Coronary Insufficiency in Infancy and Childhood

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SUMMARY

Thirteen cases of coronary insufficiency diagnosed in childhood are presented. The aetiology, signs and symptoms and course of the patients are described. Some of the causes of coronary insufficiency are amenable to treatment.


Coronary artery disease is generally regarded as a rare condition during childhood. Over the last 14 years, 13 infants and children suffering from either myocardial ischaemia or infarction have been identified at the H. F. Verwoerd Hospital. Of these patients 11 were found to have abnormal coronary arteries. Two patients had ischaemia secondary to left ventricular outflow obstruction. A major reason for presenting these case reports is to demonstrate that in a significant number of paediatric patients the causation of myocardial ischaemia is surgically remediable.

CASE REPORTS

Case 1

An 11-year-old Black boy was admitted to hospital during May 1965. He was in congestive cardiac failure and complained of episodes of upper abdominal pain. Clinical examination and further investigation, including heart catheterization, showed him to have mitral and aortic incompetence and a right coronary artery arising from the pulmonary trunk. The ECG did not show signs of myocardial ischaemia or infarction. At operation for replacement of aortic and mitral valves with Starr-Edwards prostheses, an area of fibrosis was noted on the heart surface. There was marked postoperative improvement, but after 2 months the patient was again admitted with congestive cardiac failure and severe epigastric pain. Profuse sweating, an irregular pulse and dyspnoea were present. The erythrocyte sedimentation rate was normal. The ECG showed abnormal ST-segment depression, a Q wave of 3 mm, and an inverted T wave in lead V6.

He died 3 months after the operation. Postmortem examination confirmed the presence of the coronary artery lesion, as described. The mitral and tricuspid valves were in good condition, and no antemortem thrombus was present. The left coronary artery was open; the right coronary artery had been ligated at its origin from the pulmonary artery. The rest of this artery was open and nowhere was it thrombosed or occluded. The myocardium and endocardium of the apex of the left ventricle had an area of old fibrosis and thrombus. Sections of the heart showed myocardial fibrosis and organization of a fresh infarct.

Case 2

A 9-year-old White girl had seemingly been well until the year before, when she began to complain of excessive tiredness, nocturnal dyspnoea and exertional pain over her chest and in the left arm. She had a grade 2/6 systolic murmur over the pulmonary area. The heart was not enlarged. The ECG showed slight ST-segment elevation in the left leads, which became pronounced after exercise. Selective angiocardiography demonstrated a left coronary artery arising from the pulmonary trunk. This artery acquired additional blood from collaterals from the right coronary artery, and the ultimate flow was directed into the pulmonary circulation. Anastomosis of the abnormal artery to the aorta was carried out surgically and she has since been well.

Case 3

A 2-week-old White male infant developed attacks of dyspnoea, profuse sweating and crying when taking feeds. Congestive cardiac failure and circulatory collapse developed and the patient died at the age of 1 month. At postmortem examination an anomalous origin of the left coronary artery from the pulmonary trunk and myocardial infarction of the left ventricular wall were found.

Case 4

At the age of 10 weeks a cardiac lesion had been found in this Black male child. He was free of symptoms until the age of 7 years when a diagnosis of congestive cardiac failure was made and treatment with digoxin and diuretics was initiated. He was then referred for investigation. At examination there was no evidence of cardiac failure. There was a mild left parasternal systolic impulse, a grade 3/6 ejection systolic murmur over the pulmonary area and moderate splitting of the second heart sound. On chest radiography the pulmonary conus was prominent. The ECG was remarkable in that on admission it showed a QRS axis of 30° with normal precordial complexes and a week later the axis was −90° with an rR pattern in V1, the height of the R being 20 mm. Cardiac catheterization showed that the right coronary artery arose from the pulmonary artery, and that blood flowed back into the pulmonary artery. The size of the left-to-right shunt was 10% of pulmonary flow, a figure confirmed by isotope studies. In addition, a systolic pressure gradient of 6 mmHg over the right ventricular outflow tract was found. The investigation was repeated a week later in order to carry out a coronary arteriogram. On this occasion the
outflow tract gradient was 25 mmHg. The abnormal artery was freed and anastomosed to the aorta. The patient recovered and has since been well.

**Case 5**

A Black male infant, aged 7 months, presented with diarrhea and vomiting. On examination he was marasmic and in a state of cardiovascular collapse. A grade 2/6 systolic murmur was heard over the apex of the heart. The heart was enlarged and pulmonary oedema was present. The ECG showed deep Q waves and inverted T waves in leads I, V5 and V6, an R wave of 25 mm in V6 and an S wave of 28 mm and V1. Cardiac catheterization showed that the left coronary artery arose from the pulmonary artery and that the blood flow through it was retrograde into the pulmonary artery. Surgical correction of the lesion was carried out, but the patient died shortly thereafter.

**Case 6**

A 9-year-old Black girl suffering from post-infectious cutis laxa was found to have an early diastolic murmur over the base of the heart. She collapsed one morning and became comatose. She had signs of a right hemiplegia, and dyspnoea, shock, and congestive cardiac failure. A gallop rhythm was present. On radiological examination her heart was found to be much larger than it had been a few weeks previously. Her ECG had also changed markedly, ST-segment elevation, deep Q waves and abnormally inverted T waves being present. She died within a few hours. Postmortem examination revealed idiopathic aortitis of the first section of the aorta, occlusion of both ostia of the coronary arteries by the aortic lesion, and an embolus in the left internal carotid artery. There was widespread focal infarction of the septal and posterior walls of the left ventricle, notably at the bases of the papillary muscles. Histological examination showed that the infant affected the inner third of the myocardium, sparing the sub-endocardial fibres. The aortic valve cusps were thickened and there was antemortem thrombus in the right atrial appendage.

**Case 7**

A White female child, aged 14 months, was admitted for investigation and treatment of severe systemic hypertension. The blood urea, electrolyte, calcium and phosphatase levels were normal, as was catecholamine excretion. No abnormality of adrenal function could be found. Cardiac arrest developed while renal angiography was being carried out and the procedure was discontinued. The patient responded to treatment for the cardiac arrest. Seven months later he developed attacks of pallor, tachycardia, abdominal pain and sweating. Congestive cardiac failure initially responded to treatment, but later became refractory. On radiological examination the heart was enlarged and the ECG showed elevation of the ST segment and negative T waves over the left precordium. His condition deteriorated steadily and he died. Postmortem examination showed calcification of the coronary and renal arteries and several areas of myocardial infarction in the anterior and lateral walls of the left ventricle.

**Case 8**

A 2-month-old White male infant became acutely ill, with signs of shock, congestive cardiac failure, dyspnoea and profuse sweating. The child appeared to be in pain. A gallop rhythm was heard. Death occurred within an hour. Postmortem examination revealed the presence of numerous areas of myocardial infarction in the region of the apex and lateral wall of the left ventricle. The lamina elastica of the arteries of the coronary circulation, thyroid and pancreas and the iliac artery were calcified. There were deposits of calcium in some of the renal tubules and the umbilical artery was calcified. The left atrium and ventricles showed fibro-elastosis of the endocardium.

**Case 9**

A 14-year-old White male child had repeatedly been admitted to hospital for investigation and treatment of severe systemic hypertension. The blood urea, electrolyte, calcium and phosphatase levels were normal, as was catecholamine excretion. No abnormality of adrenal function could be found. Cardiac arrest developed while renal angiography was being carried out and the procedure was discontinued. The patient responded to treatment for the cardiac arrest. Seven months later he developed attacks of pallor, tachycardia, abdominal pain and sweating. Congestive cardiac failure initially responded to treatment, but later became refractory. On radiological examination the heart was enlarged and the ECG showed elevation of the ST segment and negative T waves over the left precordium. His condition deteriorated steadily and he died. Postmortem examination showed calcification of the coronary and renal arteries and several areas of myocardial infarction in the anterior and lateral walls of the left ventricle.

**Case 10**

A White female child, aged 14 months, was admitted with a history of restlessness, irritability and poor appetite of 2 months' duration, and diarrhoea which had begun a few days previously. She was undermass, anaemic and in congestive cardiac failure. The urine contained albumin 1+. The erythrocyte sedimentation rate was 115 mm/h. The heart was enlarged, but an ECG appeared normal.

During her stay in the hospital it was noticed that the patient chewed her tongue. Because the blood uric acid level was normal, this was regarded as a possible indication that the child was suffering pain. Fifteen days after admission she died suddenly. At postmortem examination the coronary arteries were found to have nodular thickening with chronic inflammatory cell infiltration and severe intimal hyperplasia. There were areas of ischaemic fibrosis and a small area of infarction in the myocardium. Similar changes were found in the arteries of the lungs, liver and kidneys. The aorta showed chronic inflammatory cell infiltration throughout all its layers.

**Case 11**

A White male child, 4 months of age, developed a cough, dyspnoea, pallor and lack of appetite, and 3 days later had an attack during which he became blue and
shocked. Shortly thereafter he was admitted to hospital. On admission his pulse rate was 150/min and the blood pressure 170/120 mmHg. There was evidence of congestive cardiac failure and cardiomegaly and, on ECG, evidence of left ventricular hypertrophy. An aortogram showed that both the external iliac arteries were markedly narrowed and had irregular lumens, especially on the left. The origin of the right renal artery appeared to be stenosed.

After the child’s condition had been discussed with the parents, they decided to take him home. After 5 days he was readmitted in severe congestive failure. His ECG then had grossly abnormal Q waves, ST-segment displacement and inverted T waves. He died within a few hours. A postmortem examination was not performed.

Case 12

A 3-kg White male infant, 35 days of age, was admitted to hospital because of congestive cardiac failure. On examination there was a soft systolic ejection murmur over the aortic area and signs of left ventricular hypertrophy. Cardiac catheterization showed valvular aortic stenosis and mild coarctation of the aorta. The child died 26 hours later. At postmortem examination, in addition to stenosis of a bicuspid aortic valve and coarctation, a patent ductus arteriosus and widespread infarction of the septum and free wall of the left ventricle were found. The left ventricle was severely hypertrophied and dilated.

Case 13

This patient, a 14-year-old White girl with hypertrophic obstructive cardiomyopathy, had attacks of angina associated with myocardial ischaemia which had begun at the age of 10 years. Treatment with propranolol has relieved her of her angina.

DISCUSSION

Ischaemic heart disease in infancy and childhood is correctly regarded as uncommon. At an annual meeting of the Association of European Paediatric Cardiologists, however, 44 cases of myocardial infarction, proved at necropsy, and excluding cases of anomalous origin of the left coronary artery, were presented. Profuse sweating was observed in almost all the patients under the age of 2 years, and typical precordial pain in about half of the older patients. Other common signs were shock, dyspnoea and heart failure. Of the 13 patients in the present series, 3 had a gallop rhythm, 7 were in a state of shock, 11 were in congestive cardiac failure, 7 perspired excessively, and 7 appeared to have pain. The younger children could not localize their pain, and the presence of pain in the babies was deduced from the type of crying.

Anomalous origin of the left coronary artery from the pulmonary trunk is the best-known cause of myocardial infarction in childhood. The usual age at which symptoms present is within a few weeks after birth, but it may be much later. At birth the pulmonary artery systolic blood pressure is about 60 mmHg, but this falls to the normal adult level of about 30 mmHg a few weeks later. This pressure is too low to perfuse the myocardium adequately and ischaemia and infarction can occur (cases 3 and 5). If the collateral blood supply between the coronary arteries is well developed, the left coronary artery receives blood from the right. If this supply is adequate, there will be minimal ischaemia, as in patient 2 who had profuse collaterals. The left coronary artery may steal blood from the right, the direction of flow then being retrograde into the pulmonary artery. Mitral incompetence secondary to infarction of the papillary muscles can develop. The prognosis depends on the adequacy of collaterals and the direction of flow in the left coronary artery, which is largely determined by pulmonary arterial pressure. Dyspnoea, sweating, crying, and, in older children, pain, are common symptoms. The heart is enlarged and the ECG shows signs of anterolateral myocardial infarction with broad Q waves and ST-segment elevation and T-wave inversion in leads I, AVL and the left precordial leads. The ST-segment elevation may be persistent. It is important to realize that the Q waves of these patients are frequently deep but not necessarily broad. Angiography should confirm the diagnosis and surgical treatment can be successful. Anomalous origin of the right coronary artery from the pulmonary trunk is a far less common condition and is usually less serious, but may be fatal if accompanied by other cardiac defects.

Left bundle-branch block is commonly associated with ischaemic heart disease in adults. Coronary artery disease can also affect the right bundle branch. It is likely that the right bundle-branch block with left anterior hemiblock in case 4 was the result of ischaemia.

Idiopathic aortitis in South Africa is seen mostly in the Black population. Coronary artery occlusion is very uncommon in this condition, but these arteries may also be occluded at their origins, as usually occurs in other major peripheral arterial branches. Idiopathic calcinosis of the coronary arteries is part of a widespread arterial disease of uncertain pathogenesis. It appears that at least two forms exist. One is a rapidly fatal familial condition affecting infants. The other type tends to affect older children, has no familial tendency and develops more slowly. Chest X-ray films of the correct penetration may reveal the calcification which is easily demonstrable in the arteries of the thyroid. Any cause of hypertrophy of the myocardium may result in relative coronary insufficiency if the blood supply to the heart muscle is not adequate for myocardial oxygen perfusion. A common cause of this type of ischaemia is left ventricular outflow obstruction, where the high intraventricular and low aortic pressures contribute to the decreased myocardial blood supply. The aetiology of coronary arteritis is not clear in all cases. Infantile peri-arteritis, polyarteritis nodosa, the mucocutaneous lymph node syndrome and rheumatic fever are the commonest causes. Whether infantile peri-arteritis nodosa and the mucocutaneous lymph node syndrome are different entities has yet to be proved.

Some causes of myocardial ischaemia in childhood are as follows: infective endocarditis and embolism, rheumatic carditis, aortitis, infantile peri-arteritis nodosa, disseminated lupus erythematosus, syphilis, calcification of coronary arteries, atherosclerosis, progeria, muco-
TABLE I. CLINICAL FEATURES OF PATIENTS WITH POSTMORTEM EVIDENCE OF CORONARY INSUFFICIENCY

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Race</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Shock</th>
<th>Cardiac failure</th>
<th>Gallop rhythm</th>
<th>Pain</th>
<th>Perspiration</th>
<th>Dyspnoea</th>
<th>ECG</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>B</td>
<td>11 yrs</td>
<td>Mitral and aortic incompetence. Origin of right coronary from pulmonary artery</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Left ventricular hypertrophy, deep Q wave</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>W</td>
<td>2 wks</td>
<td>Origin of left coronary from pulmonary artery</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Not obtained</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>B</td>
<td>9 yrs</td>
<td>Cutis laxa, aortitis with coronary orifice occlusion</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Deep Q waves, elevated ST segment and inverted T in AVL. T wave inverted in V3 - 6</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>W</td>
<td>8 mo.</td>
<td>Calcified coronary arteries</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Not obtained</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>W</td>
<td>2 mo.</td>
<td>Calcified coronary arteries</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Not obtained</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>W</td>
<td>4 yrs</td>
<td>Calcified coronary arteries and systemic hypertension</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>ST segment elevated in V2 and V3. T wave inverted in V1 - 6</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>W</td>
<td>1 yr</td>
<td>Coronary arteritis</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>W</td>
<td>1 mo.</td>
<td>Aortic stenosis, PDA, coarctation of the aorta</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Left ventricular hypertrophy</td>
</tr>
</tbody>
</table>

TABLE II. CLINICAL FEATURES OF PATIENTS WITHOUT POSTMORTEM EVIDENCE OF CORONARY INSUFFICIENCY

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Race</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Shock</th>
<th>Cardiac failure</th>
<th>Gallop rhythm</th>
<th>Pain</th>
<th>Perspiration</th>
<th>Dyspnoea</th>
<th>ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>F</td>
<td>W</td>
<td>9 yrs</td>
<td>Origin of left coronary from pulmonary artery</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td>ST segment elevated over V4 - 6</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>B</td>
<td>7 yrs</td>
<td>Origin of right coronary from pulmonary artery</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>Left axis, rR pattern in V1. ST segments elevated</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>B</td>
<td>7 wks</td>
<td>Origin of left coronary from pulmonary artery</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Deep Q and inverted T waves in S1, and V5 - 6</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>W</td>
<td>14 yrs</td>
<td>Idiopathic hypertrophic cardiomyopathy</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>Left ventricular hypertrophy, ST segment elevated</td>
</tr>
</tbody>
</table>

polysaccharidosis,\(^2\) Friedreich's ataxia,\(^3\) fibro-elastosis,\(^7\) trauma,\(^7\) tumour,\(^1\) hypertension,\(^1\) ventricular outflow obstruction, abnormal origin of the coronary arteries, and coarctation of the aorta. Familial type IIa hypercholesterolaemia as a cause merits special attention, although no patient with this condition is included in the present series.

A summary of the causes and some clinical features in this series is in Tables I and II. With regard to the ECG, it seems that the diagnosis could have been made more often if it were easier to distinguish between a left ventricular strain pattern and infarction.

The time that elapsed between diagnosis of the acute episode and death was often short. It is not known whether serious arrhythmias were the important precipitating causes of death. Five of the children had structural defects which were potentially amenable to surgical treatment. Two were, in fact, successfully treated by operation. It is likely that early diagnosis and more energetic and intensive investigation and treatment might have saved more of the patients. Earlier diagnosis will also provide time for investigation of the obscure causes of this condition.
Hepatic Infections

Part I. A Serological Evaluation of Fab Antigens (Fab' and F (ab)₂) and Antibodies in Patients and Asymptomatic Carriers of Hepatitis B Virus

G. H. VOS, T. MARIMUTHU, D. VOS

SUMMARY

Evidence for the association of Fab (antigen-binding) fragments of IgG and antibodies directed against receptors of these fragments (Fab' and F(ab)₂) has been found in patients and asymptomatic carriers of hepatitis B antigen. Fab fragments of IgG are often detected in hepatitis B surface antigen (HBsAg)-positive sera where the intensity of antibody activity to these determinants is significantly reduced. The formation of strong antibodies to Fab fragments is often observed in association with the presence of hepatitis B surface antibodies (HBsAb). Comparative studies show that the appearance of Fab fragments in HBsAg-positive sera is not linked to the presence of hepatitis e antigen. This observation was supported by the finding of autologous Fab fragments of IgG in e antibody-positive sera. It was also established that the amount of Fab fragment in the serum is closely associated with the detection of high HBsAg titres. Preliminary investigations suggest that the Fab fragments of IgG detected in the serum of HBsAg-positive patients represent in vivo-digested HBsAb attached to the surface membrane of virus B particles. Further studies are in progress to determine the relationship of Fab fragments with a variety of other immunological events, especially the role of liver enzymes in the cleavage of intact antibodies.


REFERENCES


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MATERIALS AND METHODS

Subjects Investigated

The hepatitis antigen laboratory of the Natal Blood Transfusion Service provides extensive facilities for the specialized investigations of infectious hepatitis. This enabled us to have direct access to serum samples routinely