving hospital he was again re-admitted with severe cor pulmonale which failed to respond to treatment, and died on the 28th hospital day.

Autopsy Findings

There was slight oedema of the lower limbs. The heart was markedly enlarged (weight 225 G., expected weight about 56 G.) from hypertrophy and dilatation of the right ventricle and right auricle. The anterior wall of the right ventricle measured 9 mm. at the outflow tract. The epicardium, myocardium, and all the valves appeared normal, but the main pulmonary trunk was slightly wider than the aorta. There was no evidence of any congenital cardiac defect.

The lungs (combined weight 310 G.) were almost double the expected weight. The pleural surfaces were smooth and presented a mottled appearance, dark-red areas alternating with paler greyish areas. Scattered sub-pleural petechiae were present. There was slightly increased resistance on cutting the lungs, and the parenchyma also presented a mottled-red appearance. In addition there were about 12 small, round, greyish-white nodules, measuring about 1 mm. in diameter, scattered throughout the parenchyma of both lungs.

The hilar and tracheobronchial lymph nodes were of normal size and appeared healthy. The pulmonary vessels were normal and the remaining organs showed congestion only.

Microscopic Examination

The heart showed hypertrophy of the muscle fibres of the right ventricle. There was no evidence of rheumatic carditis and the valves were normal.

The lung picture was fairly uniform in multiple sections from both lungs. There were numerous macrophages in most of the alveoli. They were large, many had lobed nuclei, and many were multinucleated (Figs. 3 and 4). Their cytoplasm contained granules which were periodic-acid-Schiff (PAS) positive, and remained so after diastase digestion. A few macrophages showed cytoplasmic vacuoles; some contained small quantities of lipid and many contained haemosiderin granules. No inclusion bodies were found. The alveolar septa were thickened, and the septal capillaries congested and increased in number. There was minimal septal cellular infiltration, consisting of occasional lymphocytes, histiocytes and rare neutrophil leucocytes (Fig. 5). Some alveoli showed swelling of their lining cells. Silver impregnation showed a moderate increase in the thickness and number of reticulin fibres. In some areas these formed a broad interlacing meshwork surrounding the septal capillaries (Fig. 6).

Sections of the small nodules showed them to be granulomata with necrotic eosinophilic centres. Outlines of the septal capillaries were still visible in the granular debris. Surrounding

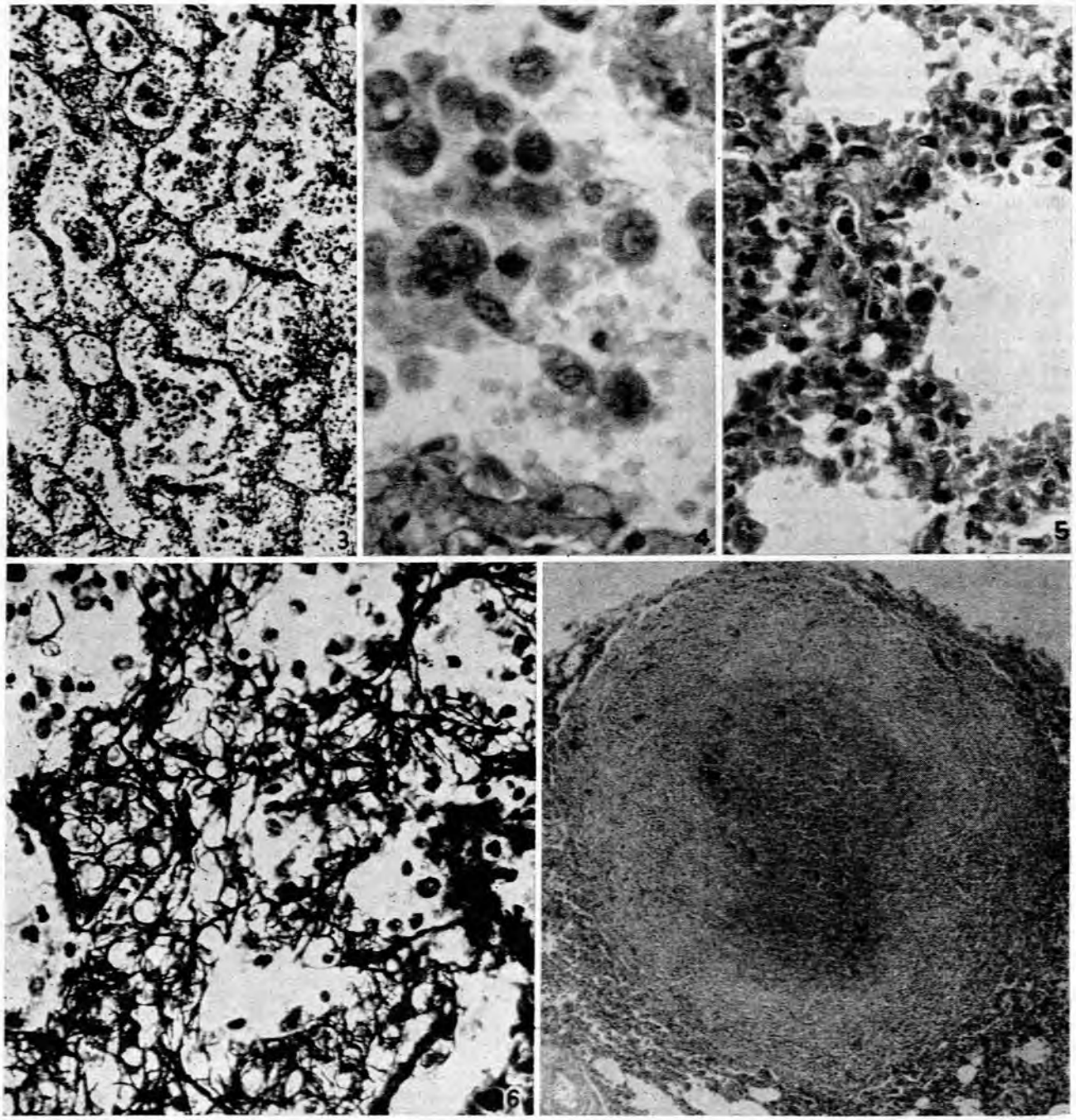

Fig. 3. Low-power section of lung showing numerous macrophages in the alveoli (haematoxylin and cosin × 120).
Fig. 4. High-power photograph of Fig. 3 showing numerous large macrophages in the alveoli.
Fig. 5. Thickened alveolar septa with moderate cellular infiltrate (haematoxylin and eosin × 120).
Fig. 6. Moderate reticulin proliferation in alveolar septa (Gordon and Sweet silver impregnation × 480).
Fig. 7. Section of a granuloma showing necrotic centre (haematoxylin and eosin × 45).

the necrotic centres there was a zone of macrophages, fibroblasts and occasional foreign-body-type giant cells. Stains for tubercle bacilli and fungi were negative (Fig. 7).

The bronchi and bronchioles were normal. The pulmonary arteries were in the main normal, although a few small branches showed slight recent intimal thickening, and, in 1 or 2 instances, recent antemortem thrombi.

The hilar lymph nodes showed non-specific reactive hyperplasia with marked congestion and some haemosiderosis.

Sections of the remaining viscera showed passive congestion only.

SUMMARY OF CLINICAL AND PATHOLOGICAL FINDINGS IN REMAINING 4 CASES

The clinico-pathological features of these 4 cases were those of cor pulmonale of unknown aetiology. The ages of the children varied from 10 months to 2½ years, and they all presented at hospital with cough, oedema and dyspnoea, all of about 2 weeks' duration. All the subjects presented during a 2-month period.

Clinically, the signs were those of cor pulmonale with congestive cardiac failure. While in the ward, over a period of a few months, the cardiomegaly increased rapidly. Laboratory investigations were negative. There was no evidence of whooping cough, bronchiectasis, emphysema, asthma, fibrocystic disease, rheumatic fever or tuberculosis. Three patients gave a past history of bronchopneumonia and 1 had had whooping cough 1 year previously. The family histories were non-contributory. These children failed to respond to the usual measures adopted for cardiac failure, and they all died 1½ - 11 months after the onset of symptoms.

At autopsy, the pertinent findings were confined to the heart and lungs. The hearts were grossly enlarged owing to right ventricular hypertrophy, the weights varying from 1½ to 4 times the expected weight. There were no congenital cardiac abnormalities. The lungs were uniformly enlarged, heavier than normal, and showed increased resistance to cutting. The parenchyma showed a diffuse mottling, dark-red areas alternating with those of normal colour. Some of the other cases showed focal bronchopneumonia. The hilar lymph nodes were normal in all cases. The remaining organs showed the effects of chronic passive congestion.

Microscopic examination of the hearts showed muscle hypertrophy only. There was no evidence of a rheumatic carditis. Sections of the lungs showed a fairly uniform picture. Numerous macrophages were present in the alveoli and these often contained haemosiderin and some PAS-positive material. Occasional macrophages contained small amounts of fat. Areas of intra-alveolar haemorrhage were frequent, and scanty hyaline membrane was seen in one case. The alveolar septa showed proliferation of the capillaries. None of these cases showed the granulomata observed in case 1. There was no evidence of tuberculosis, and the features were not those of alveolar proteinosis. Stains for fungi, bacilli and inclusion bodies were uniformly negative.

Bronchopneumonia of varying severity was seen in most cases. There was no evidence of pneumocystis carinii. Pulmonary vascular changes, when present, were mild and probably secondary to pulmonary hypertension.

DISCUSSION

The difficulty in these cases was that of identifying the disease process in the lungs. There was perhaps some resemblance to diffuse interstitial fibrosis of the lungs of the Hamman-Rich type.[1] Although rare in children, several cases have been described under the age of 10 years, the youngest being 7 months,[2-6] and recently a similar condition has been described in premature infants.[6] Heppleston[7] was the first to note that the fibrous proliferation in the alveolar septa in the Hamman-Rich syndrome was of reticular rather than collagenous type. Golden and Bronk[8] considered that the fundamental lesion was reticular hyperplasia associated with vascular changes. True fibrosis does occur, but tends to be focal rather than diffuse and does not obscure the fundamental vascular and reticular hyperplasia.

It is possible that some of the changes in the alveolar septa in our cases could have been brought about by oxygen administration. Pratt[9] presented evidence to show that, with oxygen inhalation for as little as 2 days, pulmonary alterations, consisting of capillary congestion and proliferation, may be observed. After continuous inhalation for approximately 2 weeks, diffuse fibrosis has been encountered. The lesions are thought to be reversible until fibrosis supervenes. Our subjects were admitted with cor pulmonale and then given oxygen. While the oxygen could thus not have caused the initial heart failure, it may have played a part in accentuating the reticular proliferation in the lungs.

Intra-alveolar haemorrhage was a frequent finding in our cases and macrophages containing haemosiderin were prominent. These changes were, however, probably from the congestive cardiac failure and not severe enough to warrant a diagnosis of idiopathic pulmonary haemosiderosis. The changes in the pulmonary elastic tissue were not remarkable, and foreign-body giant cells containing engulfed elastic tissue were not observed.

The significance of the granulomata in case 1 remains uncertain.

SUMMARY

Five cases of cor pulmonale of obscure aetiology in children are described. A possible relationship to the Hamman-Rich syndrome is discussed.

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