MEDICAL MEMORANDA

Ischaemic Myocardial Damage in Chronic Renal Failure

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Metastatic calcification of coronary arteries in secondary hyperparathyroidism is well documented (Brown and Richter, 1941; Andersen and Schlesinger, 1942; Katz *et al.*, 1969; Pendras, 1969; Moorhead *et al.*, 1970). Heart failure resulting from coronary calcification, however, is an uncommon complication. It has been only coincidentally mentioned in several review articles (Andersen and Schlesinger, 1942; Pendras, 1969; Moorhead *et al.*, 1970) and we have been unable to find a well-documented case report in the English literature. The object of this paper is to describe such a case resulting from renal failure in which death was due to coronary insufficiency resulting in myocardial fibrosis.

Case Report

A 22-year-old Caucasian man was first noted to have kidney disease at age 18, when at a preinduction physical examination hypertension and proteinuria were found. Several months later, in October 1966, renal biopsy showed chronic glomerulonephritis of unknown aetiology. At that time his serum creatinine was 1·8 mg/100 ml, creatinine clearance 74 ml/min, and 24-hour urinary protein 10·8 g. Blood urea nitrogen (B.U.N.) was not recorded. During 1967-8 he became easily fatigued and his diastolic blood pressure rose to 110 mm Hg, the B.U.N. rose from 65 to 90 mg/100 ml, and the creatinine reached 9·1 mg/100 ml. An intravenous pyelogram showed small kidneys bilaterally. A diagnosis of end-stage renal failure from chronic glomerulonephritis was made and later confirmed histologically.

After several months of peritoneal dialysis he underwent bilateral nephrectomy and renal transplantation from a sister donor with whom he had four major mismatches by leucocyte typing. Though the graft functioned well initially it later failed because of uncontrolled rejection and was removed one month after transplantation. He was subsequently maintained on haemodialysis, and during this time developed severe peripheral neuropathy necessitating confinement to a wheel-chair. Thirteen months later another transplant was attempted but failed because of hyperacute rejection. Between September 1969 and his death in February 1970 he remained relatively stable biochemically, with the B.U.N. between 27 and 47 mg/100 ml and the creatinine ranging from 8·1 to 10·8 mg/100 ml. Serum phosphate rose progressively from 6 to 8 mg/100 ml, serum calcium remained between 9·4 and 10·5 mg/100 ml, and alkaline phosphatase rose to 150 units. His blood pressure varied from 130/90 to 170/110 mm Hg, and E.C.G. showed first-degree heart block and widespread S-T segment depression and T-wave inversion compatible with ischaemia.

X-ray examination in January 1970 showed a 2 to 3 cm increase in heart size as well as pulmonary congestion and incipient oedema. Bony survey showed soft-tissue calcification adjacent to the proximal and distal ends of the left humerus and around the proximal interphalangeal joints of the hands. In early February 1970 he presented with a 24-hour history of sore throat and a temperature of 39°C. W.B.C. count was 3,300/mm^3. Throat cultures grew moderate numbers of *Haemophilus parainfluenzae* and β-haemolytic streptococci. He was started on erythromycin therapy. Several days later he died at home.

At necropsy the main findings were those of renal osteodystrophy and metastatic calcification. Death was caused by congestive cardiac failure resulting from ischaemia due to severe coronary calcification.

The patient was extremely wasted. There was no peripheral or sacral oedema. The heart was enlarged, weighing 500 g, and the left ventricle hypertrophied (1·7 cm in width). The endocardial surfaces of both ventricles and atria were grey-white. Numerous flecks of calcification and extensive fibrosis were present in the left ventricle and to a less degree the right ventricle and specifically involved the bundle of His (Fig. 1). The valves were normal but the valve rings were calcified. The major coronary vessels and the aorta were normal. Microscopically the primary lesion was found in the small arteries and arterioles, which showed calcification of the internal elastic lamina and often of the media. In many vessels the calcification had caused disruption of the medial coat. Most

FIG. 1—Myocardium of left ventricle showing white flecks of fibrosis and calcification.

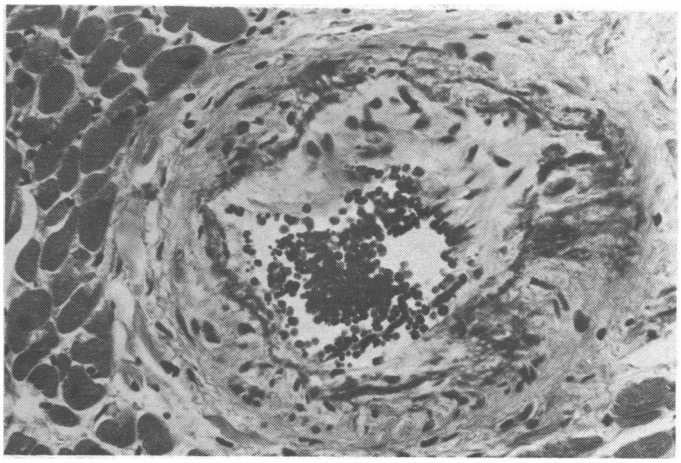

FIG. 2—Small artery of left ventricle showing granular calcification of media and internal elastic lamina, intimal proliferation, and narrowing of lumen. (H. and E. × 310.)

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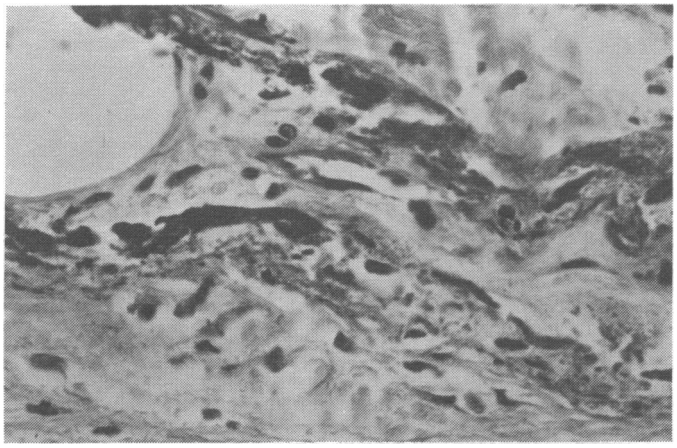

FIG. 3—Arteriole of left ventricle showing medial calcification and intimal proliferation producing complete occlusion of lumen. Patent end of lumen is seen to the left. (H. and E. × 310.)

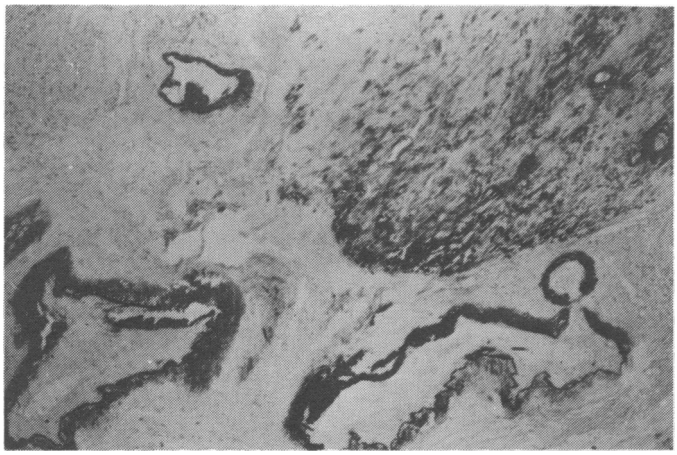

FIG. 4—Low-power magnification of left ventricle showing calcification of vessels and dystrophic calcification of myocardium. (von Kossa. × 31.)

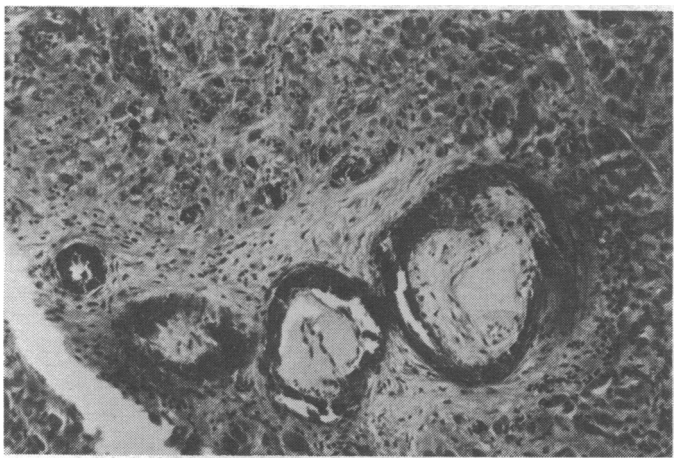

FIG. 5—High power magnification of left ventricle showing medial calcification of vessels, intimal proliferation, dystrophic calcification, and fibrosis of myocardium. (H. and E. × 125.)

vessels showed pronounced intimal proliferation leading to narrowing or occlusion of the lumen, and in some this proliferation also involved the media and adventitia (Figs. 2 and 3). There was widespread myocardial fibrosis and some calcification centred around most of the diseased vessels (Figs. 4 and 5). There was no calcification of the large coronary arteries or of the aorta.

There was extensive metastatic calcification of the small arteries of all organs examined with the exception of the brain; however, none of these showed intimal proliferation of any severity. The lungs showed extensive calcification of the bronchi, alveolar septa, and arteries. The parathyroids were all enlarged, each measuring about 1 by 0·5 cm. Microscopically they showed chief-cell hyperplasia. The bones were grossly normal but microscopically showed severe renal osteodystrophy. There was also a segmental demyelination of the peripheral nerves and neurogenic muscular atrophy, which was thought to be consistent with a uraemic neuropathy.

Comment

Though metastatic calcification of medium-sized arteries is common in hyperparathyroidism this case is unusual because the small vessels were involved and were accompanied by intimal proliferation. Normally medial calcification starts in the internal elastic lamina and spreads to involve the entire thickness of the media (Mulligan, 1947; Katz *et al.*, 1969; Parfitt, 1969). Rarely, calcification evokes intimal proliferation resulting in ischaemic damage, usually of the lower limbs (Bryant and White, 1901; Friedman *et al.*, 1969; Parfitt, 1969), but reference to the heart has also been made (Brown and Richter, 1941; Pendras 1969).

This appears to be the mechanism in the present case, though hypertension may have been a complicating factor. However, since only the vessels of the heart were involved this seems unlikely. Furthermore, experimental hypervitaminosis D in animals has shown similar selective involvement of vessels with medial calcification and intimal thickening (Haas *et al.*, 1958).

The E.C.G. changes were not those of hyperparathyroidism but those of conduction defects and ischaemia, and are well explained by our findings. Since many patients with renal failure are hypertensive the superposition of ischaemic myocardial damage might be of major significance in precipitating left ventricular failure and death.

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