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INVOLUTION OF POLYCYSTIC KIDNEYS DURING ACTIVE TREATMENT OF TERMINAL UREMIA

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Abstract. Following institution of chronic dialysis and/or renal transplantation for terminal uremia, four consecutive patients observed for 15–48 months with their polycystic kidneys in situ invariably showed a rapid relief of symptoms (pain, hematuria) followed by a gradual, but steady, involution of the kidneys. The mechanism and the practical clinical implications are discussed.

It is well established that polycystic kidneys usually are considerably enlarged before marked reduction in renal function is in evidence (1). Although the rate of growth of the polycystic kidneys in relation to the progression of the disease has not been studied in detail, it appears likely that the increment in kidney size decreases during progressive renal insufficiency until the stage of terminal renal failure is reached.

Among many other observations of pathophysiological and clinical significance, the advent of chronic hemodialysis and renal transplantation has made it possible to observe the development of polycystic kidney disease beyond the stage at which the patients previously died in terminal uremia. None of the larger materials on dialysis and transplantation in patients with polycystic kidneys in situ do, however, specify this problem (2, 4, 5). While perusing the literature in preparation for the present paper, we found only one publication, illustrating a marked reduction in the size of the polycystic kidneys of a 37-year-old man two years after successful grafting (3).

The present paper supports and extends this observation. In four consecutive patients, who had their polycystic kidneys in situ for more than 15 months after institution of active treatment of terminal uremia by dialysis and/or transplantation, a gradual reduction in kidney size was in evidence. The longer the period of observation, the more pronounced was the observed involution of the polycystic kidneys. The significance of this finding is discussed from the pathogenetic and clinical points of view.

PATIENT MATERIAL

In the period Jan. 1965 – June 1974, 14 patients with terminal uremia due to polycystic kidney disease were treated at Rigshospitalet.

Nephrectomized patients. One patient was totally nephrectomized during dialysis and 4 were totally nephrectomized in connection with necrokidney transplantation. Four of the 5 patients were from our early experience in 1965–1969, when bilateral nephrectomy was carried out on liberal indications in the majority of all patients actively treated for terminal uremia.

Non-nephrectomized patients. In 9 patients, the polycystic kidneys were left in situ. Five of them, 2 on chronic dialysis, 2 back on chronic dialysis after rejection of necrokidney grafts and 1 recently transplanted with a necrokidney, have been followed for less than 6 months on active treatment. In these cases, possible changes in the size of the polycystic kidneys have not yet been studied due to the short observation period.

Four patients, all transplanted with necrokidneys, have been observed for periods exceeding 15 months (range 15–48) and in these patients a study of the clinical course and of changes in kidney size has been performed. Their case histories are presented below.

CASE HISTORIES

Patient 1, woman, born in 1930 (TP 62)

Family history. Marked disposition for polycystic kidney disease on paternal side; a sister, suffering from polycystic kidneys, died from subarachnoideal hemorrhage in 1973.

Course of disease. In 1959 acute pyelonephritis followed by attacks of flank pain and macroscopic hematuria

at monthly to bimonthly intervals. In Aug. 1959 left-sided lumbotomy with puncture of cysts without evident relief; in Dec. 1959 surgical drainage of right-sided perirenal abscess. Rising serum creatinine since 1962. In terminal renal failure in the spring of 1970, still having frequent attacks of recurrent flank pain and hematuria.

Diagnostic verification. I.v. urography in 1959, inspection of kidneys at surgery in 1959, renal angiograms in March 1970 and May 1974.

Kidney and liver size before transplantation. Both kidneys considerably enlarged from 1959 to 1970. No liver enlargement.

Transplantation was carried out without antecedent dialysis with a necrokidney on May 21, 1970. Immediate onset of graft function.

Course of disease after transplantation. No episodes of flank pain or hematuria after transplantation. Kidney size gradually decreasing. Kidneys no longer palpable from Sept. 71, 16 months after grafting.

Present status (June 74, 49 months after transplantation). Excellent clinical condition. Revalidated to housework plus part-time work as secretary. Kidneys not palpable. No liver enlargement. Serum creatinine 0.09 mmoles/l, 24-hour endogenous creatinine clearance 80–90 ml/min, BP 115/70. Urine less than 100 mg protein/24 hours, sterile on culture. Medication: azathioprine 100 mg and prednisone 2.5 mg/day.

Patient 2, man, born in 1919 (TP 124)

Family history. No known cases of polycystic kidney disease in the family.

Course of disease. No definite urologic symptoms. In March 1971 examined by own doctor due to uremic symptoms. Transferred to Rigshospitalet with creatinine clearance of 8 ml/min.

Diagnostic verification. Renal angiograms in April 1971 and in Oct. 1972. Autopsy in Dec. 1972.

Kidney and liver size before dialysis and transplantation. Neither kidneys nor liver were palpable, possibly due to marked obesity.

Dialysis and transplantation. Regular dialysis in July–Nov. 71. Transplanted on Nov. 2, 1971 with necrokidney. Immediate function, which remained good until July 1972, when chronic rejection was diagnosed clinically and by graft biopsy. Died in uremia with terminal septicemia on Dec. 27, 1972. Autopsy revealed a few 1 cm large cysts in the liver and typical polycystic kidneys measuring 16×10×10 cm each.

Course of disease during dialysis and after transplantation. As before active treatment, no local urologic symptoms. Kidneys not palpable, liver not palpable.

Patient 3, man, born in 1921 (TP 133)

Family history. Marked disposition to polycystic kidney disease on maternal side. One older brother died from uremia at the age of 40. A twin brother, suffering from polycystic kidney disease, was transplanted at another hospital in 1973.

Course of disease. Between 1950 and renal transplantation in 1971, numerous episodes of flank pain and macroscopic hematuria. Rising serum creatinine since 1964. In terminal renal failure in 1971.

Diagnostic verification. I.v. urography in 1964. Renal angiograms in Oct. 1970 and March 1974.

Kidney and liver size before transplantations and dialysis. Kidneys large and readily palpable between 1964 and 1971. No liver enlargement.

Transplantations and dialysis. Transplanted without antecedent dialysis with a necrokidney on Dec. 3, 1971. Acute rejection, followed by graftectomy on Dec. 9, 1971. On regular hemodialysis between Dec. 9, 1971 and Feb. 2, 1973, when retransplanted with a necrokidney, which is still functioning.

Course of disease on dialysis and after successful transplantation. Since admission to the regular hemodialysis program following failure of first graft there have been no episodes of flank pain or hematuria. Polycystic kidneys, gradually decreased in size, were no longer palpable in July 1972, 7 months after start of hemodialytic treatment.

Present status (June 1974, 30 months after institution of dialysis and 16 months after successful transplantation). Clinically in good condition, works 6 hours per day in previous job as accountant. Kidneys not palpable. Liver 4–5 cm below right costal margin. (It is not possible to state from the records when the liver, which was not palpable before dialysis, started to increase in size.) Serum creatinine 0.10–0.11 mmoles/l, 24-hour endogenous creatinine clearance 60–65 ml/min, BP 140–150/90–100. Urine less than 150 mg protein/24 hours and sterile on culture. Medication: azathioprine 125 mg and prednisone 15 mg/day.

Patient 4, woman, born in 1914 (TP 135)

Family history. Not conclusive.

Course of disease. Slight uremic symptoms since 1966. No flank pains or hematuria. In terminal uremia in June 1971.

Diagnostic verification. I.v. urography in 1966, renal angiograms in May 1971 and March 1974.

Kidney and liver size before dialysis and transplantation. Kidneys palpable and slowly growing since 1966. Liver not palpable.

Dialysis and transplantation. On regular dialysis between June 1971 and Dec. 21, 1971, when transplantation with a necrokidney, which is still functioning, was performed.

Course of disease on dialysis and after transplantation. As before, no flank pain, no hematuria. Kidneys very large and readily palpable at transplantation in Dec. 1971. Kidneys still palpable in Jan. 1973, no longer palpable in Aug. 1973, 26 months after start of dialysis and 20 months after grafting.

Present status (June 74, 36 months after institution of dialysis and 30 months after successful transplantation). General condition good. Receives pension, but manages full-time housework. Kidneys not palpable, liver not enlarged. Serum creatinine 0.09 mmoles/l, 24-hour endogenous creatinine clearance 60–70 ml/min, BP 140–160/90–100. Urine less than 100 mg protein/day. Intermittent asymptomatic bacteriuria. Graft urogram normal. Medication: azathioprine 100 mg and prednisone 5 mg/day.

ANGIOGRAPHIC TECHNIQUE

All patients with terminal renal failure are examined with renal angiograms and arteriography of the iliac vessels as part of our "pretransplantation survey". Routine ultrasonic scanning was not carried out and i.v. urography, even with high doses of contrast and nephrotomography, does not reveal the kidney area in polycystic kidneys with very poor function. Therefore, apart from physical examination, the only possibility of reexamining the patients with the aim of demonstrating a change in kidney size was to repeat the renal angiograms.

Like urography, renal angiography does not give a sharp delineation of the kidney surface in polycystic kidneys with exceedingly low function. It was therefore necessary to search for the most peripheral arterial ramifications in the right and left kidneys which chould be verified as anatomically identical in the first and the second renal angiogram of each patient. The ramification points were connected by straight lines, and the area of the resulting polyeders was measured by planimetry (Fig. 1). The percentage reduction in the size of the polyeders was taken to represent the percentage reduction in total kidney size.

Possible errors caused by slight variations in the film–focus distance were corrected for by planimetry of the area of the same corpora vertebralia in both examinations. This correction only proved to be of importance in one case, in whom the first and second angiograms were carried out by slightly different techniques.

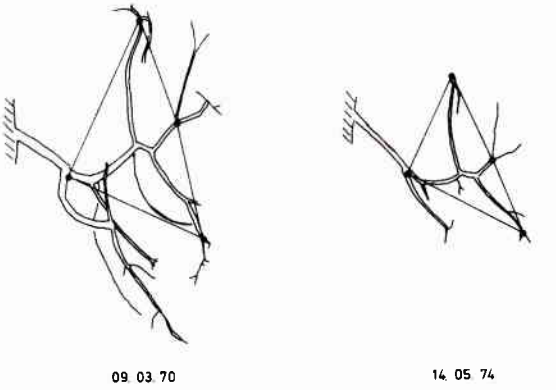

Fig. 1. The most peripheral arterial ramifications which could be shown to be identical in two arteriograms on patient 1 taken with an interval of 50 months.

RESULTS

Clinical symptoms and signs. As illustrated by the case histories, hematuria and flank pain subsided rapidly following grafting (pat. 1) as well as after institution of regular dialysis (pat. 3). In the three patients, in whom the kidneys were clinically palpable (nos. 1, 3 and 4), they gradually diminished in size and were no longer palpable 16 months after grafting (pat. 1), 7 months after institution of regular dialysis (pat. 3) and 20 months after grafting (pat. 4).

Thus clinical symptoms apparently vanish long before reduction in kidney size is in evidence. The results are summarized in Table I.

Kidney size. As described above, an attempt was made to estimate the percentage reduction in kidney size by renal angiography. Table II shows that a reduction was found in all four patients and that it was roughly parallel to the active treatment period.

DISCUSSION

The present material of 4 consecutive patients with their polycystic kidneys in situ for more than 15 months after institution of chronic hemodialysis and/or renal transplantation demonstrates that the kidneys invariably undergo a gradual involution and that the degree of shrinkage is roughly proportional to the observation period. This supports and extends the only other published observation of a similar phenomenon in a male patient, who was

Table I. *Clinical data of the four patients*

Pat. no.	Sex	Born in		Pain	Hematuria	Infection	Palpable kidney	Palpable liver
1	♀	1930	Before TP	+++	+++	+	++	0
			After TP	0	0	0	0	0
2	♂	1919	Before dial. and TP	0	0	0	0	0
			After dial. and TP	0	0	0	0	0
3	♂	1921	Before dial and TP	+++	+++	(+)	+++	0
			After dial. and TP	0	0	0	0	++
4	♀	1914	Before dial. and TP	0	0	0	+++	0
			After dial. and. TP	0	0	0	0	0

Table II. *Reduction in kidney size in the four patients*

Pat. no.	1st angiography	2nd angiography	Interval (mo.)	Active treatment period before 2nd angiography (mo.) Dialysed	Functioning graft	Total	Calculated reduction in kidney size (%)
1	March 9, 1970	May 14, 1974	50	0	48	48	Left 48 Right 38
2	April 13, 1971	Oct. 25, 1972	18	4	11	15	Left 27 Right 11
3	Oct. 30, 1970	March 27, 1974	41	14	14	28	Left 10 Right 12
4	May 11 1971	March 26, 1974	34	6	27	33	Left 41 Right 50

observed for 2 years following a successful grafting (3).

Furthermore, it is apparent that local clinical signs and symptoms from the polycystic kidneys (pain and gross hematuria) disappear rapidly and that symptomatic relief precedes palpable reduction in kidney size.

In one patient (no. 4) we have found that liver enlargement has increased over a period of 3 years. Neither our small material, nor other materials known to us, do, however, clearly elucidate the course of polycystic liver affection following successful grafting.

The cause of the reduction in kidney size remains unknown. It is possible that the involution is simply a continuation of the process of replacement fibrosis, which is in evidence already before the stage of terminal uremia. It cannot be excluded, however, that effective dialysis as well as transplantation of a normally functioning kidney alter the function of the polycystic kidneys in such a manner that intracystic pressure is reduced, with the result that the process of replacement fibrosis is accelerated.

The practical implication of the present clinical and morphological findings is of significance, since it has previously been our policy, and has been recommended by more experienced workers (2), to carry out total nephrectomy on liberal indications in patients with end-stage polycystic kidney disease to relieve pain, hematuria and mechanical distress. The present results strongly indicate that a more conservative attitude may be warranted in many cases and that the potentially hazardous surgical removal of large polycystic kidneys should be confined to patients in whom manifest infection is present and may represent a threat to the patient, not least after renal transplantation when immunosuppressive drugs have to be administered. It should, moreover, be kept in mind that removal of polycystic kidneys is only rarely indicated to regulate high BP and that total nephrectomy during dialysis is followed by an accentuation of anemia with consequent need for blood transfusions. If indicated on account of infection, total nephrectomy in patients with polycystic kidney disease should therefore ideally be carried out in conjunction with grafting and not during dialysis.

REFERENCES

1. Dalgaard, O. Z.: Polycystic disease of the kidneys. In: Diseases of the kidney, 2nd ed. (ed. M.S. Strauss and L. G. Welt), p. 1223. Little, Brown and Co., Boston 1972.
2. Lazarus, J. M., Baily, G. L., Hampers, C. L. & Merrill, J. P.: Hemodialysis and transplantation in adults with polycystic renal disease. J. Amer. med. Ass. 212: 1821, 1971.
3. Martin, D. C. & Goodwin, W. E.: Renal transplantation in polycystic renal disease. J. Amer. med. Ass. 202: 202, 1967.
4. Nakamato, L. & Kolff, W. J.: Chronic uremia due to polycystic renal disease treated by the artificial kidney. Int. J. Med. 101: 921, 1958.
5. Salvatierra, O., Kounty, S. L. & Belzer, F. O.: Polycystic renal disease treated by renal transplantation. Surg. Gynec. Obst. 137: 431, 1973.