MEDICAL PRACTICE

Hospital Topics

Clinical importance of acquired cystic disease of the kidney in patients undergoing dialysis

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Abstract

From 1976 to 1982 five patients undergoing haemodialysis at Oxford Renal Unit suffered serious complications from acquired cystic disease of the kidney and two died as a direct result. Clinical features seen were pain, haematuria, palpable renal enlargement, massive haemorrhage, resolution of anaemia, and metastatic malignancy. The clinical histories emphasise the features of a disease that is likely to assume increasing importance in patients undergoing haemodialysis.

Introduction

Cystic degeneration of kidneys in patients with end stage renal failure was first reported in 14 of a postmortem series of 30 patients undergoing haemodialysis[1] and is now agreed to be common.[2-7] Cysts are multiple and may occur throughout both kidneys, which may remain small or become massively enlarged. Tumours may be associated with these cystic changes and usually take the form of papillary, tubular, or solid adenocarcinoma.[1] Both the incidence and extent of cystic change rise with duration of dialysis and since large numbers of patients undergoing haemodialysis are living longer, the disease will become important in their management.

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We report five cases of serious complications from acquired cystic disease of the kidney in patients undergoing haemodialysis.

Case histories

Case 1—A 37 year old garage proprietor began dialysis treatment six months after he developed malignant hypertension. Intravenous urography showed small smooth kidneys, and biopsy was not performed. For 12 years he remained well while undergoing haemodialysis, and between 1975 and 1977 haemoglobin concentration rose from about 7 g/dl to almost 10 g/dl, after which the patient developed microcytosis (mean cell volume 70 fl) and haemoglobin concentration fell to about 8 g/dl (fig 1). In 1980 he developed a non-productive cough and chest pain. A chest radiograph disclosed multiple round

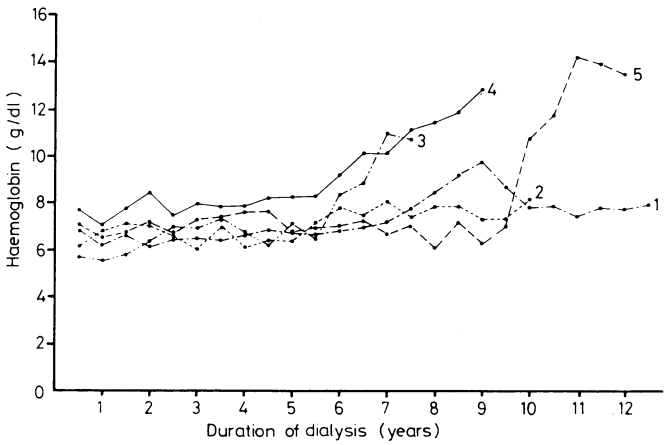

FIG 1—Changes in haemoglobin concentration with duration of dialysis. Each point represents mean of all haemoglobin estimations within six months.

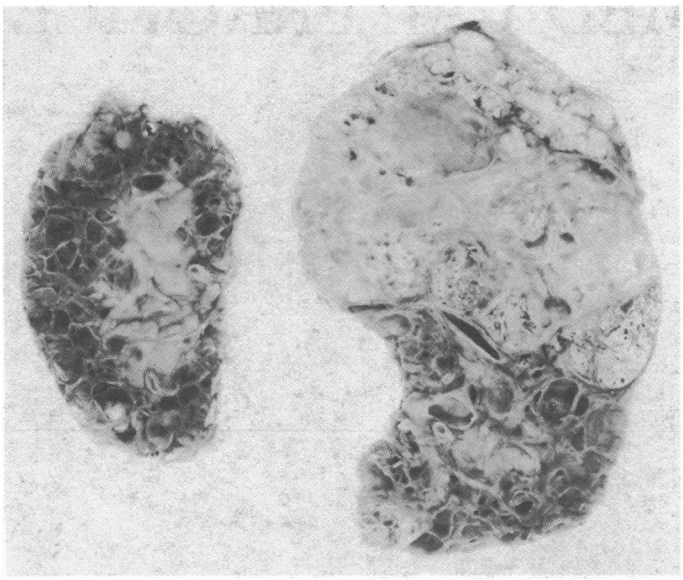

FIG 2—Acquired cystic change in both kidneys with large tumour at upper pole of right kidney and small one at lower pole.

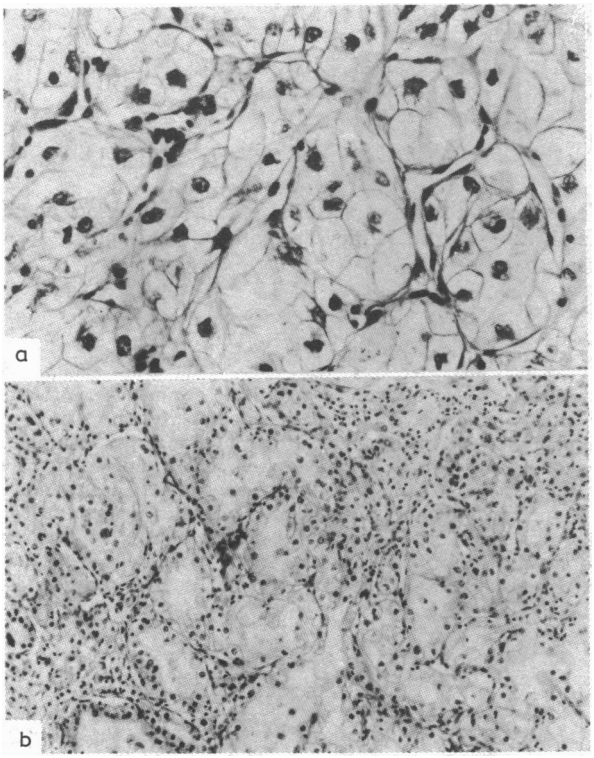

FIG 3—(*a*) Typical clear cell adenocarcinoma of kidney. Haematoxylin and eosin × 240. (*b*) Secondary clear cell adenocarcinoma from kidney in lung. Haematoxylin and eosin × 80.

opacities. Shortly afterwards the patient died, and necropsy showed cystic change throughout both kidneys, which weighed 820 g and 290 g (fig 2). There was an 8 cm tumour at the upper pole of the right kidney. Histological examination confirmed clear cell renal adenocarcinoma with metastatic tumour in the lungs (fig 3).

Case 2—A 30 year old housewife presented with hypertension and uraemia. Intravenous urography showed small kidneys, and retrograde pyelography showed clubbing of the calyces. Renal biopsy showed end stage renal disease. In 1969 she began dialysis treatment and was given anticoagulants because of recurrent thrombosis of her arteriovenous shunt. In 1976 she developed severe right sided abdominal pain on the day after undergoing dialysis. Anticoagulation was reversed, and she was given a transfusion. Temporary peritoneal dialysis produced heavily bloodstained effluent. Anticoagulation was not restarted, but in 1980 she developed similar pain on the left while undergoing dialysis. On admission blood pressure was 80/50 mm Hg and she had guarding over the left side of her abdomen. She was resuscitated with a blood transfusion but the next night became hypotensive again and died. Necropsy showed cystic change throughout both kidneys, which weighed 38 g and 82 g. There was no tumour but at the lower pole of the left kidney there was haemorrhage from a ruptured cyst tracking around the kidney and bursting into the peritoneal cavity, which contained one litre of blood.

Case 3—A 28 year old schoolteacher began dialysis treatment in 1968, two years after presenting with malignant hypertension. Intravenous urography showed normal sized kidneys with smooth outlines, and renal biopsy showed chronic glomerulonephritis with pronounced hypertensive arterial damage. From 1970 to 1976 he had biochemical evidence of mild hepatitis, and biopsy in 1976 showed granulomatous hepatitis. In 1972 he developed acute left loin pain 48 hours after dialysis. Temporary peritoneal dialysis was performed, producing bloodstained effluent. In 1973 he suffered a similar episode.

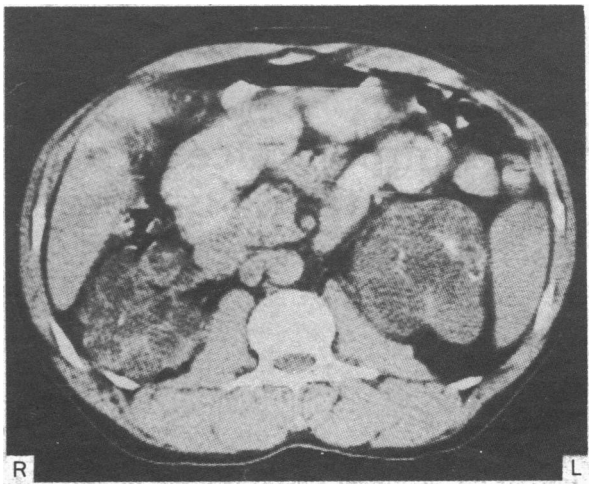

FIG 4—Both kidneys are enlarged and occupied by low density cysts, some of which show peripheral calcification.

There was now a mass palpable in the left loin, and plain abdominal radiography showed calcification within the left kidney. Between May 1974 and January 1976, haemoglobin concentration rose to 11 g/dl having been stable at 6-7 g/dl for the first five and a half years of dialysis (fig 1). In 1976 he became slightly feverish, and repeat radiological examination showed further enlargement of the kidneys. Renal angiograms showed abnormal vascularisation at the lower pole of the left kidney. In preparation for renal transplantation bilateral nephrectomy was performed, together with splenectomy. Unfortunately, the patient died from postoperative haemorrhage. Nephrectomy specimens each weighed 340 g and showed cystic change with tumour formation, the largest tumour being a 3 cm mass in the left kidney. Histological examination showed these to be clear cell tumours. There was no metastatic spread.

Case 4—A 30 year old joiner started dialysis treatment in 1974, one year after presenting with hypertensive encephalopathy. Intravenous urography showed normal sized kidneys, and renal biopsy disclosed chronic glomerulonephritis with severe hypertensive arterial damage. Two renal transplants were acutely rejected and required graft nephrectomy. From 1976 he suffered several episodes of haematuria, right loin pain, and fever. Renal angiography showed abnormal renal vasculature suggesting cystic change in both kidneys. In 1981, because of continued pain and haematuria, right nephrectomy was performed. The kidney weighed 180 g and was replaced with multiple cysts. There was no tumour. Unfortunately, in January 1982 the pain recurred on the left together with haematuria. The patient's haemoglobin concentration rose from 8·2 g/dl in October 1978 to 12·9 g/dl in April 1983 (fig 1).

Case 5—A 34 year old driver developed malignant hypertension. Intravenous urography showed normal sized kidneys, and renal biopsy showed fibrinoid necrosis and sclerosed glomeruli. He started dialysis treatment in 1971. In 1974, two days after undergoing

dialysis, he developed acute left sided abdominal pain with tenderness. There was dullness at the base of the left hemithorax, and pleural aspiration removed 200 ml blood. Temporary peritoneal dialysis showed intraperitoneal haemorrhage, which stopped after transfusion of eight units of blood. In 1975 he had a further episode of left loin pain and haematuria. In 1976 and 1978 he received two renal transplants which were both rejected acutely and abandoned. The patient remained well while undergoing haemodialysis, and between October 1980 and March 1982 haemoglobin concentration rose from 6·2 g/dl to 14·0 g/dl (fig 1). Computed tomography in April 1983 showed greatly enlarged kidneys with multiple cystic areas (fig 4).

Discussion

Survival while undergoing maintenance dialysis has increased the importance of many complications of chronic renal failure and created a new set of diseases such as accelerated atheroma, renal osteodystrophy, and aluminium toxicity in patients undergoing dialysis. Acquired cystic disease of the kidney is another such complication which has received comparatively little attention though important clinical problems may result.

AETIOLOGY

The aetiology of acquired cystic disease of the kidney is unknown, though theories based on cyst production in animals are interesting. Hepler[8] produced cysts in rabbits with a combination of ischaemia produced by ligation of segmental arteries and obstruction by papillary cauterisation.[8] Severe arterial disease is seen in kidneys of patients with end stage renal failure,[9] which may cause ischaemia, and tubular obstruction may occur by oxalate crystals or fibrosis.[1] Microdissection has shown continuity between cysts and tubules.[5] In rats cystic disease can be induced by feeding certain diphenyl compounds,[10–12] and it has been suggested that the accumulation of similar substances in patients undergoing haemodialysis might cause acquired cystic disease of the kidney.[13] In view of the association between acquired cystic disease and renal tumours this hypothesis is made particularly attractive by microdissection studies on rats fed nordihydroguaiaretic acid,[12] indicating that cystic change is consequent on focal cellular hyperplasia in the outer medullary segment of the collecting duct. This hypothesis has not been investigated in man, and there are no studies of the incidence of acquired cystic disease in patients undergoing continuous ambulatory peritoneal dialysis or in transplant recipients after a short spell of haemodialysis when exposure to "uraemic" toxins should be less.

CLINICAL FEATURES

Although most reported series have concentrated on the pathological features of acquired cystic disease of the kidney it is becoming apparent that it may mimic many of the clinical features of polycystic kidney disease: abdominal mass, pain, haematuria, intrarenal and perirenal haemorrhage, a relatively high haemoglobin concentration, and tumour formation were all seen in our patients.

Haemorrhage—Haemorrhage may lead to haematuria or painful renal enlargement or may burst retroperitoneally causing pain in the loin, hypotension, and a fall in packed cell volume without external blood loss. The first reports of spontaneous retroperitoneal haemorrhage in patients undergoing dialysis did not establish the source of bleeding but pointed out an association with anticoagulation.[14 15] In the original description of acquired cystic disease of the kidney[1] three patients had retroperitoneal haemorrhage and this association has been confirmed, though there have been only rare reports of serious cases and no fatalities. Four of the five patients we describe suffered recurrent retroperitoneal haemorrhage. In three patients persistent haemorrhage necessitated temporary peritoneal dialysis to avoid the need for heparin and in each case intraperitoneal extension of the haemorrhage was shown. One patient developed an associated haemothorax, presumably from direct extension of the haematoma. Another patient died of massive retroperitoneal haemorrhage, rupturing intraperitoneally. We therefore believe that it is justified to regard all such haemorrhages as potentially serious. Though only one of our patients was taking coumarin derivatives anticoagulant treatment should be used with care in patients known to have acquired cystic disease of the kidney, and after an episode of retroperitoneal haemorrhage careful observation is needed in hospital. Renal angiography may show the site of bleeding,[16] and embolisation through the catheter, which is effective in controlling haemorrhage from other renal lesions,[17] may be particularly useful in cases of haemorrhage where nephrectomy is likely to be hazardous.

Anaemia—Whether acquired cystic disease leads to an increase in haemoglobin concentration is uncertain. In their survey of 32 patients undergoing dialysis Mirahmadi and Vaziri found no difference in haemoglobin concentrations between 15 with cystic change and the rest.[4] No patient had tumours, however, and the degree of cystic change in their patients was small. Though details are not given for each patient, it was stated that all cysts were less than 1·5 cm diameter and the average weight of both groups was considerably less than the normal adult renal weight of 140-160 g. More recently Goldsmith,[18] using ultrasonography, studied 20 patients who had been undergoing haemodialysis for more than six years and noted a correlation between the extent of cystic change, haemoglobin concentration, and duration of dialysis. Of our patients, three had large rises in haemoglobin concentrations and large cystic kidneys. One with very small cystic kidneys had no rise in haemoglobin concentration. The remaining patient had large cystic kidneys and a rise in haemoglobin concentration, which subsequently fell as he developed microcytosis; concomitant iron deficiency may have complicated his anaemia. After several years of stable anaemia a dramatic rise in haemoglobin concentration is unusual,[19] and the association with unusually extensive acquired cystic disease in three of our patients supports Goldsmith's observation. Though one patient had granulomatous hepatitis, this preceded the rise in haemoglobin concentration by four years. There was no other explanation for the change in haemoglobin concentration in any of the patients. In polycystic kidney disease the anaemia of chronic renal failure is less severe, and it is tempting to suggest that the development of acquired cystic change has a similar effect, though further study is required to prove that the association is causal. In theory, increased production of erythropoietin could result from neoplasia or the stimulation of erythropoietin producing cells by local hypoxia consequent on spatial distortion by cysts or associated with severe arterial disease. Surprisingly, however, Goldsmith showed a negative correlation between haemoglobin and erythropoietin concentrations as measured by mouse liver cell bioassay. Whatever the explanation these cases do indicate the ability of the uraemic marrow to respond sufficiently to maintain a near normal haemoglobin concentration under appropriate circumstances, despite the presumed persistence of uraemic toxins. Furthermore, the increased production of a haemopoietic factor by some cystic kidneys in end stage renal failure could result in erythrocytosis after transplantation.

Neoplasia—Renal tumours are found in up to 45% of patients with acquired cystic disease of the kidney[1–7] and are frequently bilateral and multiple. Their malignant potential is uncertain. Histological differentiation of renal cell carcinoma from adenoma is difficult, and size is an important factor in predicting the behaviour of these tumours. According to Bell, renal cortical tumours less than 3 cm in diameter rarely metastasise,[20] though there are exceptions.[21] In acquired cystic disease of the kidney death from metastatic spread of tumour is unusual and has been described only once before in seven reported series. Clearly, these cases show some malignant potential, and as patients

survive longer while undergoing dialysis it may become a greater problem, raising the question of whether it is justified to screen patients undergoing dialysis with a view to prophylactic nephrectomy. Computed tomography will show both cystic change and tumour formation and is probably the method of choice,[22 23] though the changes can also be shown well by ultrasonography. In our patient the primary was clinically silent and a screening programme of asymptomatic patients undergoing dialysis would have been required to make the diagnosis before metastatic spread. As tumours may be bilateral and bilateral nephrectomy will seriously exacerbate anaemia assessment of malignant potential before nephrectomy is necessary. Size may be helpful and as this tumour is the largest we have seen in acquired cystic disease it might be argued that malignant spread was likely and death preventable by nephrectomy; screening of the older patients undergoing dialysis may therefore be justified.

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Influence of imaginative teaching of diet on compliance and metabolic control in insulin dependent diabetes

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Abstract

Dietary non-compliance is an important cause of poor metabolic control in insulin dependent diabetes. Patients are often blamed, but teaching methods may be at fault, so a prospective study was set up to compare the effect of three different teaching methods. After a three month run in, 40 adults with longstanding poorly controlled insulin dependent diabetes (mean haemoglobin A_1 13·0%) were allocated at random to three teaching methods: conventional diet sheet instruction (group 1); practical lunchtime demonstrations (group 2); videotape education (group 3). Knowledge was assessed by questionnaires, compliance by seven day food records, and glycaemic control by serial glycosylated haemoglobin measurements. During six months of follow up there was no improvement in knowledge, compliance, or HbA_1 in group 1, but in groups 2 and 3 both knowledge and compliance improved. In group 2 HbA_1 fell to 10·6 (SD 2·1)% and in group 3 to 9·6 (2·3)%. The change in HbA_1 showed an appreciable correlation with dietary compliance as judged by day to day consistency in carbohydrate intake.

These findings show that new and interesting educational methods can have a major influence on knowledge, compliance, and metabolic control in insulin dependent diabetes.

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Introduction

For patients treated with insulin to achieve and maintain good diabetic control they need to pay attention simultaneously and continuously to many variables including insulin dose, correct site of injection, and the effects of exercise and diet.[1] Rollo in 1798 was the first to point out that patients find it very difficult to adhere to prescribed dietary restrictions.[2] Yet, however many advances have been made in the treatment of