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POSTPARTAL CARDIOMYOPATHY

JOHN V. O. REID, M.R.C.P., *Department of Medicine,* University of Natal, and King Edward VIII Hospital, Durban*

Postpartal heart disease has been described in an increasing number of publications since the first report by Virchow[1] in 1870. The literature has been reviewed in 2 recent papers by Rosen[2] and by Benchimol *et al.*[3] The most important papers on this subject have been those by Hull and co-workers,[4,5] Gouley *et al.*,[6] Musser *et al.*,[7] Meadows,[8] and Benchimol *et al.*[3]

Analysis of this literature shows that many of the cases described as postpartal had their beginning during or even before pregnancy; many had an aetiology referable to specific disease, especially pre-eclamptic toxaemia of pregnancy, nephritis, and hypertension of other origin. Some had a non-specific inflammatory myocarditis, and some were so complicated by pulmonary thrombosis or embolism as to leave doubt whether the postpartal state was significant in the aetiology or not. Benchimol *et al.*[3] considered that, on careful assessment, cases described as occurring postpartum could be allocated to aetiological types, so that doubt concerning the identity of a specific postpartal heart disease remains. The majority of authors emphasize the haemodynamic changes that occur in pregnancy and continue after delivery, which may lead to an uncovering of heart disease in the puerperium.

The present study is of 13 female patients, considered to be suffering from the cardiomyopathy of Africans seen in the southern part of Africa, whose illness began postpartum. No claim is made that they represent a specific postpartal heart disease; the implication of the occurrence is that whatever factors cause this cardiomyopathy may be exaggerated in the postpartal state. The patients were carefully selected to exclude the possibility of other aetiology; all but 2 had their onset sufficiently far removed from the delivery to render the haemodynamic changes of pregnancy and the puerperium irrelevant (i.e. 1 month or more). The other 2 with a shorter interval were so similar that their inclusion seemed justifiable.

AFRICAN CARDIOMYOPATHY

African cardiomyopathy is now generally considered to be of 2 broad groups: the endomyocardial fibrosis of North, East and West Africa, and the cardiomyopathy of Southern Africa which is largely free from this fibrosis.[9,10] Clinical studies of the Southern African type were first reported by Gillanders,[11] and pathological studies were reported by Higginson *et al.*[12] and Becker *et al.*[13] who emphasized the endocardial changes that do occur, though they are very different in degree from the gross changes of the northern group. Whether these 2 groups are fundamentally different, or differ only in some superadded factor, remains to be seen.

The cardiomyopathy seen at King Edward VIII Hospital is of the southern type. No cases corresponding to the endomyocardial fibrosis of North, East and West Africa have been seen. The clinical presentation is a familiar one, and the cases to be described were such orthodox examples that the possibility of the postpartal cases being of different aetiology from the usual cardiomyopathy is considered minimal.

MATERIAL

Seventeen female patients have been seen in heart failure in whom no primary non-myocardial cause for the heart failure could be found. Strict criteria for inclusion were adhered to in these cases of cardiomyopathy. Any patient whose diastolic blood pressure was known to be more than 90 mm.Hg at rest either at previous incidental admission, at delivery, after response of the heart failure therapy, or at subsequent follow-up, was excluded. Hypertensive retinopathy of Grade 1 or more excluded the patient. Any patient with signs or symptoms suggesting pulmonary embolism at or near the beginning of the illness was excluded, as was any with primary pulmonary dysfunction. Any patient with more than slight albuminuria, or with granular casts or cells in the urine, was excluded. Evidence of a purely left ventricular lesion on radiography disallowed the patient. The only cardiac murmurs allowed were ordinary soft ejection murmurs, and mitral or tricuspid pansystolic murmurs of Grade 2/4 or less, which disappeared with recovery from heart failure and decrease in heart size. Any significant fever, leucocytosis or anaemia caused exclusion. Finally, occasional cases of tuberculous pericarditis occur in Africans in whom a thick layer of granulation tissue leads to a radiological cardiomegaly, with low amplitude, congestive cardiac failure and the clinical features of cardiomyopathy. To exclude these, any doubtful case was submitted to right atrial catheterization and angiography to demonstrate the thickness of the atrial wall. In this way 2 cases were excluded.

The strictness of the criteria in all probability disallowed several true cases from admission to the series, but they allow a corresponding security of diagnosis.

Of the 17 cases, 13 had their first symptoms in the puerperium. In 3 there was no relationship to pregnancy or the puerperium; in 1 the onset was at the 6th month of pregnancy. It is the 13 cases arising postpartum that form the substance of this report.

CASE DETAILS

History of the Illness

Some of the relevant data are given in Table I. The age range extends over nearly the whole child-bearing period; 6 of the patients were 30 years or more, 7 less than 30 years of age. The length of history in all but 4 cases was a month or less; in 1 patient it was most acute and caused admission after only a day's illness. In all these patients there was

* Now Department of Physiology.

TABLE I. SOME RELEVANT DATA CONCERNING THE PATIENTS IN THIS SERIES

	Patient	Age in years	Duration of symptoms	Interval between delivery and onset	No. of previous deliveries	Birth	B.P. on admission (mm. Hg)
1	G.A.	20	1 week	6 weeks	2	Single	130/95
2	P.N.	34	3 months	3 months	5	Single	120/90
3	D.N.	39	1 month	5 weeks	3	Single	120/75
4	P.S.	31	3 weeks	1 week	5	Single	140/110
5	A.D.	34	3 weeks	5 months	5	Single	130/85
6	B.N.	23	1 day	5 weeks	?	Twins	150/100
7	A.H.	27	4 weeks	1 month	4	Single	130/90
8	M.Q.	26	3 weeks	1 week	5	Single	150/110
9	S.M.	30	4 months	1 month	11	Twins	100/?
10	F.H.	30	1 week	3 months	?	Single	130/90
11	F.M.	28	3 days	1 month	?	Single	120/90
12	R.D.	29	3 months	6 weeks	4	Single	125/105
13	Sh.N.	23	14 months	4 months	1	Single	110/60

progressively severe dyspnoea on exertion, and in 9 there was a cough which produced either nothing or small amounts of sputum, occasionally blood-tinged. Nine had noticed swelling of the legs, and 5 complained of a tight, oppresive feeling in the chest when dyspnoeic, which in 3 could be severe enough to be called a pain.

The interval between delivery and onset of symptoms varied from 1 week to 5 months, and bore no relation to the duration of symptoms before admission. In this interval all patients felt entirely well and were fully mobile. All were breast-feeding their infants on admission, and in all this was stopped soon after. The number of previous deliveries was known in 10 cases and showed a wide scatter.

The dietary history, as is usual in this African population, was poor and largely carbohydrate. A simple method of quantitating the value of the diet in this population is by the number of days per week on which meat is eaten. On this basis, the diet when meat is taken less than once per week is Grade 0. If meat is eaten once, the diet is Grade 1; if twice, Grade 2; if 3 times, Grade 3, and if more than 3 times, Grade 4. Of the present patients, 1 took a Grade 0 diet, 4 were Grade 1, 4 were Grade 2, and 4 were Grade 3. In a control healthy group of 100 postpartal women, 4% took a Grade 0 diet, 12% Grade 1, 21% Grade 2, 17% Grade 3, and 46% Grade 4. There is no good evidence from these figures that the patients took any poorer a diet than the general population from which they came.

In 11 cases (Table I) the preceding delivery was of a single infant; in 2, twin infants were born.

Physical Examination

The findings on physical examination were fairly uniform. All except 1 patient appeared well nourished, the exception having dry lack-lustre skin and hair. They were all in congestive heart failure on admission; the heart was typically large with a hypodynamic pulsation, felt laterally and parasternally, the pulse was small and fast, and the hands cold. There was in all a diastolic gallop sound, heard best in the mitral area, which was timed on phonocardiography in 6 patients. The time after the aortic second sound was 0·08 seconds in 1, 0·14 in 3, 0·16 and 0·18 seconds in 1 each. An early gallop sound has been recorded as well in male cases proved at autopsy, and cannot be used as a differential diagnostic point for a pericardial lesion. A pansystolic murmur due to functional atrio-ventricular valve incompetence was heard in 3 patients. The murmur disappeared with rest and decrease in heart size; it was mitral in 2, and tricuspid in 1.

Treatment and Progress

The progress of the patients and their treatment was variable. Four were kept at bed rest without any medication, on a meat-free, carbohydrate diet similar to their own for an initial period of 4 days. They were then given, by injection, 100 mg. each of pyridoxine, pantothenic acid, aneurine and nicotinamide daily for 3 days; and by mouth 60 mg. of riboflavine daily for the same period. Thereafter they were followed for a further 3 days on no therapy, as in the initial period of observation. Finally digitalis with or without a diuretic was administered. During all this time accurate daily assessments were made of pulse rate, blood pressure, jugular venous pressure, heart size, urine output, weight, and the degree of oedema and hepatomegaly. In none of these 4 was there any response to the vitamins. Two other patients begun on this regime had to be treated, from the third and fourth days, because of dangerous deterioration of the clinical state.

In 2, digitalization by 18 gr. of digitalis leaf in 3 days followed by a maintenance dose of 2 gr. daily did not cause any significant change in the subjects within 5 days of the commencement of this therapy. The giving of a mercurial diuretic and restriction of salt led to rapid and marked improvement in 11 of the 13 patients. The other 2 remained refractory; 1 was eventually discharged free from heart failure, only to return after 4 weeks, again in severe decompensation. The other improved so slowly over 3 months that she was finally discharged, still in failure, on her own insistence. She was still in severe heart failure 5 months after discharge. It is noteworthy that the 2 refractory patients were those who had produced twins.

Of the 11 who improved well, 2 were apparently cured at the time of discharge, all signs and symptoms having disappeared; 1 of these was still well 1 month after discharge, having taken digitalis. Unfortunately she then failed to attend again and could not be traced, so that it is not known how far she remained in health without therapy. The other did not re-attend and could not be traced.

Six were followed for periods up to 1 year; 5 needed continued digitalis, 1 being completely symptom-free on this regime. The patient who did not need therapy was also quite free from symptoms after 3 months without treatment, but she had clear radiological evidence of persisting cardiomegaly. No patient in this series was found to be free from signs of heart disease when followed up.

The remaining 3 patients, who were followed up for less than a month, continued to show signs and need therapy, and subsequently failed to re-attend and were untraceable.

TABLE II. SERUM PROTEIN AND TURBIDITY FIGURES IN 11 PATIENTS AND IN CONTROLS

	Serum albumin (g. per 100 ml.)	Serum globulin (g. per 100 ml.)	Serum alkaline phosphatase (King-Armstrong units)	Zinc turbidity (units)	Thymol turbidity (units)
Present series	3·0 (2·4 - 3·7)	3·9 (2·9 - 5·4)	8·1 (4 - 11)	16·4 (8 - 31)	5·4 (2 - 11)
Control series	2·7 (1·5 - 3·7)	3·3 (2·2 - 4·2)			

Investigations

According to the criteria for admission to the series, none of the patients had significant anaemia, leucocytosis or urinary abnormality.

Serum-protein and turbidity tests were performed in 11 patients. The mean and range of values is given in Table II, together with those available of a control healthy postpartal female population of 27 cases.[14]

Since the serum-albumin level probably reflects the protein nutritional state there does not seem from these figures to be any greater deficiency than in the normal population.

Liver biopsies were performed in 4 patients. In 1 of the biopsies there were a few binucleate cells; in another a slight amount of fat was present. The other 2 showed nothing worth comment, and in general all 4 showed no evidence of the damage that is associated with chronic malnutrition in these African patients.

The toxoplasma complement-fixation test was performed in 3 patients and was negative in all.

Pressures were measured in the pulmonary circulation in 2 patients after clinical improvement. The right ventricular pressures were 30 and 40 mm.Hg systolic, and 0 and 5 mm.Hg diastolic respectively; the mean right atrial pressures were 5 mm.Hg in both, and the mean left atrial pressures (wedged pulmonary artery) were 12 and 20 mm.Hg respectively.

Chest X-rays taken on the first admission, when the patients were in congestive heart failure, showed large hearts and marked pulmonary congestion. On screening, both ventricles appeared to be involved in the dilatation, and their movement in contraction was small. As the patients improved the heart size came back towards normal. In the least successful it remained large, in the most successful the lung fields cleared and the heart size, though persistently abnormal, was considerably reduced.

Twelve-lead electrocardiographic examination was made in all patients on from 2 to 6 occasions, except in 1 patient where only a single tracing was obtained. Analysis of the leads on admission shows that the axis was deviated to the left in 6; the electrical position was horizontal in 6, vertical in 2, and mid-position in the remainder. The transition from dominant S wave to dominant R wave in the chest leads occurred at V_3-V_4 in 9, V_4-V_5 in 4. The maximum amplitude of P (which was in lead II in 12 cases and in lead I in 1 case) was 1 mm. mean, range 0·25-2 mm. The mean duration of the P wave was 0·08 seconds, range 0·06-0·1 seconds. It was biphasic in V_1 in 5 cases, bifid in V_2 in 2 cases and in V_4 in another. The mean P-R interval was 0·135 seconds, range 0·12-0·16 seconds. Small q waves, never greater than ½ mm. in depth, were present in V_5 and V_6 in 3, accompanying a similar wave in lead II in 2. There were similar q waves in leads I and aVL in 1 case. The mean corrected Q-T interval was 0·439 seconds, with a range, 0·379-0·514 seconds. The sum $S(V_1)+R(V_5)$ was 31·4 mm. mean, range 13·5-52 mm.; in only 3 was the sum greater than 35 mm. The sum $R(V_1)+S(V_5)$ was 1·8 mm. mean, range 0-7·5 mm. The maximum potential in the augmented limb leads had a mean of 6·6 mm., range 2·5-11 mm. Five patients had a maximum of less than 5 mm. The QRS duration in 11 patients in lead II was 0·064 seconds mean, range 0·05-0·08 seconds. The other 2 patients had a left bundle branch block pattern with a QRS duration of 0·12 and 0·14 seconds. This pattern disappeared in 1 patient in the 6th month after her discharge; she was then free from symptoms on digitalis. T waves were inverted over the left ventricular surface leads in 6, over the right in 1, over both left and right surfaces in 4. The maximum height or depth of the T wave in standard and unipolar limb leads was 1·1 mm. mean, range 0·25-2 mm. In the chest leads the maxima had a mean of 4·3 mm., range 1-10 mm. In subsequent tracings the following changes took place: in 3 the T wave inverted or deepened in leads V_1-V_3; in 1 in leads V_4-V_6. In 1 the T wave, initially inverted in leads V_4-V_6, became shallower there. Two patients showed a progressive anti-clockwise rotation, and 1 rotated clockwise.

DISCUSSION

The clinical history and findings and the results of the investigations are all typical of Southern African cardiomyopathy. The cases have not differed from male cases except in the age incidence and the prognosis. The mean age of these 13 postpartal cases was 29, and of the non-postpartal female cases, 31 years. In a comparable series of 31 male cases, personally studied, the mean age on admission was 41, and only 4 cases were below the age of 30. A possible implication is that the exaggeration of the aetiological factors in the puerperium is responsible for the earlier onset in females. So far no cases have been seen in nulliparous African females. It is of particular interest that the 2 patients who had produced twins were the only 2 completely refractory to therapy. The tendency for twin pregnancy to be associated with postpartal heart failure has been recorded before and is reviewed by Meadows[8] and Rosen.[2]

The difference in prognosis is to some extent a matter of impression, because of small numbers and poor follow-up. Two postpartal patients out of 13 were discharged completely free from symptoms and signs, clinical or investigatory. Only 1 African male out of 31 studied, and many more seen casually, responded to this extent. Two further postpartal patients, 1 of whom was still on treatment, were symptom-free at follow-up, but continued to show cardiomegaly. This degree of response occurred in only 2 out of the 31 male patients. Two postpartal patients were completely resistant to treatment: refractoriness in males is sufficiently common to have caused 6 out of 31 to die, and a further 3 to be discharged after several months of hospital regime, still in heart failure.

The better prognosis of the postpartal group was seen also in the 4 female patients whose illness started apart from the peurperium. One of these was apparently cured at the time of discharge but has not been seen without therapy; the other 3 were much improved but had persistent signs. These numbers are too small to resolve the point whether the puerperal factors are sufficiently reversible to make the prognosis better than in those females in whom these factors were not operative. However, in general, the puerperal factor alters the age incidence and the prognosis compared with male cases. A possible interpretation of the postpartal occurrence of an illness common in this population is that a postpartal process occurs which merely precipitates heart failure, the cardiomyopathy may be fundamental and the postpartal process transitory. Since the nature of both of these is unknown, one can go no further with reasonable speculation.

It is difficult to know how far the puerperal cardiomyopathies described in people of European origin are related to the present cases. On the criteria for inclusion in this series no individually reported European case could be included. On the other hand several investigators have reported cases in American negroes which may be included,[4,5,15] and Keely[9] has briefly mentioned the occurrence in this country. No cases have been seen in the Asian patients of this hospital, although their numbers are the same as Africans in the general population served by the hospital. Such racial differences frequently imply a

dietary difference. The failure of the 4 patients tested to respond to B vitamins shows only that there was no acute deficiency of these substances. Similar results were seen in 18 male cases submitted to the same trial and have been reported for this type of cardiomyopathy by Gillanders.[11] The diet of the present cases, though deficient in protein over probably their whole life-time, was no worse than that of a control sample. Moreover, except in 1 case no signs of other malnutrition were present; such signs, especially those of pellagra, are not uncommon in the hospital population, yet no tendency for these pellagra patients to have cardiac symptoms has been noted. Neither clinical beri-beri nor response to aneurine has been observed in any patients.

A simple protein-deficiency factor is rendered unlikely by the serum-protein findings and by the histological findings in the liver in 4 patients. Normal liver histology has been reported in a non-postpartal case by Higginson *et al.*,[12] who also reported absence of fibrosis in 2 others. In the 31 cases of cardiomyopathy in males that were studied, the appearance of the liver was known either by biopsy or autopsy in 15. In 6 of these there was no fibrosis, and in 4 no abnormality at all. Fibrosis may, therefore, be absent in the male cases. It has not been seen in the postpartal cases. Since it is thought to be an invariable accompaniment of prolonged protein deficiency in these adult patients, the findings argue against this deficiency factor in postpartal cardiomyopathy. Hull and Hidden[5] and Gillanders[11] have reported findings for the serum proteins similar to the present figures.

Meadows[8] also considered that there was no nutritional factor in his cases. Sodeman,[15] however, stated that nutritional deficiency was common in the patients who displayed the picture of postpartal heart failure, and 2 of the cases of Benchimol *et al.*,[3] grouped as non-specific myocarditis, had evidence of vitamin deficiency.

Although there is evidence that toxoplasmosis is a common infection in this country,[16] the complement-fixation test did not reveal this aetiology for the cardiomyopathy in the postpartal cases, and has given similar results in male cases. The myocarditis reported by Paulley *et al.*[17] has not therefore been observed.

The pressure measurements from the pulmonary circulation in 2 cases merely confirm the clinical evidence of biventricular failure, in contrast to the pulmonary hypertensive cases described by Abrahams.[18] Similar findings have been made in 6 non-postpartal cases.

The radiological features in these cases are the same as those previously described in this condition[11] and as recorded in European cases of cardiomyopathy.[19]

Electrocardiography shows, as the dominant variation, T-wave flattening and inversion, often with progressive changes. There is a tendency to small voltage QRS deflections, and a prolonged Q-T interval. Abnormal Q waves are notably absent. The findings in similar cases have been reported by Hull and Hafkesbring,[4] Gillanders,[11] Becker *et al.*[13] and Meadows.[8]

Hull and Hafkesbring[4] reported 1 postmortem examination in a 16-year-old negress. The findings, briefly reported, indicate a different picture, a myocarditis rather than a non-inflammatory cardiomyopathy. Moreover the illness began before delivery. It may be that this was in fact a different type of case, so that the pathological picture remains uncertain. The reported appearances in European cases have been quite unlike the African cardiomyopathy, the commonest description being of severe focal scarring. Higginson *et al.*[12] have reported the findings in the African variety, which consist of interstitial oedema, a fine interstitial fibrosis, hypertrophy of muscle fibres with hyperchromatic nuclei and a subendocardial fibrosis that, if present, is patchy, rarely diffuse, and usually not wider than the space occupied by about 6 muscle fibres. In occasional cases the band of fibrosis may be 10 or more fibres in diameter and macroscopically obvious. Since no deaths from postpartal cardiomyopathy have been seen here, final evidence as to the identity with non-postpartal cases is lacking, but there seems no good reason to doubt this identity.

SUMMARY

1. Thirteen patients are described in whom heart failure presumed due to 'African cardiomyopathy' developed postpartum. Electrocardiographic and other investigatory results are presented.

2. Nutritional factors as studied by dietary history, clinical appearance, vitamin replacement, plasma-protein levels, and liver biopsy gave no evidence for any specific nutritional deficiency.

3. Twin deliveries occurred in the 2 cases which were most refractory to therapy.

4. The postpartal cases showed greater improvement than a comparable male series, but none reversed completely.

5. It is postulated that some unknown postpartal process precipitates heart failure in patients with African cardiomyopathy, itself of unknown aetiology, and that the postpartal process may well be transitory.

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