Malignant hypertension and its renal complications in black South Africans

F. J. MILNE, S. H. JAMES, Y. VERIAVA

Summary

Malignant hypertension is an important cause of morbidity and mortality among urban black South Africans. Hypertension accounts for 15.9% of all patients and for 34.6% of blacks receiving treatment for end-stage renal failure. Malignant hypertension is more commonly diagnosed than benign hypertension and two-thirds of patients present in the age group 30 - 49 years. Together they are the most common preventable cause of end-stage renal failure in this country. Acute partially reversible renal failure occurs in 20% of patients with malignant hypertension who require dialysis. This is an important subgroup, who may be recognised by their younger age, female preponderance and fulminant presentation. Short-term peritoneal dialysis and effective control of blood pressure will result in satisfactory return of renal function. However, only adequate country-wide control of hypertension will prevent these costly renal complications.

Two recent reviews have covered many of the clinical and management aspects of malignant hypertension among black South Africans, but world-wide. Demographic and epidemiological data suggest that this disease has been under-emphasised in the past in the RSA and that the medical profession should be made aware not only of the extent of the problem but also the serious complications and the important challenges for clinical and basic research. This article emphasises the renal complications of malignant hypertension seen in this country.

Demographic data

Malignant hypertension is now a rare disease in the Western world but is more prevalent among black Americans than whites. The only published prevalence study in South Africa showed a hospital prevalence of 2.2% in Johannesburg during 1979/1980, while Seedat and Reddy in 1974 quoted a 7% incidence at a hypertension clinic in Durban. An unpublished survey of medical admissions to Hillbrow Hospital, Johannesburg, showed an average annual admission rate of 0.94% over the years 1985 and 1986 (S. H. James, M. Med. (Med.) dissertation, University of the Witwatersrand). There were 135 admissions for malignant hypertension from a total of 14 327 patients for the 2 years. This relatively common occurrence of malignant hypertension in blacks contrasts strikingly with its rarity in whites.

Aetiology

The terms 'accelerated hypertension' and 'malignant hypertension' cause confusion, since they are sometimes used to describe the same syndrome and sometimes to imply different phases of the same syndrome. The term 'malignant' has been used to describe patients who in addition to high blood pressure have papilloedema, while the term 'accelerated' has been used when papilloedema is absent but there are fresh bilateral haemorrhages of the flame type with or without cotton wool spots. McGregor et al. and Ahmed et al. have convincingly shown that the prognosis of so-called 'accelerated' and 'malignant' hypertension is the same. Thus we prefer the term 'malignant' hypertension to describe all patients presenting with a diastolic pressure above 120 mmHg and bilateral fresh haemorrhages and/or exudates or papilloedema.

Definition

The terms 'accelerated hypertension' and 'malignant hypertension' cause confusion, since they are sometimes used to describe the same syndrome and sometimes to imply different phases of the same syndrome. The term 'malignant' has been used to describe patients who in addition to high blood pressure have papilloedema, while the term 'accelerated' has been used when papilloedema is absent but there are fresh bilateral haemorrhages of the flame type with or without cotton wool spots. McGregor et al. and Ahmed et al. have convincingly shown that the prognosis of so-called 'accelerated' and 'malignant' hypertension is the same. Thus we prefer the term 'malignant' hypertension to describe all patients presenting with a diastolic pressure above 120 mmHg and bilateral fresh haemorrhages and/or exudates or papilloedema.

Malignant hypertension is rarely seen in whites unless there is an underlying secondary cause, usually bilateral renal parenchymal disease or renal artery stenosis. In blacks the majority of patients appear to have essential hypertension. The diagnosis is usually made on clinical grounds but has been supported histologically by tissue obtained either at autopsy or from nephrectomy specimens obtained from patients on dialysis or at the time of transplantation. Although no systematic angiographic study has been performed to exclude renal artery stenosis, which is commonly associated with malignant hypertension in white Americans, this is an unlikely cause in black South Africans. Fibrous dysplasia and aortitis even of the Takayasu type is generally rare and, because atheroma of the aorta is still uncommon in blacks, renal artery stenosis is unlikely to be an important cause of malignant hypertension in this group. The endocrine causes of malignant hypertension are anecdotally as rare in blacks as whites and, apart from pheochromocytoma, they seldom present in the malignant phase. Table I shows the distribution of malignant hypertension in three areas of the world and confirms not only the predominance of essential malignant hypertension (82%) in South Africa, but also the large numbers of patients that presented to a single medical unit in the space of 1 year.

| TABLE I. MALIGNANT HYPERTENSION AROUND THE WORLD |
|----------|----------|----------|
| Glasgow  | Melbourne | Johannesburg |
| No. of patients | Essential (%) | Secondary (%) |
| 139 | 60 | 40 | 62 |
| 83 | 20 | 80 | 82 |
| 82 | 18 | 18 | 18 |

Modified from Isles.

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Renal disease

The renal disease in malignant hypertension has been well described in a recent review. Musculomucoid hyperplasia and fibrinoid necrosis of the smaller intrarenal arteries are characteristic lesions. Fibrinoid necrosis was considered to be the hallmark of the malignant phase of hypertension. It is not clear whether this is simply a manifestation of malignant hypertension or whether it is pathogenic. If, as suspected, fibrinoid necrosis is only a manifestation of extremely high arterial pressure, then musculomucoid hyperplasia is more likely to be the basic pathological lesion in malignant hypertension. Hyaline arteriosclerosis will only be present if there has been longstanding benign hypertension. Isaacs and Milne have studied the nephropathology of malignant hypertension in blacks in Johannesburg. Unlike the findings in black Americans, they saw fibrinoid necrosis in a large proportion of their autopsy series, and also confirmed musculomucoid hyperplasia in all.

Diagnosis

The renal complications of malignant hypertension range from mild proteinuria to end-stage renal failure. The specific diagnosis of essential malignant hypertension is difficult when renal insufficiency is present. These patients commonly present with some blood and protein in the urine. Red blood cell casts or, rarely, frank haematuria may confuse the diagnosis with primary glomerulonephritis and superimposed malignant hypertension. In favour of essential malignant hypertension is the lack of past renal history, modest concentrations of protein in the urine (< 1 g/d) and normal to only slightly decreased renal size on ultrasonography. Confirmation of the diagnosis can only be obtained by renal biopsy. However, this may be hazardous in the setting of malignant hypertension. Many of the local studies quoted can be criticised on the grounds that there was no histological proof of essential malignant hypertension, but nephrologists have been reluctant to perform renal biopsies in the malignant phase.

Renal failure following malignant hypertension may present in three forms. These are acute, acute-on-chronic and chronic. Of great interest are the acute and the acute-on-chronic presentations. Complete recovery of renal function has been well documented provided the rise in serum creatinine level is modest. Serum creatinine concentrations of less than 300 μmol/l frequently return to normal values once adequate control of the blood pressure has been obtained. Less well documented is a subgroup of patients who present with oliguric renal function. Complete recovery of renal function has been well documented provided the rise in serum creatinine level is modest.

TABLE II. SOUTH AFRICAN DIALYSIS AND TRANSPLANTATION REGISTRY (1982 - 1987) — ESSENTIAL HYPERTENSION

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>White</th>
<th>Coloured</th>
<th>Asian</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients treated for ESRF</td>
<td>952</td>
<td>1771</td>
<td>640</td>
<td>269</td>
<td>3632</td>
</tr>
<tr>
<td>No. of patients with EHT causing ESRF</td>
<td>329</td>
<td>77</td>
<td>134</td>
<td>37</td>
<td>577</td>
</tr>
<tr>
<td>Occurrence (%)*</td>
<td>34,6</td>
<td>4,3</td>
<td>20,9</td>
<td>13,8</td>
<td>15,9</td>
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</table>

* 2/1 x 100. ESRF = end-stage renal failure; EHT = essential hypertension.
hypertension than the mean age in other series of malignant hypertension quoted. The greater number of patients (37.4% of all malignant hypertension patients) were started on treatment for end-stage renal failure during the decade 30 - 39 years, followed by 30.1% in the 40 - 49-year age group. This trend was found in all population groups. The survival of patients with hypertension and other causes of end-stage renal failure was similar. Furthermore, no significant difference in survival between end-stage renal failure patients with benign or malignant hypertension could be demonstrated. It is clear from the SA Dialysis and Transplantation Registry data that hypertension, both malignant and benign, is the most common preventable cause of end-stage renal failure in the RSA and the predominant cause of end-stage renal failure among South African blacks who constitute the major population group in the country.

We have found that after renal transplantation bilateral nephrectomy did not improve blood pressure control or graft survival in these patients. Our experience with survival of black transplant patients has been that there is no significant difference over 30 months comparing patients with malignant hypertension and other causes of renal failure. This is in broad agreement with the SA Dialysis and Transplantation Registry figures which show an 80% actuarial graft survival at 30 months of 1 072 patients of all races who received transplants without hypertension compared with a 75% survival of 113 patients, again of all race groups, who received transplants and who had a diagnosis of hypertension. The period of observation is short and it is possible that differences may develop as the number of black patients and the duration of follow-up increases.

### Management

A comprehensive account of the management of malignant hypertension has been presented in the two recent reviews. It is worth noting that in the past, when effective therapy was not available, the 1-year mortality rate was 80%. Advances in therapy have revolutionised the management of this disorder with reversal of the malignant state and prolonged patient survival.

Essential malignant hypertension may present in two forms: most commonly there is no immediate threat to life, but on rare occasions patients present in hypertensive crisis with either encephalopathy or severe pulmonary oedema. In this rare crisis situation the patient should ideally be admitted to an intensive care unit where the blood pressure can be rapidly controlled with intravenous sodium nitroprusside. If an intensive care unit is not available, oral or sublingual nifedipine (capsule bitten and the contents swallowed) will lower the pressure to safe levels within 30 minutes during which time other therapy may be instituted for a longer-term antihypertensive effect.

The basic aim of active therapy in the non-crisis situation is to reduce the diastolic blood pressure gradually to 110 mmHg over a 48-hour period. It must, however, be remembered that autoregulation of cerebral and renal blood flow is set at a higher arterial pressure in patients with malignant hypertension. Should the pressure fall too rapidly and to too low a level, a significant reduction in renal and cerebral perfusion may occur and result in acute tubular necrosis or cerebral ischaemia. Renal function must be closely monitored by serial serum creatinine level estimations and when these stabilise or improve, then further attempts must be made to bring the blood pressure to within normal limits. In this non-crisis situation oral atenolol or slow-release nifedipine have been shown to be safe and effective within the first 24 hours in local black patients.

The authors wish to thank Drs E. du Toit and C. G. Lawley for making available the detailed data from the South African Dialysis and Transplantation Registry, Dr C. G. Isles for reviewing the manuscript and for permission to produce the modified table, and Mrs A. Smith for typing the manuscript.

### REFERENCES


### TABLE III. HYPERTENSION CAUSING END-STAGE RENAL FAILURE

<table>
<thead>
<tr>
<th>Total No. of patients with essential hypertension</th>
<th>All groups</th>
<th>Black</th>
<th>White</th>
<th>Coloured</th>
<th>Asian</th>
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</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>577</td>
<td>329</td>
<td>77</td>
<td>134</td>
<td>37</td>
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<tr>
<td>%</td>
<td>328</td>
<td>195</td>
<td>34</td>
<td>91</td>
<td>8</td>
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<td>Benign hypertension</td>
<td>57</td>
<td>59,6</td>
<td>10,3</td>
<td>27,7</td>
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<td>No. of patients</td>
<td>249</td>
<td>134</td>
<td>43</td>
<td>43</td>
<td>29</td>
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<tr>
<td>%</td>
<td>43</td>
<td>54,0</td>
<td>17,2</td>
<td>17,2</td>
<td>11,6</td>
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</table>
Sonographic demonstration of atypical congenital anomalies in the fetus of a diabetic mother

A case report

R. SEIDER, G. VAN RENSBURG, B. DARAZS

Summary

Uncontrolled diabetes, particularly in early pregnancy during the stage of organogenesis, increases the risk of teratogenesis. A case of mixed congenital abnormalities in a fetus demonstrated ultrasonographically during the second trimester of pregnancy in an uncontrolled insulin-dependent diabetic mother is presented. Necropsy of the abortus confirmed the findings.

Case report

An affluent, 26-year-old insulin-dependent diabetic woman, who lived in a rural area, had been controlling her diabetes symptomatically with Monotard injections, the dose varying in accordance with the subjective impressions of her glucose status. At the time of presentation at hospital her random blood glucose level was 18.1 mg/ml and the haemoglobin HbA1c level was 10.9. Despite an approximately 12-year history of diabetes she had no retinal stigmata and normal renal function. The period of amenorrhoea had been 24 weeks when she was first seen in the ultrasound department and, although she had had 5 previous ultrasonographic examinations at peripheral clinics, these had failed to show any fetal abnormalities.

The findings at 1 Military Hospital included a fetal biparietal diameter of 4.5 cm, which suggested a sonographic age 5 weeks less than gestational age as calculated from the patient’s last menstrual period. A femur length of 3.3 cm also indicated a fetal age of approximately 19.5 weeks but the humerus was 3.6 cm, in keeping with a 23-week gestation. The dating in our department is in accordance with the tables published by Sabbagha et al.1 and Romero and Jeanty.2 The lower limbs were shown to be motionless and flexed throughout the examination. The cervical and cranial dorsal spine appeared ultrasonographically normal, but the caudad thoracic and lumbar spine was absent (Fig. 1). Bright sacral echoes were demonstrated. The fetal pelvis was small and contracted but a normal bladder was identified. The liver, kidneys and heart were normal, but the cardiac echoes were placed eccentrically in the chest with bowel occupying the right chest. Three vessels were identified in the cord and the amniotic fluid and placenta were normal.

A therapeutic abortion was performed 1 week later and radiographs of the fetus were taken (Fig. 2). A careful necropsy

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