BILHARZIAL HEART DISEASE IN EGYPT

COR PULMONALE DUE TO BILHARZIAL PULMONARY ENDARTERITIS

BY

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Of the various pathological causes of pulmonary endarteritis and right heart failure, schistosomiasis is probably the least familiar outside Egypt and other countries where the disease is endemic. It has long been known that bilharzia ova are sometimes deposited in the lungs (Belleli, 1885; Turner, 1909), and that adult worms of *S. haematobium*, often coupled males and females, may be found in the pulmonary vessels (Symmers, 1905; Day, 1937). In 1928, Sorour reported pulmonary bilharziasis as a common post-mortem finding in Egypt, and described small fibrous nodules due to ova deposited in the lungs, which he named bilharzial tubercles because of their semblance to the tubercles caused by Koch's bacillus. He also described a verminous lobular pneumonia due to the presence of dead bilharzial worms, and an "endobronchitis obliterans." Under the term "bilharzial atheroma," Sorour described deposits of ova in the intima of the pulmonary vessels resulting in endothelial proliferation, and he mentioned the wealth of new capillaries in the thickened intima, since recognized as a characteristic feature of bilharzial pulmonary endarteritis. In 1932 S. Azmy Pasha, of Cairo, recorded the first case of bilharzial heart disease observed clinically and pathologically. He described two cases with cardiac enlargement, gross dilatation of the pulmonary artery and pulmonary incompetence, associated with bilharzial hepato-splenomegaly. Necropsy was performed in one case and showed deposits of bilharzia ova in the lungs, obliterative endarteritis of the small pulmonary vessels, atheroma and dilatation of the main pulmonary trunks, and hypertrophy with dilatation of the right side of the heart; in addition, there were bilharzial lesions of the bladder and cirrhosis of the liver. Similar cases were later reported by Clark and Graef (1935) in a Porto Rican and by Day (1937) in Egypt. By far the most important contribution to the subject was made by Bernard Shaw and Ghareeb (1938) who described very fully the pathological changes of pulmonary schistosomiasis with special reference to the arterial lesions and to "Ayerza's disease."

Cor pulmonale with gross dilatation of the pulmonary artery is by no means a rare clinical finding in Egypt, certainly far more common than in England. It is usually encountered in young adults suffering from advanced visceral bilharziasis (Egyptian hepato-splenomegaly) or from severe genito-urinary infection with *S. haematobium*. Cor pulmonale occurred in 0.8 per cent of 520 consecutive cases of visceral bilharziasis admitted to the Kasr-el-Aini Hospital, and was found in 2.1 per cent of 282 consecutive autopsies on cases of schistosomiasis (Shaw and Ghareeb). The clinical diagnosis of "Bilharzial Ayerza's disease" is not infrequently made in the wards, and cases have been shown at clinical meetings (Mousa, 1942), yet the number of cases on record, in which both clinical and pathological findings are given, is scanty. The following new case is therefore reported.

CASE REPORT

A farmer, aged 34, was admitted to the Kasr-el-Aini Hospital under Dr. Gaafar. For three years he had suffered from dyspnoea on exertion, cough with slight expectoration, and præcordial pain. For several years he had noticed hæmaturia at the end of micturition.

On examination he was breathless at rest, but not obviously cyanosed. There was no clubbing of the fingers. The neck veins were not engorged and there was no œdema. The rhythm was regular; the blood pressure, 120/80 mm. The apex was in the fifth interspace, four inches from the mid-line. There was visible and palpable pulsation in the first and second left interspaces, with dullness on percussion to the left of the sternum in this area. Auscultation showed an accentuated first sound and soft systolic murmur at the apex, and a much accentuated pulmonary second sound. The chest was emphysematous in shape, but there were no added sounds over the lungs. The liver and spleen were enlarged and firm.

X-ray of the chest (Fig. 1) showed an aneurysmal swelling in the region of the main

FIG. 1.—Radiograph showing aneurysmal dilatation of pulmonary artery and its right branch in the hilum. The aortic knob is invisible.

pulmonary trunk without any visible aortic knob, and the right pulmonary artery in the hilum formed a swelling of aneurysmal proportions. The heart was enlarged to right and left. There was no obvious fibrosis of the lungs. Urine contained a trace of albumin, red cells, pus cells, and living ova of *bilharzia hæmatobium*. The stools contained *ankylostoma* ova. Wassermann reaction, negative: blood-count; red cells 4,660,000; white cells 7800 (polymorphs 62 per cent, lymphocytes 26 per cent, eosinophils 10 per cent, monocytes 2 per cent).

Three weeks after admission he became suddenly worse. He complained of pain over the liver, the cervical veins became engorged, marked cyanosis appeared, and gallop rhythm was audible at the apex. The liver became more swollen, jaundice developed, and he died a few days later.

NECROPSY

Heart weight, 550 g. (approx.). The pulmonary trunk was grossly dilated, forming a sac 6.5 cm. in diameter; the circumference just above the valves was 13.5 cm. Both main branches of the pulmonary artery formed aneurysmal swellings which were almost circular, and 7 cm. in diameter. On opening up the artery, the main trunk showed thickening of its wall and intimal atheromatous plaques. The walls of both main branches were thickened and the seat of advanced ulcerated atheroma; their lumina were filled and almost occluded

by ante-mortem thrombus of some standing. Atheroma extended into the medium-sized arterial branches in the lungs (see Fig. 2 and 3).

The aorta was hypoplastic, with a circumference above the valves of 6 cm., and showed slight intimal atheroma but no evidence of syphilitic aortitis. The heart itself showed gross enlargement of the right side, both ventricle and auricle being dilated to about three times their normal capacity. The right ventricle was much hypertrophied, its wall being 1.3 cm.

FIG. 2.—Heart and attached left lung with anterior wall of pulmonary artery and of its left branch removed to show contained thrombus.

FIG. 3.—Heart and aorta viewed from right, showing aneurysmal dilatation of right pulmonary artery and occluding thrombus.

thick, and the auricle was also hypertrophied. The left ventricle was normal. All the valves were healthy, and both inter-auricular and ventricular septa were intact.

The lungs were congested but free from bilharzial tubercles. The liver weighed 1400 g.; it was coarsely granular and congested, and the naked eye appearance was suggestive of bilharzial cirrhosis. The spleen weighed 750 g.; its capsule was thickened and its pulp fibrotic. The intestines appeared normal. The bladder showed a "sandy patch" at the trigone, and ova of *S. hæmatobium* were present in scrapings. The ureters were normal and the kidneys showed congestion only.

HISTOLOGY

Lungs. Sections from both lungs were examined. The alveoli were normal except for some degree of venous congestion and extravasation of red cells. The pulmonary arterioles were much thickened and showed marked obliterative endarteritis (Fig. 4). There were numerous "angiomas," both of capillary and cavernous type, typical of bilharzial pulmonary arteritis (Fig. 5). Bilharzia ova were seen in relation to some of the arterioles;

FIG. 4.—Section showing small pulmonary vessel occluded by canalized intimal thickening.

the ova were distorted and shrivelled and sometimes occupied by giant cells (Fig. 6 and 7). In the interstitial tissues, ova were scanty and calcified. Sections stained by Levaditi's method did not show any spirochætes.

Pulmonary arteries. Sections from the trunk and two main branches showed atheroma with calcification. The adventitia showed thickened vasa vasorum with perivascular infiltration by lymphocytes and plasma cells. There were minute foci of cellular infiltration in the media, but no destruction of the musculo-elastic coat suggestive of syphilis, and no spirochætes could be found in sections stained by Levaditi's method. In the main branches, there was organized thrombus of moderate age.

Aorta was normal, except for some cellular infiltration of the adventitia, and there was no evidence of a syphilitic lesion.

Liver showed periportal cirrhosis of the type usually produced by bilharzial disease in Egypt.

Spleen showed hyalinosis of the central arterioles of the lymphoid bodies. Sinusoids were filled with red cells and histiocytes. The trabeculæ were prominent and there were fibro-siderotic nodules which gave the prussian blue reaction. Bilharzial pigment both intra-

and extra-cellular was present, but no parasites or ova were seen. The histological picture was that usual in endemic splenomegaly.

Bladder and colon showed deposits of calcified ova in the submucosa.

Anatomical diagnosis. Pulmonary endarteritis due to bilharziasis; atheroma and aneurysmal dilatation of the pulmonary artery and main branches, with thrombotic occlusion. Hypertrophy and dilatation of the right heart. Cirrhosis of liver; bilharzial splenomegaly; bilharzial cystitis.

DISCUSSION

Pathology. Adult worms may be found in the lungs where, when dead, they produce a focal verminous pneumonia, and later become calcified. The more important pulmonary lesions are, however, caused by the ova which reach the lungs as emboli from the normal habitat of the worms and become impacted in the pulmonary arterioles. In the case of *S. hæmatobium*, the ova travel direct from the systemic veins to the right heart and lungs. In the case of *S. Mansoni*, which inhabits the portal tract, ova must reach the systemic veins via collateral venous channels which develop when the liver has become cirrhotic.

Shaw and Ghareeb classify pulmonary bilharzial lesions as follows:

- (1) Parenchymatous tubercles.
- (2) Focal arterial lesions.
- (3) Widespread arterial lesions causing "Ayerza's disease."

Ova of both *S. hæmatobium* and *S. Mansoni* infest the lungs, but the latter more often cause arterial lesions. The ova become impacted in the arterioles causing a necrotizing arteriolitis, and may then pass through the vessel wall, destroying the media, and so become extravascular, when they form bilharzial tubercles. Healing of the vascular lesion causes

FIG. 5.—Drawing of section showing angioma-like formation round occluded and vascularized pulmonary vessel.

FIG. 6.—Section of thickened pulmonary vessel with adjacent giant cell filling shell of ovum.

FIG. 7.—Section showing obliterative endarteritis of pulmonary arteriole, the wall of which contains a calcified bilharzia ovum and adjacent angiomatoid formation.

obliterative endarteritis. Shaw and Ghareeb have shown that the distinctive histological feature of bilharzial arteritis in the lungs is the formation of "angeiomatoids." The occluded vessel becomes canalized by new capillaries, some of which dilate forming blood spaces lined by endothelium and, in the absence of an intact medial coat, this vascularized tissue expands beyond the normal confines of the vessel and may reach cavernous dimensions. They found no evidence that angeiomatoid formation was the result of thrombosis followed by canalization of the arterioles, for when this happens the vascular tissue is contained within an intact media. Clark and Graef (1935) also described highly vascularized tissue expanding the vessels in bilharzial arteritis of the lungs, and they too excluded canalized thrombosis as the explanation; they also noted extravascular granulomas containing endothelial lined channels. Serial sections are necessary in order to demonstrate the relation of the angeiomatoids to the vessel lumen.

In the earlier stages of bilharzial infection of the lung, ova may be seen in the vessel walls (Fig. 8) and in extravascular tubercles, but later, when there is widespread obliterative arterio-
litis, and enlargement of the right heart, the ova may be scanty or absent, and angeiomatoids

FIG. 8.—Section showing bilharzia ova embedded in intima of small pulmonary vessel.
(By the courtesy of Prof. Sorour.)

may then be the only evidence of a bilharzial aetiology. Shaw and Ghareeb believe that massive and repeated embolism of the lungs by ova is necessary to cause pulmonary hypertension and enlargement of the right ventricle.

Vessels proximal to the obstruction show medial hypertrophy and intimal thickening which is a reaction to pulmonary hypertension, and the larger branches show atheroma. Occlusion of the main pulmonary arterial branches in the hila by organized thrombus, as occurred in the present case, has also been reported in aneurysmal dilatation of the pulmonary arterial tree due to atrial septal defect (Bedford, Papp, and Parkinson, 1941); it occurred in three of Brenner's cases of primary pulmonary arteriosclerosis, and in others cited by him (Brenner, 1935). In Azmy's case of bilharzial pulmonary arteritis, one main branch was occluded by clot regarded as embolic.

While changes in the pulmonary vessels are undoubtedly the cause of the cardiac enlargement and failure in bilharziasis, the myocardium is, occasionally, directly involved, and Clark and Graef found scanty ova of *S. Mansonii* surrounded by miliary foci of fibrosis, in both ventricles. In the case of *S. Japonicum*, Strong (1944) cites a case reported from Japan in which numerous bilharzial tubercles with giant cells occurred in the ventricular myocardium, so that sections viewed by low power resembled tuberculosis.

Clinical features. In Egypt, bilharzial cor pulmonale usually occurs in young adults aged 20 to 35 years, but proven cases as young as 12 and 13 years have been recorded (Shaw and Ghareeb). The condition is encountered mainly in residents of the Nile Delta, where infection with *S. Mansoni* is endemic and where hepato-splenomegaly is prevalent. Compared with other forms of chronic cor pulmonale, the bilharzial variety affects younger subjects and does not usually cause much cyanosis or clubbing of the fingers. The absence of cyanosis has been attributed to an associated anæmia due to hookworm infestation, but even in the absence of anæmia cyanosis is seldom severe, except as a terminal event. A more probable explanation is the fact that, in bilharzialis, the pulmonary lesion may be almost confined to the arterioles, leaving the alveolar and capillary structure intact (Mousa, 1942). In fact, bilharzial lung infection may amount to a primary pulmonary arteritis, and its main effect is to cause pulmonary hypertension and hypertrophy of the right heart. In the more common varieties of cor pulmonale, the vascular lesion is associated with chronic disease of the lung parenchyma, and it is the latter that interferes with oxygenation of the blood in the lungs and thus causes cyanosis. Radiographs of the chest in bilharzial heart disease rarely show any significant changes in the lung fields apart from vascular dilatation, and evidence of fibrosis is usually lacking.

Brenner (1935), in discussing primary pulmonary vascular sclerosis states that cyanosis is usually intense, but he cites cases, including syphilitic ones, in which it was absent. In theory, provided the lesion is limited to the arterioles and the hypertrophied right ventricle can maintain an adequate flow against the increased resistance, there is no reason why cyanosis should occur; it would be expected only when the right ventricle fails. Indeed, the classical clinical picture of so-called Ayerza's disease is really one of chronic lung disease and heart failure combined.

Mainzer (1938) has described the X-ray appearance of miliary infiltration of the lung fields in pulmonary bilharziasis, but at the Kasr-el-Aini Hospital these miliary shadows in the lung fields have only been observed during the course of antimony treatment, and are regarded as due to an allergic reaction around the ova. Clinically, some degree of emphysema, with or without bronchitic signs, is the usual finding in the chest.

The radiological appearance of the heart may be indistinguishable from that of atrial septal defect. Not only is the pulmonary trunk grossly dilated, but the hilar branches may also reach aneurysmal size, a feature regarded as especially characteristic of atrial septal defect. Pulmonary incompetence from enlargement of the valvular orifice is common in both conditions.

The main diagnostic problem is, therefore, to differentiate between bilharzial and congenital heart disease. The presence of bilharzial lesions elsewhere is, of course, important. All recorded cases of bilharzial heart disease and all cases that we have observed have also had hepato-splenomegaly, and some have also had lesions of the urinary tract. The presence of ova in the stools and urine should always be sought. The blood may show an eosinophilia, but less frequently and to a lesser degree than in the earlier stages of bilharzial infection. The intradermal reaction of Fairley may be positive even when ova are no longer to be found in the stools or urine.

SUMMARY

A case of chronic cor pulmonale with aneurysmal dilatation of the pulmonary artery, due to bilharzial endarteritis of the pulmonary arterioles, is described, and the pathological and histological findings are given.

The clinical and pathological features of the disease as it occurs in Egypt are briefly reviewed. It affects young adults, aged 20 to 35 years or even younger, infected with *S. Mansoni* or *S. haematobium* or both, and suffering from Egyptian hepato-splenomegaly.

Cyanosis and clubbing of the fingers are slight compared with that seen in other forms of chronic pulmonary heart disease, and clinical and radiological signs of lung disease are slight or absent. Dilatation of the pulmonary artery may amount to aneurysm, and relative pulmonary incompetence is common. The X-ray appearance of the heart is similar to that of atrial septal defect.

Pathologically, the changes are mainly vascular, and consist of an obliterative endarteritis of the pulmonary arterioles, atheroma and dilatation of the main vessel, and hypertrophy and dilatation of the right ventricle. Histologically, bilharzia ova may be identified in the walls of the small vessels and in extravascular tubercles. In the later stages, the occluded vessels become expanded by highly vascularized tissue to form "angiomatoids," which are a distinctive feature of bilharzial arteritis.

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