Mycotic Aneurysms of the Intrapulmonary Arteries

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SUMMARY
In the case presented, multiple aneurysms of the peripheral pulmonary arteries occurred in a child with secondary pulmonary hypertension complicated by bacterial endocarditis. Study of other reported cases suggests that pulmonary hypertension may be significantly associated with the development of mycotic aneurysms. As surgical resection of aneurysms has been at least temporarily successful, increased attention may be given to control of infection in these patients and to the appreciation of the frequency of aneurysms of the main pulmonary artery as well as peripheral pulmonary arteries in patients with congenital heart disease and pulmonary hypertension complicated by bacterial endocarditis.

Additional Indexing Words:
Congenital cardiac disease
Bacterial endocarditis
Mycotic aneurysms
Recurrent infections
Pulmonary hypertension

Mycotic aneurysms of the intrapulmonary arteries have been the subject of several recent reviews in which the development of such aneurysms in association with recurrent thromboembolism has been stressed. It has also been appreciated that patients with congenital heart disease and with primary pulmonary hypertension have developed mycotic aneurysms. Septic embolization apparently occurs from infected thrombi in the former cases and from valvular endocarditis and sepsis in the latter groups. The suggestion that pulmonary hypertension might be an underlying factor in these different groups led us to review the available clinical and pathological data in the literature. This review, together with a brief case report, forms the basis of the present paper.

Report of Case

Clinical Summary
A 9-year-old Negro male was admitted to the Kings County Hospital Center, September 16, 1961, with respiratory distress, facial edema, and chest pain. Congenital heart disease was first recognized at 3 months of age and since then his physical endurance had been limited.

Physical examination revealed a pale Negro boy who weighed 49 lb, had a respiratory rate of 60 per minute, and blood pressure of 120/80 mm Hg. The heart was enlarged and there was a grade IV to V pansystolic murmur over the second and third left intercostal spaces which was transmitted along the left sternal border to the apex of the axilla; a grade III to IV diastolic murmur at the same location with transmission was also present.

The liver was enlarged, and there was pitting edema of the hands, feet, and legs. The patient was digitalized and treated for bacterial endocarditis with procaine penicillin, 1.2 million units per day, and chloromycetin, 95 mg/kg/day. He was given packed red cells and, later, several transfusions because of anemia. A blood culture taken on admission grew out beta hemolytic streptococci. Electrocardiograms showed combined ventricular hypertrophy, predominantly left ventricular. Chest roentgenograms (fig. 1), indicated pleural effusion at the right base with infiltration. The latter persisted in subsequent films even as the effusion cleared.

The patient appeared to improve over the first 3 to 4 weeks, although his temperature reached 101 F on three occasions despite continuous antibiotic therapy. Four blood cultures...
MYCOTIC ANEURYSMS

Figure 1

Chest x-rays taken shortly after admission. Pleural effusion obscures aneurysm in the right lower lobe.

were negative, and treatment with antibiotics was discontinued 1 month after admission. Chest x-rays showed a round density in the left lower lung field. Subsequent films in the fifth and sixth weeks in the hospital showed similar densities in the right lower lobe which had increased in size, compared with those taken 1 and 2 weeks previously (fig. 2). Three months after admission the patient suddenly coughed up a large amount of blood and expired. The clinical diagnoses were severe pulmonary hypertension secondary to a large left-to-right shunt, bacterial endocarditis, and pulmonary infarcts, or possibly, metastatic carcinoma.

Autopsy Summary

The heart, which weighed approximately 300 g was left attached to the left lung, and the right lung was separated for injection. Both ventricles were hypertrophied and the right was dilated as well. The right ventricular wall measured 0.5 cm and the left, 1.5 cm in thickness. The foramen ovale could be probed to a diameter of 2 mm. A 1.0-cm ventricular septal defect lay inferior to the crista supraventricularis and between the septal and anterior leaflets of the tricuspid valve. The pulmonary outflow tract was narrowed and the endocardium here was thick (fig. 3). The pulmonary cusps were thickened and distorted and their ulcerated free margins were occupied by calcified vegetations. The medial edge of the posterior cusp was torn from its attachment at the commissure.

The intima of the main pulmonary artery was thick and corrugated in patchy areas. This intimal thickening ended abruptly at the bifurcation of the pulmonary artery.

Numerous small and large aneurysms measuring 1 mm to 1.5 cm in diameter occupied the main pulmonary artery (fig. 4). A pedunculated thrombus or vegetation hung from the superior wall of the orifice of the right pulmonary artery. The left atrium, mitral and aortic valves were normal and the ductus arteriosus was closed. Measurements of valve circumference were as follows: tricuspid, 8.5 cm; pulmonic, 6.0 cm; mitral, 8.0 cm; and aortic, 5.0 cm.

Both lungs were adherent to the parietal pleura by fine fibrous adhesions, especially at the bases, and small infarcts were seen under the pleura. The tracheobronchial tree was filled with fresh and clotted blood. The left lung contained four aneurysms (fig. 4); the largest of these in the left lower lobe measured 4 cm in diameter and had ruptured into the adjacent bronchus. Post-mortem injection and x-rays of the right lung showed two large aneurysms, and subsequent reconstruction of the injected and sectioned lung showed that one was in the lower lobe and one was in the lower portion of the middle lobe. All aneurysms had thickened, rough intima which was at least partially covered by organized thrombus (fig. 5).

Microscopic Examination

The ventricular myocardium showed small focal areas of fibrosis in both ventricles; the coronary arteries were normal. A partially calcified

Figure 2

Chest x-ray 5 weeks after admission shows aneurysms in the left-lower and right-lower lung fields. (Compare with figure 4).
vegetation attached to the left anterior cusp of the pulmonary valve contained colonies of gram-positive cocci. The valve itself consisted of thickened and hyalized collagen and contained numerous small vessels.

The main pulmonary artery showed partial persistence of the fetal elastica pattern with rather elongated parallel bands of elastic tissue. Adventitial thickening was marked, both in the pulmonary artery and adjacent base of the aorta, and some of the lymphatics were filled with calcified thrombi containing gram-positive cocci. The vessels were cuffed by lymphocytes and plasma cells. Walls of the aneurysms showed destruction of elastica with fibrosis and focal calcification. There was marked intimal fibrosis (fig. 6).

The peripheral pulmonary aneurysms showed the same destruction of elastic tissue with replacement by organized granulation tissue. The wall of the large ruptured aneurysms was necrotic and contained foci of calcified thrombi and gram-positive cocci. Some of the small and medium-sized arteries also contained similar thrombi. The large muscular arteries were extremely tortuous, and many contained organized recanalized thrombi (fig. 7). Elastosis was common and muscular hypertrophy marked in the large and medium-sized muscular arteries.

Figure 3
The heart as seen from the outflow tract of the right ventricle showing pulmonary valve and pulmonary artery. The pulmonary cusps are the site of calcified vegetations and the posterior cusp is partially destroyed and torn from its attachment. Note the multiple aneurysms of the main pulmonary artery.
Multiple blocks of lung tissue were examined in step serial section for angiomatous and plexiform lesions, and in only one area distal to a large organized, recanalized thrombus was one found. Many thin-walled vessels led from the recanalized arteries to enter capillaries directly. Elastic pulmonary arteries showed intimal fibrosis as well as medial hypertrophy.

**Review of the Literature**

A summary of the present case and of the cases in the literature (excluding traumatic, syphilitic, and what appear to be congenital aneurysms) is shown in tables 1 to 3. Cases where only the main pulmonary artery was involved were also excluded.

The 22 cases were divided into three groups: group 1, patients with congenital heart disease; group 2, patients with recurrent infections and thrombophlebitis (Hughes–Stovin syndrome); and group 3, patients without congenital heart disease or known thromboembolism.

**Group 1**

The nine patients in this group (table 1) had congenital heart disease complicated by bacterial endocarditis and died either of heart failure, infection, or rupture of a pulmonary aneurysm. Blood cultures were positive for *Streptococcus viridans* in four cases and *Corynebacterium diphtheriae* in one.

At autopsy, six patients had patent ductus arteriosus, three had a ventricular septal defect, and all had bacterial endocarditis. Hypertrophy of both ventricles was found in seven cases with the thickness of the right heart exceeding that of the left in five of these cases.

Aneurysms of the main pulmonary artery were frequent in this group, occurring in six of the seven cases in which the pulmonary artery was described. Aneurysms of the intrapulmonary elastic arteries were bilateral and multiple in six, unilateral and multiple
in two, and single in one. Descriptions of the microscopic appearance of the aneurysms were essentially similar to those of our case and were usually interpreted as mycotic by the
author, whether or not bacteria were demonstrated.

Unfortunately, descriptions of the medium-sized and small pulmonary arteries were rarely

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**Figure 5**

Section of the small aneurysm in the left-lower lobe. Fresh and organized thrombus partially covers the surface. Note fragmentation of elastica and destruction of wall in lower artery from which aneurysm arises (Verhoff-van Gieson stain).

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**Figure 6**

Main pulmonary artery showing the details of the intimal puckering and thickening illustrated in figure 3. The area of destruction of elastica is a site of potential aneurysmal dilatation. Note the fetal elastica pattern between destroyed areas (Verhoff-van Gieson stain).
given, and the presence of pulmonary hypertension can only be inferred from the nature of the communications between the systemic and venous system and the presence of right ventricular hypertrophy.

**Group 2**

This group consisted of eight male patients; seven had the recognized syndrome of recurrent thrombophlebitis and pulmonary aneurysms. The eighth patient (case 11) had a similar course except that no thrombophlebitis was recognized. Their course of recurrent infections, unexplained fever, and symptoms accompanying thrombosis of systemic veins was usually prolonged (average 3 to 4 years). It terminated in rupture of pulmonary aneurysm into the tracheobronchial tree or pleural cavity in seven of the eight patients. Resection of aneurysms was done in three patients, but two later died of rupture of another aneurysm, and the third survived.

At autopsy, five had multiple bilateral aneurysms, one had two aneurysms in one lung, and one had a single aneurysm. No disease of the pulmonary valve or main artery was described in contrast to the group with congenital heart disease. Mural thrombi were found in the right heart in four of six cases, but the authors usually excluded these as a source of emboli. Generalized cardiac enlargement was not described in any of the patients, but the right heart was slightly hypertrophied in two (cases 12 and 15). Some comment was made about the small pulmonary arteries in six cases. In three, they contained organizing or recanalized thrombi, and in two, both medial hypertrophy and intimal sclerosis were seen. The muscular arteries were said to be normal in one patient (case 16). In one (case 17), catheterization studies showed mild to moderate elevation of pulmonary pressures.

Although the source of infection in some of these patients was not identified, the descriptions of the aneurysms were similar in all cases which leaves little doubt that they were mycotic.

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**Figure 7**

*A medium-sized pulmonary artery with both a recanalized thrombus and a recent calcified thrombus containing bacterial colonies (Verhoff-van Gieson stain).*
Table 1

Pulmonary Aneurysms Associated with Congenital Heart Disease and Bacterial Endocarditis (Group I)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Defect</th>
<th>Vegetation</th>
<th>Aneurysms</th>
<th>Trunk</th>
<th>Branches</th>
<th>Culture</th>
<th>Cardiac hypertrophy</th>
<th>RV</th>
<th>LV</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidd12</td>
<td>22</td>
<td>F</td>
<td>PDA</td>
<td>A,D,P</td>
<td>Single</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Krysowski13 (1902)</td>
<td>17</td>
<td>F</td>
<td>PDA</td>
<td>P</td>
<td>Multiple, left lung</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Humphry14 (1912)</td>
<td>18</td>
<td>M</td>
<td>VSD, FO</td>
<td>VSD</td>
<td>Multiple, right lung</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Ruptured aneurysm</td>
</tr>
<tr>
<td>4</td>
<td>Sherman and Roman15 (1926)</td>
<td>7½</td>
<td>M</td>
<td>VSD</td>
<td>M</td>
<td>Multiple, bilateral</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Meningitis</td>
</tr>
<tr>
<td>5</td>
<td>Palmer and Kemp16 (1939)</td>
<td>44</td>
<td>M</td>
<td>PDA</td>
<td>P</td>
<td>Multiple, bilateral</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Cardiac failure</td>
</tr>
<tr>
<td>6</td>
<td>Hora and Wendt17 (1941)</td>
<td>37</td>
<td>M</td>
<td>PDA</td>
<td>A,LV</td>
<td>Multiple, bilateral</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Infection</td>
</tr>
<tr>
<td>7</td>
<td>Lelli18 (1941)</td>
<td>12</td>
<td>M,A,LV</td>
<td>PDA</td>
<td>M,A,LV</td>
<td>Multiple, bilateral</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Cardiac failure</td>
</tr>
<tr>
<td>8</td>
<td>Lillian19 (1949)</td>
<td>17</td>
<td>F</td>
<td>PDA</td>
<td>D</td>
<td>2, bilateral</td>
<td>+</td>
<td>Uniform</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Ruptured aneurysm</td>
</tr>
<tr>
<td>9</td>
<td>Present case</td>
<td>9½</td>
<td>M</td>
<td>VSD</td>
<td>P</td>
<td>Multiple, bilateral</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Ruptured aneurysm</td>
</tr>
</tbody>
</table>

Abbreviations: A = aortic; D = ductus; M = mitral; P = pulmonary; T = tricuspid; LV = left ventricle; VSD = ventricular septal defect; PDA = patent ductus; and FO = foramen ovale.
### Table 2

**Pulmonary Aneurysms Associated with Recurrent Thromboembolism (Group 2)**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Infection, fever</th>
<th>Aneurysms, branches</th>
<th>RVH</th>
<th>Small pulmonary arteries</th>
<th>Duration of symptoms</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Beattie and Hall²⁰ (1912)</td>
<td>21</td>
<td>M</td>
<td>+</td>
<td>Multiple, bilateral</td>
<td>-</td>
<td>Thrombosis</td>
<td>7 mo</td>
<td>Ruptured aneurysm +</td>
</tr>
<tr>
<td>11</td>
<td>Thompson and Gerstl²¹ (1946)</td>
<td>27</td>
<td>M</td>
<td>+</td>
<td>Single, left lung</td>
<td>0</td>
<td>Several recanal. thrombi</td>
<td>2 yr</td>
<td>Ruptured aneurysm +</td>
</tr>
<tr>
<td>12</td>
<td>Pirani et al.²² (1949)</td>
<td>10</td>
<td>M</td>
<td>+</td>
<td>Multiple, bilateral</td>
<td>Stl.</td>
<td>Thick, hyalinized, some obl. by org. thrombi</td>
<td>4 yr</td>
<td>Ruptured aneurysm +</td>
</tr>
<tr>
<td>13</td>
<td>Hughes and Stovin¹ (1959) (case 1)</td>
<td>35</td>
<td>M</td>
<td>-</td>
<td>Multiple, bilateral (resection)</td>
<td>0</td>
<td>Medial hypertrophy, intimal fibrosis</td>
<td>3 yr</td>
<td>Lobectomy, later ruptured aneurysm +</td>
</tr>
<tr>
<td>14</td>
<td>Calenoff³ (1964) (case 2)</td>
<td>11</td>
<td>M</td>
<td>+</td>
<td>2, left lung</td>
<td>0</td>
<td>Medial hypertrophy, intimal fibrosis</td>
<td>3 yr</td>
<td>Ruptured aneurysm +</td>
</tr>
<tr>
<td>15</td>
<td>Hurlimann and Reymond²³ (1961)</td>
<td>25</td>
<td>M</td>
<td>+</td>
<td>Multiple, bilateral (2 resections)</td>
<td>2-9 mm</td>
<td>-</td>
<td>5½ yr</td>
<td>Ruptured aneurysm +</td>
</tr>
<tr>
<td>16</td>
<td>Kopp and Green² (1962)</td>
<td>30</td>
<td>M</td>
<td>+</td>
<td>Multiple, bilateral</td>
<td>0</td>
<td>Normal</td>
<td>8 yr</td>
<td>Lobectomy, ruptured aneurysm +</td>
</tr>
<tr>
<td>17</td>
<td>Frater et al.⁴ (1965)</td>
<td>23</td>
<td>M</td>
<td>+</td>
<td>Single (resection)</td>
<td>Pulmonary hypertension</td>
<td>-</td>
<td>5 mo</td>
<td>Alive 9 mo. P.O.</td>
</tr>
</tbody>
</table>

*See table 1 for abbreviations.

### Table 3

**Pulmonary Aneurysms not Associated with Congenital Heart Disease or Thromboembolism (Group 3)**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Blood culture</th>
<th>Aneurysms Trunk</th>
<th>Site of vegetation</th>
<th>Cardiac hypertrophy RV</th>
<th>Pulmonary arteries (small)</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Sancetta et al.²⁴ (1958)</td>
<td>11</td>
<td>F</td>
<td>Staph. (coag -)</td>
<td>Single (resected)</td>
<td>-</td>
<td>-</td>
<td>Intimal thickening</td>
<td>Living</td>
</tr>
<tr>
<td>19</td>
<td>Taber and Ehrenhaft²⁵ (1956)</td>
<td>5</td>
<td>F</td>
<td>Staph. (coag +)</td>
<td>Multiple (2 resections)</td>
<td>-</td>
<td>-</td>
<td>Medial hypertrophy</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>20</td>
<td>Trevor²⁶ (1912)</td>
<td>24</td>
<td>F</td>
<td>Strept. (coag +)</td>
<td>Multiple, bilateral</td>
<td>P.A. and lt. pul. art.</td>
<td>+</td>
<td>-</td>
<td>Ruptured aneurysm</td>
</tr>
<tr>
<td>21</td>
<td>Charlton and DuPlessis²⁷ (1961)</td>
<td>25</td>
<td>M</td>
<td>Staph. (coag +)</td>
<td>0 Multiple, bilateral</td>
<td>T</td>
<td>+</td>
<td>-</td>
<td>Ruptured aneurysm</td>
</tr>
<tr>
<td>22</td>
<td>Calenoff³ (1964) (case 2)</td>
<td>47</td>
<td>M</td>
<td>Sterile</td>
<td>Multiple, bilateral</td>
<td>T</td>
<td>?</td>
<td>?</td>
<td>-</td>
</tr>
</tbody>
</table>

*Abbreviations as before.
+Patient's brother has pulmonary hypertension.
Group 3

These five patients, none of whom had congenital heart disease or known thromboembolism, form a heterogeneous group. The only survivor was an 11-year-old girl with primary pulmonary hypertension whose single pulmonary aneurysm was resected (case 18). Four years later, cardiac catheterization demonstrated increasing pulmonary hypertension, but she had no new aneurysms. The patient’s brother also had primary pulmonary hypertension. Another child, 5 years old, had successful resection of one aneurysm but died after the second was removed. Examination of the surgical specimen showed medial hypertrophy of the muscular pulmonary arteries. Both of these patients had positive blood cultures for Staphylococcus aureus and endocarditis was diagnosed clinically.

Three other patients in this group had right-sided endocarditis and multiple bilateral aneurysms. Unfortunately, no descriptions were given of the small pulmonary arteries. Right ventricular hypertrophy was present in two cases.

Discussion

Our review of 21 cases of mycotic aneurysms of the intrapulmonary arteries shows that the majority of these patients had diseases usually associated with pulmonary hypertension, either chronic recurrent thromboembolism or significant left-to-right shunts. Two patients had primary pulmonary hypertension. In cases of Hughes-Stovin syndrome (recurrent thromboembolism and pulmonary aneurysms), the descriptions of pulmonary vessels, when given, are compatible with pulmonary hypertension in most cases. Actual measurement of pulmonary pressures was made in only one of these cases, and in this case it was elevated (case 17). Of the three patients who had only right-sided bacterial endocarditis, two showed right ventricular hypertrophy. Unfortunately no descriptions were given of the pulmonary arteries in any of these cases, so it is not certain whether bacterial endocarditis in the absence of vascular disease may lead to mycotic aneurysms. Resection has been done for the aneurysms in several cases (cases 13 and 16 to 19); however, the diffuse nature of the vascular disease increases the likelihood of development and subsequent rupture of another aneurysm. The only patients who survived any length of time each had a single aneurysm which was resected (cases 17 and 18).

In our case, the rupture of an aneurysm was associated with acute necrosis and the presence of bacterial colonies. Despite repeated negative blood cultures, numerous bacterial colonies were demonstrated on the pulmonary valve at autopsy. The apparent relationship between acute infection and rupture of the aneurysm in our case suggests giving prophylactic antibiotic therapy to these patients.

In addition to aneurysms in the intrapulmonary vessels, six of nine patients with congenital heart disease and endocarditis had aneurysms of the main pulmonary artery. In our case, clumps of bacteria were present in lymphatics of the pulmonary artery, and this presumably was the method of local spread of infection with subsequent destruction of the vessel wall and aneurysm formation. This type of pulmonary arteritis is rare and is to be differentiated from that of syphilis and that associated with rheumatic heart disease. Involvement of the main pulmonary artery was not found in any of the patients with recurrent thromboembolism, nor did they have bacterial endocarditis.

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References


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