Fatal Myocardial Necrosis*
PROBABLY DUE TO TOXOPLASMA MYOCARDITIS

R. VAN DER HORST, M.B., CH.B., Part-time Senior Physician and Cardiologist, Cardiac Unit, Wentworth Hospital; PAULINE KLENERMAN, M.D., Part-time Senior Paediatrician, Addington Children’s Hospital; MARY SCHONLAND, M.B., B.CH., Lecturer, Department of Pathology, and M. GOTSMAN, M.D., Professor of Cardiology, University of Natal, Durban

SUMMARY

This report describes a 10-year-old girl, with a congenital neurological abnormality, whose terminal illness was rapid in onset and abruptly fatal.

The patient developed cardiogenic shock from myocardial necrosis. The electrocardiogram showed diaphragmatic myocardial damage, left anterior hemiblock and later features of increasing intraventricular conduction disturbance. Autopsy showed disappearance of myocardial fibres, with interstitial fibrosis and cellular infiltration. Circumstantial evidence suggested a diagnosis of toxoplasma myocarditis.


Extensive myocardial damage is rare in the paediatric age group and the causes are unusual. This is in contrast to the adult, in whom occlusive coronary artery disease is common. This report describes a 10-year-old girl with electrocardiographic evidence of severe transmural myocardial injury due to chronic myocarditis, probably a result of toxoplasmosis.

CASE REPORT

The patient was born in 1960, the third child of normal healthy parents. The pregnancy and labour were normal, birth weight was 3,3 kg and the neonatal course uneventful. Motor development (sitting and walking) and speech development were delayed, and later she was difficult to educate because of an IQ of 58. X-ray studies of the skull, examination of the fundi, urinalysis, a full blood count, the VDRL and Wassermann reactions were normal. An EEG at the age of 5 years was considered normal, but at the age of 7 years an EEG showed a diffuse abnormality in the right temporal area. The serum complement-fixation test tested against *Toxoplasma gondii* antigen was positive in a dilution of 1:4 and the end titre was 1:8. The indirect toxoplasma fluorescent antibody test was positive (2+) in a serum dilution of 1:25, and at a dilution of 1:400 there was a trace reaction. These results indicated active or recent infection with toxoplasma. The child was treated with pyrimethamine (Daraprim; Burroughs Wellcome) and sulphadiazine for 4 weeks, and 6 months later, when the toxoplasma tests were repeated, they were still positive. Further treatment was not given.

At the age of 10 years she presented with a 25-day history of recurrent vomiting. A full blood count was normal. Seventy-two hours after admission to hospital, during which time she was afebrile, she developed acute peripheral circulatory failure with anxiety, restlessness, cold and sweaty extremities, cyanosis, hypotension; and heart failure with a puffy face, ankle oedema, increasing hepatic enlargement and tachycardia. Cardiac murmurs were not present but a loud pathological 3rd heart sound was heard. The electrocardiogram (Fig. 1) showed sinus rhythm with a PR interval of 0.18 seconds; left atrial hypertrophy, left axis deviation (mean frontal QRS axis of −60°); and incomplete left bundle-branch block. The
initial and terminal QRS vectors were directed to the left of $-30^\circ$, and this we interpreted as a diaphragmatic myocardial necrosis with left anterior hemiblock. Radiography (Fig. 2) showed great enlargement of the heart. The serum transaminase level exceeded 350 units. Oliguria occurred. The serum potassium level rose to 6.8 mg/100 ml and the blood urea to 99 mg/100 ml. Her clinical state deteriorated rapidly and she died 18 hours later, despite active attempts at resuscitation with a low fluid intake, digoxin, diuretics, sodium bicarbonate, pethidine, oxygen, lignocaine, and isoprenaline. An electrocardiogram shortly before death (Fig. 3), showed an atrial rate of 75 per minute, second-degree heart block with a Wenckebach phenomenon, and wide, varying QRS complexes which showed a pattern of right bundle-branch block and left superior hemiblock. Sequential cardiograms showed a progressive disturbance of intraventricular conduction.

Death was due to an irreversible, low cardiac-output syndrome.

A limited autopsy disclosed that the heart was enlarged, flabby and weighed 245 g (the expected weight for age being 120 g) (Fig. 3). The coronary arteries were normal. A small, organizing thrombus was found on the endocardial surface of the left ventricle. Microscopically, muscle fibres in sections taken from the right and left ventricles showed marked hypertrophy. The fibres were widely separated by delicate, oedematous connective tissue (Figs. 4 and 5). Many fibres showed granular or fatty degeneration, but normal muscle striations and nuclei. No encysted parasites were seen and pericarditis and endocarditis were absent. Occasional leucocytes (basophils and mast cells) were present in the connective tissue. These are the features of a diffuse chronic myocarditis. Histologically the lungs, kidneys, and liver showed the changes of congestive cardiac failure. A virus could not be isolated from fresh sections of the heart, liver, lungs, kidneys and tracheal swabs when introduced into baby mice, and on tissue culture.
Many infectious agents can damage the heart, but a pathological examination of the myocardium rarely identifies the cause, and many patients would be diagnosed as having 'idiopathic cardiomyopathy', were it not for the inflammatory cell infiltration. Histological studies in this patient demonstrated a chronic myocarditis which, although nonspecific, suggested that an infectious agent was the likely cause. Viruses could not be cultured directly from various organs including fresh heart tissue.

Toxoplasma infection occurs universally and is not uncommon in South Africa. Infection in a patient can be confirmed either by procedures which measure the level of circulating toxoplasma antibodies, or which demonstrate the organism in various tissues. The evidence for toxoplasmosis as a cause for the myocarditis in our patient is inferential and is based on the serological findings, the exclusion of viral myocarditis, and a failure to identify another cause. These indirect criteria are often used to diagnose toxoplasma myocarditis.

Severe myocardial damage from any cause, can produce an electrocardiographic pattern which simulates myocardial infarction. The extent of the abnormality is determined by the location of myocardial necrosis or fibrosis. In infants and children, an electrocardiographic pattern indistinguishable from myocardial infarction has been reported in occasional instances of endocardial fibro-elastosis, viral myocarditis, thrombocytosis, glycogen storage disease, cardiac tumours, and obstructive cardiomyopathy. Other disorders may cause myocardial infarction in infancy and childhood, and these include congenital heart malformations, coronary artery anomalies, anomalous origin of the left coronary artery from the pulmonary artery, coronary artery disease (calcinosi), coronary embolism, systemic hypertension, trauma, periarteritis nodosa and necrotizing arteritis, perinatal anoxia, anaemia, and sepsis. Diffuse interstitial myocardial fibrosis has been described in the Bassen-Kornzweig syndrome and in Friedreich's ataxia. None of these were present in this patient.

Toxoplasmosis can cause extensive myocardial damage, which is responsible for an electrocardiographic pattern of transmural myocardial infarction, and which can impair intraventricular and atrioventricular conduction, and produce various arrhythmias which depend upon the extent of the disease. Our patient started with an electrocardiographic pattern indistinguishable from diaphragmatic myocardial infarction with left anterior hemiblock, and later severe atrioventricular conduction delay was added. Eventually the picture was that of bilateral bundle-branch block with alternating left and right bundle branch block.

Different pathological patterns have been described in toxoplasma myocarditis, but histologically they are fairly uniform. Focal inflammatory lesions are present and asso-
associated with cellular infiltration. In some instances central necrosis of an inflammatory focus and interstitial oedema or fibrosis is observed, depending on the stage of the disease. Myocardial fibres surrounding inflammatory foci may show various stages of degeneration; toxoplasma cysts are not often demonstrated in the myocardial cells.

It is interesting to speculate on the facts responsible, for some years, for the well-being of this patient, which was followed by the sudden onset of cardiac failure with a rapid, downhill clinical course. It has been suggested that, although the pyrimethamine and sulphasalazine combination is parasiticidal to the free forms, and prevents multiplication of the encysted form of Toxoplasma gondii, a short course of treatment allows proliferation of surviving parasitic cells which rupture later and produce an intense reaction. It is for this reason that Martin et al. and Gellis advise therapy for only 6 weeks. The source of the infection in this patient is unknown. She had delayed neurological and motor development and an abnormal EEG, which suggest that she acquired the toxoplasma infection during intra-uterine life. The cardiac lesion could have been present for some time although the heart was clinically normal. The factor which precipitated her final cardiac failure is uncertain but was probably related to the incomplete treatment of the toxoplasma infection.

This study was supported by a grant from the Anglo-American Corporation of South Africa.

Boeke Ontvang: Books Received


