From the Department of Child Health, Dr. Soetomo Hospital, University of Airlangga, Surabaya.

Congestive Heart Failure in Diphtheric Myocarditis

by

A.M. PRASODO, M. NARENDRA, A. JOERNIL, WAHJOENARSO and F. KASPAN.

Abstract

The picture of congestive heart failure in diphtheric myocarditis was mainly determined by poor general condition, hepatic enlargement ± epigastric pain, dyspnea. Basal rales and peripheral edema were not observed. Cardiomegaly on X-ray examination supported the diagnosis.

Congestive heart failure as a complication of diphtheric myocarditis occurred in 31.2% — 52% of cases with severe ECG changes and only in 5% of cases with ST depression or T wave changes.

Of 29 cases with congestive heart failure only 3 survived. Apparently good results of digitalis treatment were obtained when only gallop rhythm, as an early sign of heart failure, was found.

Extensive myocardial damage by diphtheria toxin may explain why no beneficial effect of digitalis treatment was obtained. Prophylactic digitalization before signs of congestive heart failure appeared, as suggested by several authors; was not performed in this study.

Received 27th. June 1975.

Introduction

Myocarditis diphtherica, a frequent complication of toxic diphtheria still has a high mortality rate, depending on the severity of the disease. Most of the patients will die suddenly with signs of shock, dyspnea with or without hepatic enlargement (Kwari et al., 1965; Yap and The, 1962). Cardiac decompensation as a complication of myocarditis diphtherica is a serious condition and remains a problem which is difficult to be managed (Kwari et al., 1965; Morgan, 1963; Yap and The, 1962). The picture of congestive heart failure in children varies depending on the etiology of the heart disease (Mc Namara, 1971).

The purpose of this study is to evaluate the incidence and clinical picture of heart failure in diphtheric myocarditis and the results of its treatment. The mortality rate and causes of death other than cardiac in myocarditis diphtherica will also be discussed.

Materials and methods

Patients subjected to this study were cases with diphtheria of varying severity admitted to the Dr. Soetomo Hospital during the period of January 1, 1969 to January 1, 1974. The diagnosis of diphtheria was based on the following clinical criteria:

1. The presence of a membrane in the pharynx with bullneck appearance or with inspiratory stridor.
2. The presence of a membrane on one or both tonsils covering more than half of the tonsils.
3. A membrane outside the tonsil (posterior wall of the pharynx, uvula).
4. Borderline cases were first treated with penicilline 600.000 IU; if after 3 days no improvement occurred or they even became worse it was considered to be of diphtheric origin.

Clinical criteria were considered to be of more importance than laboratory diagnosis, since a negative culture did not rule out the presence of diphtheria. The incidence of the various types and the degree of the severity of the disease in this study was not determined.

Electrocardiograms were recorded on admission with the Siemens Cardiostat T and repeated every 5 days, if necessary in a shorter time. The main problem was to recognize acute cardiac failure as early as possible, since frank edema almost never occurred (Kwari et al., 1965; Morgan, 1963; Mc Namara, 1971; Yap and The, 1962). The following criteria have been taken for the presence of cardiac failure: 1. gallop rhythm, 2. dyspnea, 3. acute hepatic enlargement, 4. poor general condition such as weakness, pallor, anorexia, sweating, 5. the presence of ECG abnormalities, 6. X-ray changes.

Hepatic enlargement could also occur because of the diphtheric toxin, however hepatic enlargement was considered to be caused by congestion if it was accompanied by dyspnea and other signs mentioned above and when the enlargement occurred rapidly. Distended neck veins as a sign of heart failure was difficult to evaluate in smaller children and was also unreliable when they were crying.

Dyspnea was considered to be of cardiac origin if other causes such as respiratory obstruction, bronchopneumonia or other respiratory factors could be excluded. When three or more of these criteria were present the patient was then considered to have cardiac failure.

Treatment

1. Anti diphtheria serum was given in a dose of 40.000 to 60.000 IU depending on the severity of the cases.
2. Prednison in a dose of 2 mg/kg BW in toxic cases for two weeks.
3. Penicillin procaine 600.000 IU for ten days.
4. Digitalization was done with cedilanid parenterally in a dose for children less than 5 years of age 0.03 mg/kg BW as initial dose, over 5 years of age 0.02 mg/kg BW, divided in 3 doses followed by a maintenance therapy orally in a dose of 0.01 mg/kg BW of lanoxin.
5. Suportive treatment as vitamin, intravenous fluid, oxygen, when indicated; alupent was given in cases of AV block.

Result

Sixteen hundred and forty nine (1649) patients with diphtheria of varying severity were admitted during a 5 year-period with an overall mortality rate of 9.7% (160 deaths) (Table 1). Electrocardiograms were recorded on 1567 patients, 82 had no ECG because of several circumstances and were therefore excluded. They were patients who were very ill and died before ECG was taken. Of these 1567 patients with ECG recordings, 331 showed abnormalities of varying severity. To these 331 patients special attention was paid for the occurrence of cardiac failure and other features preceding the death.

TABLE 1 : *Mortality rate in diphtheria cases with normal/abnormal ECG.*

ECG	No. of patient	ECG	Mortality
+	1567	abnormal : 331 normal : 1236	92 (27.4%) 16 (1.2%)
—	82	—	52 (63.4%)
Total	1649		160 (9.7%)

TABLE 2 : *Incidence of various types of ECG abnormalities in diphtheria.*

ST depression ± T wave changes	97 cases	(29.5%)
Flat/low T wave	81 ,,	(24.4%)
Sinus tachycardia	74 ,,	(22.3%)
Intraventricular conduction defect ± nodal rhythm	19 ,,	(5.7%)
RBBB	9 ,,	(2.7%)
LBBB ± nodal rhythm	32 ,,	(9.6%)
Complete AV block	13 ,,	(3.9%)
Prolonged QT	3 ,,	(0.9%)
Nodal rhythm with normal QRS complex	2 ,,	(0.6%)
Ventricular extrasystole	1 ,,	(0.3%)
T o t a l	331 patients	

Mortality rate (Table 1 — 2)

The overall mortality rate was 9.7% and the mortality rate of cases with ECG abnormalities was 27.4%. The high mortality rate (63.4%) of the cases (82), which had no ECG recorded, could be explained by the fact that they came already in a very bad condition and died within 24 — 48 hours after admission with numerous complications.

When we look at the various types of ECG abnormalities it was evident that the highest mortality rate was associated with severe ECG changes (Table 3). The lowest was found in cases with flat T wave (7.3%), the highest (100%) with complete AV block followed by intraventricular conduction defect ± nodal rhythm, LBBB + nodal rhythm and RBBB.

TABLE 3: *Causes of death (cardiac/non-cardiac) in diphtheric myocarditis.*

ECG abnormalities	No. of patient	Causes of death cardiovasc.	Non-cardiac	Total death
Sinus tachycardia	7	—	14	14 (18.9%)
Flat/low T wave	81	—	6	6 (7.3%)
ST-depression ± T wave changes	97	7	5	12 (12.3%)
RBBB	9	4	1	5 (55.5%)
LBBB ± nodal rhythm	32	17	4	21 (62.5%)
AV block	13	13	—	13 (100%)
Intraventricular conduction defect	19	13	4	17 (89.4%)
Prolonged QT interval	2	—	2	2 (100%)
Nodal rhythm with normal QRS	2	—	2	2 (100%)

The cause of death was determined to be of non-cardiac origin if the patient died because of respiratory paralysis, respiratory obstruction (tracheostomy), bleeding tendency, sepsis, bronchopneumonia, atelectasis. In cases the patient died without any complicating condition mentioned above but with severe ECG changes the cause of death was considered to be of cardiac origin. If other complicating factors were present making the condition severe enough to cause the death (respiratory paralysis) but no signs of cardiac failure were present, the cause of death was considered to be non-cardiac. However, it does not mean that the patient would necessarily survive if the complications did not occur.

The cause of death was considered to be of cardiac origin if :

1. Signs of cardiac failure were present.
2. Shock in the presence of severe ECG changes preceded by hypotension was considered to be caused by low cardiac output.
3. Sudden death in cases with severe ECG changes.

Signs of cardiac failure

Attention was focused on the 331 patients with ECG abnormalities to check for the presence of cardiac failure.

TABLE 4 : *Signs of acute congestive heart failure observed in diphtheric myocarditis (35 cases).*

Signs	Number of patient	%
Gallop rhythm	6	
Dyspnea	35	100%
Basal rales	—	—
Acute hepatic enlargement ± epigastric pain	30	87%
Peripheral edema	—	—
Poor general condition (weakness, pallor, sweating)	35	100%
Cardiomegaly	9	—

The cardinal signs appeared to be: dyspnea, acute hepatic enlargement in the presence of poor general condition, Gallop rhythm was only found in 6 cases, while none of the patients had basal rales or peripheral edema. X-ray examination of the chest was only carried out on 9 patients because of several reason (patients died before X-ray could be taken, technical problems etc.). The heart size in these cases varied between CTR 52% — 60%.

TABLE 5 : *Incidence of acute congestive heart failure in the various ECG abnormalities in diphtheric myocarditis.*

Type of ECG abnormalities	No. of cases with CHF	%
Sinus tachycardia	—	—
Low/ lat T wave	—	—
ST depression ± T wave changes ...	5 out of 97 cases	5.1%
RBBB	4 „ 9 „	44.4%
LBBB	10 „ 32 „	31.2%
Intraventr. conduct. defect	10 „ 19 „	52.5%
Complete AV block	6 „ 13 „	46%

A total number of 35 patients showed signs of acute congestive heart failure and its incidence was high in the intraventricular conduction defect, complete AV block, RBBB and LBBB. Signs of cardiac failure were not observed in cases with sinus tachycardia and T wave changes. Four dead cases with RBBB had left axis deviation on ECG, while three of 10 dead cases with LBBB had right axis deviation on ECG. Shock without other signs of congestive heart failure occurred in 28 cases and was fatal.

Results of treatment

When the patient was considered to have cardiac failure digitalization was carried out. Only 29 cases were digitalized as outlined in our methods.

TABLE 6 : *Digitalization in 29 cases of myocarditis diphtherica with congestive heart failure.*

Type of ECG abnormality	No. of cases	No. of death
ST depression ± T wave changes ...	5	4
RBBB	4	4
LBBB	10	8
Intraventric. conduct. defect	10	10
T o t a l	29	26

Six cases of complete AV block with cardiac failure were not digitalized and were therefore excluded from the evaluation. Of the 29 cases which were digitalized only 3 survived. These 3 cases were one with ST-depression inverted T and 2 cases with LBBB, which only had gallop

rhythm. After digitalization the parents were checked for the pulse, blood pressure and ECG. Only one case with LBBB got complete AV block. Six patients died within 24 hours after digitalization, while the remainder could survive for 2 and a few only for 3 days. The general impression was that as soon as acute congestive heart failure occurred, the condition of the patients deteriorated rapidly and digitalis appeared to be of little help.

Discusion

Three hundred and thirty one ECG abnormalities (21%) were found in 1567 patients admitted with diphtheria of varying severity. The overall mortality of diphtheria was 9.7%, however the mortality of the cases with ECG abnormalities was 27.4% as opposed to 1.2% of the cases with normal ECG. The morbidity and mortality of myocarditis were clearly determined by the type of the ECG changes. Sinus tachycardia did not necessarily mean a myocardial involvement since this abnormality was usually observed in cases with respiratory obstruction and cases with fever. After a few days to one week the heart rate usually returned to normal.

Flat to low T waves without other clinical signs of myocarditis were non-specific changes which would not bring much concern. It was also noted that the cause of death in these two groups was mostly of non-cardiac origin (respiratory obstuction etc.).

ST depression with inverted T wave, bundle branch block, complete AV block, intraventricular conduction defect, nodal rhythm, certainly indicated myocarditis and these patients should be observed for the occurrence of acute cardiac failure or shock. The picture of congestive heart failure in children varies a great deal, depending on the age of the patient and the type of heart disease (Mc Namara, 1971). In newborns or infants with congenital heart disease, peripheral edema and basal rales are usually not found (Mc Namara, 1971). In older children with congestive heart failure caused by rheumatic heart disease, the classical picture of lung edema with pulmonary congestion and basal rales is a frequent finding and peripheral edema is also not uncommon, while ascites occasionally may occur in long standing congestive heart failure.

Firstly the congestive heart failure caused by myocarditis diphtherica is acute. As a sensitive parameter for congestion appeared to be the acute hepatic enlargement, mostly accompanied by epigastric pain, which occurred in 30 out of 35 cases with congestive heart failure and almost always was this accompanied by dyspnea. Gallop rhythm appeared to be not a constant finding. Only 6 out

of 35 cases with signs of congestive heart failure showed gallop rhythm. The general condition of the patients such as weakness, excessive sweating, pallor, anorexia was of great help, when one was hesitating whether or not congestive heart failure was present, since the hepatic enlargement was due to toxic degeneration of the liver the patient was usually in a good condition. X-ray examination was only performed in 9 cases and the heart size varied from mild to severe cardiomegaly.

The incidence of congestive heart failure was related to the severity of the myocarditis as evidenced by the type of ECG abnormalities. Congestive heart failure was not observed in cases with sinus tachycardia or cases with flat to low T waves, it occurred in only 5.1% of cases with ST depression with or without inverted T waves, while the incidence was high in other ECG abnormalities (intraventricular conduction defect, complete AV block, Bundle Branch Block).

Shock was another fatal complication in 13 cases with complete AV block, 7 died with signs of shock. We believe that this shock state which occurred in severe myocarditis was of cardiac origin and was the result of a low cardiac output. In the absence of severe ECG abnormalities peripheral vascular collapse would be the major cause of this shock.

Out of 35 cases with congestive heart failure 29 were digitalized, only 3 of them survived. These 3 cases were one with ST depression plus inverted T wave and 2 cases with LBBB which only had gallop rhythm. A study (Yap and The, 1962) conducted in the years 1958, 1959 — 1961, on diphtheria in this same hospital, showed also poor results of digitalis therapy in diphtheric myocarditis with decompensaton; 4 out of 5 cases with cardiac decompensation died. But of 20 cases with diphtheric myocarditis which had gallop rhythm, poor general condition and ECG changes, only 4 died after digitalis treatment. Controversial opinion arose about the use of digitalis in diphtheric myocarditis (Barnett and Einhorn, 1968; Friedman et al., 1973; Gillis ad Kagan, 1971; Hugkes, 1967; Kempe et al., 1970; Nadas, 1972; Nelson et al., 1969). Some authors believe one should avoid digitalis (Friedman et al., 1973), others recommend the use of digitalis even before signs of congestive heart failure appear (Barnett and Einhorn, 1968; Kempe et al., 1970; Nelson et al., 1969).

From this study and from the results of Yap and The (1962), we learn that satisfactory results were obtained in cases with only gallop rhythm as a sign of myocardial failure. Another factor which is also of influence is the severity of myocarditis as judged by the severe ECG changes.

Cases as complete AV block, particularly with slow ventricular rate (less than 60) had mostly a fatal outcome with or without signs of congestive heart failure.

Diphtheric myocarditis causes severe changes in the heart muscle, which consist of hyaline degeneration, necrosis and myolysis. Histochemical studies on autopsy revealed mitochondrial damage with loss of enzyme activity, depletion of glycogen and accumulation of lipid droplets in the damage myofibrils (Burch et al., 1968). In complete AV block external destruction was found in the ventricular septum. If we are aware how severe the diphtheric toxin can damage the myocardium, then we could understand why digitalis is of little or no help, since a sick myocardium will not be benefited by digitalis. Once cardiac decompensation occurred the condition usually deteriorated quickly and the patient will die despite all measurements. Some authors (Friedman et al., 1973) suggest that measurements such as absolute bedrest which can prevent cardiac failure be intensified and excitement or physical stress be avoided. Others (Friedman et al., 1973) believe that the administration of diuretics (lasix) would be more beneficial that digitalis (Friedman et al., 1973; Gillis and Kagan, 1971).

REFERENCES

1. BARNETT, H.L. and EINHORN, A.H.: Pediatrics, 14 th ed. p. 588 — 589, 1212 (Appleton — Century — Crofts, New York 1968).
2. BURCH, G.E., SHIN-CHIEN, S., SOHAL, R.S., KANG, C.C. and COLCALOUGH, H.L. : Diphtheric myocarditis, a histochemical and electron microscopic study. Am. J. Cardiol. 21 : 261 (1968).
3. FRIEDMAN, F.W., LESCH, M. and SONNENBLEEK, E.H. : Progress in Cardiovascular Diseases, Neonatal Heart Disease pp. 215 — 217 (Grunne & Stratton, New York 1973).
4. GILLIS, G. and KAGAN : Current Pediatric Therapy. 5th Ed p. 557 (Saunders, Philadelphia 1971).
5. HUGHES, G.J. : Diphtheria, Synopsis Pediatr. 2nd ed. p. 714 — 718 (Mosby, Saint Louis 1967).
6. KEMPE, C.H., SILVER, H.K. and O'BRIEN, D. : Current Pediatric Diagnosis & Treatment, ed. p. 580 (Lange. Med. Publ., Los Altos 1970).
7. KWARI, S., YAP, K.N. and THE, S.L.: Clinical study of diphtheria with special reference to cardiac complications. Paediatr. Indones. 5 : 928 (1965).
8. Mc. NAMARA, D.G. : Recognition of Congestive Heart Failure. Pediatr. Clin. N. Amer. Pediatr. Cardiol., 18 : 1197 (1971).

9. MORGAN, B.C.: Cardiac complications of diphtheria. Pediatr. 32 : 549 (1963).

10. NADAS, F. : Pediatric Cardiology, 3rd ed. p. 236 (Saunders, Philadelphia 1972).

11. NELSON, W.E., VAUGHAN, V.C. and Mc. KAY, R.J. : Textbook of Pediatrics, 9th Ed., (Saunders, Philadelphia 1969).

12. WATSON, H. : Pediatric Cardiology, 1st ed. pp. 868 (Mosby, Saint Louis 1968).

13. YAP, K.N. and THE, S.L. : Diphtheria, M.I.P.I. Congr., Yogyakarta, October, 1962.