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DILATED CARDIOMYOPATHY IN YOUNG ADULT AFRICANS: A SEQUEL TO INFECTIONS?

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Summary

Over a period of 6 years, only twelve cases of dilated cardiomyopathy were clinically diagnosed in Nigerians between the ages of 11 – 30 years at the University College Hospital, Ibadan, Nigeria. Eleven presented with heart failure, while the twelfth patient presented with a cerebrovascular accident. Two other patients also had a cerebrovascular accident.

A history of febrile illness was obtained in seven, but in only three was fever unresponsive to antimalarials, documented on admission. Antistreptolysin-O titre was normal and erythrocyte sedimentation rates elevated in each of the patients. Leucocytosis was present in six, three had a four-fold rise or fall in antibody titres against Coxsackie-B viruses and one, a four-fold rise or fall against *Toxoplasma gondii*.

Histological evidences of myopericarditis were found in three of the six patients who died.

It is concluded that dilated cardiomyopathy is rare in young adult Nigerians, and that constitutional upset is common, as in children, but prognosis is poorer. Infections by Coxsackie-B viruses, *T. gondii* and possibly other viruses appear to be of major aetiological factors.

Résumé

Au cours de 6 années de diagnostics cliniques faits au Centre Medical Universitaire d'Ibadan (University College Hospital, Ibadan), on n'a trouvé que douze cas de cardiomyopathie dilatée parmi les Nigerians de l'age de 11 – 30 ans. Onze de ceux-ci ont terminé on syncope, et le douzieme a subi, comme deux autres malades, un accident cerebrovasculaire.

Sept d'entre ces malades avaient une histoire de maladie febrile, dont trois n'ont pas repondu aux traitements antipyretiques, comme documente au moment de leur entrée a l'hôpital. L'Antistreptolysine-O titre était normal et la sedimentation erythrocyte s'est elevée dans chacun de ces malades. La leucocytose s'est presentée dans six; trois autres avaient une augmentation ou dimunition quadruples de titres anticorps contre le virus Coxsackie-B; un malade avait une augmentation ou dimunition quadruples contre *Toxoplasma gondii*.

On a trouve des evidences histologiques de myopericardite dans trois des six décèdés.

On a donc tiré la conclusion que la cardiomyopathie se trouve trés rarement chez les jeunes-adultes Nigerians par contraste aux indispositions constitutionnelles qui sont plus frequentes comme on trouve normalement chez les enfants, sans pourtant des prognostics suffisants. Les infections causées par le virus Coxsackie-B, *T. gondii*, et d'autres virus encore, semblent resulter des facteurs etiologiques.

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Introduction

Dilated cardiomyopathy (DC) is a common cause of heart failure in the tropical and subtropical countries of the world including Nigeria (WHO Bulletin, 1965; Lauckner, Rankin & Adi, 1961; Edington & Jackson, 1963). It occurs in all ages, (Edington & Jackson, 1963) but predominates in patients above the age of 30 years, with a peak incidence around 60 years

(Falase, 1977).

Most studies of this disease have concentrated on patients within two age groups, children below 10 years of age and adults above the age of 30 years. These studies have shown that the disease in the two age groups are different in their clinical presentations, natural history and possibly, aetiology. While systemic upsets such as fever, anorexia and malaise are common in children (Antia, Cockshott & Thorpe, 1969) these are uncommon in adults (Parry, 1968). The prognosis is good in children in whom the symptoms and signs in over a third of the patients followed by Antia (Antia *et al.*, 1969) returned to normal, unlike in adults where the mortality was as high as 40% over a 4 year follow-up (Falase, 1978). Furthermore, infection has been suggested as the cause of the disease in children (Ikeme, 1976), while hypertension, excessive alcohol ingestion, malnutrition, high parity, thiamine deficiency and infections have been shown to play some role in the aetiology of the disease in adults (Falase, Fabiyi & Ogunba, 1977).

There are no studies of DC among Nigerians who fall within the age group of 11–30 years in Nigeria. For the past 6 years at the University College Hospital, Ibadan, Nigeria, we have been collecting such patients to find out whether their clinical presentation and natural history are different from those in the other age groups and whether there will be pointers to the aetiology of the disease in the older age group. This paper is a report of our findings.

Subjects and materials

The patients were diagnosed as suffering from DC if they had cardiac enlargement confirmed on plain chest radiograph, if they had a poor systolic ejection fraction on angiocardiography, echocardiography and systolic time intervals and if other known causes of cardiac enlargement such as hypertension, anaemia, congenital heart disease, rheumatic heart disease, organic valvular heart disease, endomyocardial fibrosis and hypertrophic cardiomyopathy had all been excluded on clinical grounds. The patients were unselected and constituted a consecutive series admitted either as emergencies or from the out-patient clinic. They were classified into upper and lower socio-economic groups as defined by Osuntokun (1977).

A detailed history was taken and a full physical examination performed on each patient on admission. All the patients also had full routine investigations for heart failure including anti-streptolysin-O (ASO) titre and the erythrocyte sedimentation-rate (ESR).

Cardiac catheterization, angiocardiography and echocardiography were performed using standard techniques. Paired antibody titres were determined against *Toxoplasma gondii* in the serum by the latex slide-agglutination method (Beverly, Freeman & Watson, 1973) while a neutralization test in Vero tissue-culture cells was used to detect antibodies against Coxsackie-B viruses. A four-fold increase or decrease in antibody titres was considered significant.

All the patients had the usual routine treatment for heart failure; complications were treated when present. Autopsy examination was performed on all the patients who died.

Results

Over 200 patients with DC were seen during the 6-year period but only twelve were so diagnosed within the 11–30 year age-group. The twelve patients comprised seven females and five males and were aged between 14–30 years (24·9 ± 1·5 s.e. mean) years. Three were from the high, and nine from the low socio-economic classes. Only one was judged to be clinically malnourished.

TABLE 1. Summary of the clinical features of the twelve patients

Symptoms and signs	No. of patients
Heart failure	11
Cough	10
Dyspnoea	10
History of febrile illness	7
Documented fever on admission	3
Pleuritic chest-pain	4
Triple rhythm	12
Tachycardia	11
Cardiac murmurs	
Mitral incompetence (MI)	3
Tricuspid incompetence (TI)	1
MI + TI	2
Hemiplegia	3
Pleural effusion	2

Clinical presentation (Table 1)

Eleven of the twelve patients presented with heart failure; eight biventricular, two left ventricular, and one right ventricular failure. Two of the eleven patients also had a cerebrovascular

accident; one of the two patients was admitted in coma.

The only patient who had no heart failure had a 2-day history of fever and developed a left hemiplegia on the third day, while driving home from work.

Six of the eleven patients who presented with heart failure gave a history of febrile illness, the duration of which varied between 2 and 7 weeks before the onset of symptoms of heart failure, but in only three was fever actually documented on admission. The duration of symptoms of heart failure ranged from 2 hours – 3 years before presentation.

Of the seven females, two were nulliparous while two have had five or more pregnancies. All the five parous patients had symptoms of heart failure within 10 months of the last delivery. The two grand-multiparous patients developed symptoms in late pregnancy and one of them had the most severe heart failure.

A history of pleuritic pain was obtained in four patients and three of these gave a history of febrile illness, but in only two was fever present on admission.

Three had persistent low grade pyrexia unresponsive to antimalarial drugs while on admission. The blood pressure was normal in all. Eleven had tachycardia and one, ventricular extra systoles. All the patients had a triple-rhythm — eight, a third, one a fourth and three both a third and a fourth heart sounds. None had a pericardial friction rub. Mitral incompetence was present in three and tricuspid incompetence in two. Pleural effusion was found in two.

Laboratory investigations

None of the patients had a packed cell volume below 30% but leucocytosis was found in six patients and eosinophilia in four. The ASO titre was normal but the ESR was raised in all the patients.

Electrocardiographic findings

These were: sinus tachycardia (ten patients), ST depression with T-wave inversion (ten patients), left ventricular hypertrophy (three patients), right atrial hypertrophy (two patients), left atrial hypertrophy (one patient), and right ventricular hypertrophy (one patient). Fascicular blocks were less common and took the form of left anterior hemiblock (one patient), left bundle branch block (one patient) and right bundle branch block (one patient). Ventricular tachycardia occurred in one patient.

Table 2 shows the distribution of antibody titres to *T. gondii* and Coxsackie-B viruses in the six patients in whom they were measured. A four-fold rise or fall in antibody titres against *T. gondii* was found in only one (16·6%), but high titres were obtained in three patients. A four-fold rise or fall in antibody titres against the Coxsackie-B viruses was obtained in three (50%). One of the patients (Case 6) had a persistently high serum antibody against *T. gondii* 1 year after presentation.

Response to treatment and follow-up

Six patients recovered fully from heart failure and remained well throughout follow-up. Two of them who had cerebrovascular accidents also recovered fully.

Six patients died and at autopsy, they all had grossly dilated flabby ventricles. All of them had left ventricular mural thrombi, and in three, additional right ventricular mural thrombi. Renal infarction was present in four, cerebral infarction in two, pulmonary infarction with haemorrhages in three and hepatic infarction in two.

TABLE 2. The distribution of antibody titres against the Coxsackie-B viruses and Toxoplasma gondii in six patients

Case	Coxsackie-B viruses												*T. gondii*	
	B_1		B_2		B_3		B_4		B_5		B_6			
1	—	—	—	—	—	—	1:4	1:4	—	—	—	—	1:1024	1:516
2	1:32	1:32	1:32	—	—	—	1:516	1:64	—	—	—	—	—	1:4
3	—	—	1:16	1:4	—	—	—	—	1:16	1:32	1:16	1:8	—	—
4	1:32	1:32	—	—	1:32	1:32	—	—	—	—	1:4	1:4	1:1024	1:28
5	—	—	—	—	—	—	1:1024	1:516	—	—	—	—	—	—
6*	—	—	—	1:1024	—	—	—	—	—	—	—	—	1:1024	1:516

* Titre of 1 : 128 1 year after

FIG 1. Section through the myocardium of Case 5 showing extensive lymphocytic and monocytic infiltration.

Histological examination of the heart showed that three had definite evidence of myocarditis and pericarditis with extensive lymphocytic and monocytic infiltrations of the myopericardium (Fig. 1). Two of the three patients had low grade pyrexia during their hospitalization and the two had high antibody titres to Coxsackie-B viruses.

Discussion

The small number of patients in this series emphasizes the rarity of DC in the age group studied, as opposed to its predominance in the over 30 years age group (Ikeme, 1972; Falase, 1977). This finding is also similar to that of Botreau-Roussel *et al.* (1979) in Martinique.

The study also re-emphasizes the important differences in the mode of presentation, clinical course and response to treatment between children, young adults and the older age group. The presentation in the 11–30 year age group tends to be similar to that of children (Antia *et al.*, 1969), but different from adults (Edington & Jackson, 1963). Thromboembolic phenomenon is however, rare in children (Antia *et al.*, 1969) but common in the 11–30 year age-group (28% in this study) and in the older age group (Stuart & Hayes, 1963). The response to treatment is good in children (Antia *et al.*, 1969), poor in adults (Falase, Fabiyi & Ogunba, 1977) and in the 11–30 year age-group as shown in this study.

There are many causes of myocardial damage (Oakley, 1972) and some of these (hypertension, excessive and prolonged alcohol ingestion, malnutrition, high parity, thiamine deficiency and infections from *T. gondii* and the Coxsackie-B viruses) have been implicated as the probable causes of DC in adult Nigerians (Falase *et al.*, 1977). Of these, only the infectious causes were shown to be present in the 11–30-year-old patients studied, and the evidence for infections was strong. There was a history of fever in six patients, three of whom had definite low grade pyrexia on admission and of the three, two had histological evidences of myopericarditis at autopsy but had no pyrexia before death. Other evidence of infection included leucocytosis in six patients, a high ESR in all the patients and significant antibody titres to *T. gondii* and Coxsackie-B viruses in the six tested.

Toxoplasmosis and Coxsackie-B virus infection have been shown to be endemic in Nigeria (Olurin, Fleck & Osuntokun, 1972; Fabiyi & Odegbo-Olukoya, 1974) probably as a result of over-crowding and poor sewage disposal. It is therefore likely that infection from these agents and other agents not yet identified was the only cause of DC in this age group, just as in children.

It is also possible that myocarditis is common in the community, but in only a few patients is it so severe as to precipitate heart failure in children and young adults. Repeated infections and further insults from other factors such as excessive and prolonged alcohol ingestion, hypertension and high parity later in life may account for the preponderance of DC in the middle and older age groups.

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