Scleroderma Hypertensive Renal Crisis and the Changing Pattern of Mortality in Systemic Sclerosis (Scleroderma)

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Dear Sir,

We have recently reviewed the causes of death amongst 243 patients with systemic sclerosis [1], followed prospectively between 1979 and 1989 [2]. There were 42 deaths, 5 (12%) due to renal failure. Only 1 patient died from scleroderma renal crisis (SRC). This unusually low mortality rate from renal failure, especially that due to SRC, prompted us to undertake a more detailed review of our experience.

Seven of the 243 patients developed SRC. There were 6 females and 1 male with a mean age, at the time of development of SRC, of 32 years (range 22–46). The mean disease duration, from time of diagnosis, was 53 months (range 8–120), being less than 2 years in 4 patients. Skin involvement was diffuse in 6 and restricted to the distal extremities in 1 patient. SRC developed abruptly in all cases, with severe hypertension (systolic pressure: mean 206 mm Hg, range 175–230; diastolic pressure: mean 119 mm Hg, range 110–140) and rapidly progressive renal insufficiency (maximum serum creatinine: mean 705 $\mu\text{mol/l}$, range 337–922). Five of the patients presented with seizures, 1 on the basis of a subarachnoid hemorrhage. One patient presented with cortical blindness, due to bilateral occipital infarcts, and micro-angiopathic hemolytic anemia.

Hypertension was treated with a variety of drugs including intravenous sodium nitroprusside, captopril, minoxidil, nifedipine, apresoline and β -blockers. Combinations of oral agents were required for adequate blood pressure control in 5 patients, while in 2, initial treatment was with sodium nitroprusside followed by captopril alone. In 2 patients there was spontaneous recovery of renal function after their blood pressure had been controlled. Although the other 5 patients required dialysis, this was subsequently discontinued in 3 following recovery of adequate renal function, in 1 after several

months of anuria. Three of the 7 patients have died: 4, 11 and 48 months following development of SRC. The causes of death were renal failure, hemorrhage following accidental administration of heparin and infection. Two developed chronic renal failure requiring maintenance dialysis. SRC is characterized by the abrupt onset of malignant arterial hypertension with rapidly progressive renal failure. While the pathogenesis of SRC is uncertain, there is a marked decrease in renal cortical blood flow associated with vasoconstriction, intimal hyperplasia and intravascular coagulation, involving small arteries and afferent arterioles [3]. It has been reported to

develop in 20% of patients with diffuse scleroderma but in only 1% of those with limited skin involvement [4]. Patients with early disease (less than 3 years) and rapidly progressive skin thickening are particularly susceptible [5]. However, between 1979 and 1989, we only encountered 7 new cases of SRC amongst 243 (3%) patients. Since 120 of the patients being followed had diffuse scleroderma and 6 of them developed SRC, the prevalence in this subset is 5%.

Prior to the last decade, the survival of patients with SRC was no more than 6 months [4], and at autopsy renal failure accounted for 43% of deaths [6]. In another study, all patients developing renal failure died within 1 year [7]. Since then dialysis treatment has increased survival in patients developing renal failure. An improvement in the prognosis of SRC is also attributed to the use of captopril, an angiotensin-converting enzyme inhibitor [8–11]. The 5-year cumulative survival rate increased to 75% amongst those treated with captopril [12]. The same investigators also noted a decline in the frequency of SRC from 27 (1972–1978) to 14% (1979–1985).

While captopril is claimed to improve survival in SRC, this cannot be verified with our limited experience. Although 6 of the 7 patients in our series were treated with captopril, in none was this the sole antihypertensive

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agent used. In fact, our experience indicates that captopril, while useful in the treatment of SRC, is often inadequate when prescribed alone. There is no doubt that the key to the successful management of SRC is early aggressive treatment of the hypertension.

In conclusion, our study supports previous evidence of a decline in the frequency of SRC in patients with systemic sclerosis. Survival from SRC has improved markedly as a result of early aggressive management with newer antihypertensive agents, including captopril and the institution of dialysis therapy. As in our series, renal function may subsequently improve sufficiently to allow discontinuation of dialysis. This reduction in the frequency of SRC and improved survival from this manifestation may explain the observed reduction in mortality from renal failure in patients with systemic sclerosis.

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