Secondary polycythaemia associated with bilateral renal lymphocoeles

I.E. Burton, P. Sambrook and L.J. McWilliam

Departments of Haematology, Diagnostic Radiology and Histopathology, University Hospital of South Manchester, Withington, Manchester M20 8LR, UK

Summary: A patient with a 15 year history of secondary polycythaemia due to renal erythropoietin hypersecretion is presented. Subsequent spontaneous development of bilateral renal lymphocoeles, which contained high erythropoietin levels, was shown by computerized tomography. The lymphocoeles were successfully treated by bilateral peritoneal marsupialization. No cause for the persistent polycythaemia or lymphocoeles was found at laparotomy or on renal biopsy.

Introduction

Renal lymphocoeles and secondary polycythaemia are well-recognized complications of renal transplantation.^{1–4} We are unaware of any previous record of spontaneous bilateral renal lymphocoele occurring in association with polycythaemia in the absence of previous surgery, renal tumour or cystic disease.

Case report

An asymptomatic Caucasian male aged 35 years was found to have mild hypertension (160/110 mmHg) at a routine medical examination in 1978. At presentation, examination was otherwise normal. Haemoglobin was raised at 21.7 g/dl, haematocrit 0.62, MCV 89 fl, MCH 89 pg, white cell count $7.0 \times 10^9/l$ with a normal differential and platelet count of $155 \times 10^9/l$. Blood gases were normal, urea 8.3 mmol/l, creatinine 140 $\mu\text{mol/l}$, creatinine clearance 65 ml/minute, 24 hour urine vanillyl mandelic acid (VMA) 81 mmol/l (normal 7–85 mmol/24 hours). Plasma cortisol was 345 mmol/l (normal 9.00 hour 328 mmol/l). Chest X-ray, electrocardiogram and intravenous pyelography were all normal. Bone marrow showed normoblastic erythroid hyperplasia but no increase in other haemopoietic elements. During the following month he was venesected a total of 6 units to a haemoglobin of 14.5 g/dl.

One year later his haemoglobin had risen again to 17.8 g/dl. Confirmation of secondary polycythaemia was obtained by finding raised erythropoietin levels on radioimmunoassay (RIA) of

> 400 mU/ml (normal < 30). He was treated with four further venesections during 1981. Bilateral renal angiography, ultrasound and computed tomographic (CT) scanning of chest and abdomen revealed no abnormalities. For the next 10 years his blood pressure varied between 130/90 and 150/100 mmHg with creatinine levels averaging 100 $\mu\text{mol/l}$ and haematocrit 0.50–0.55. In 1987 he developed the symptoms and blood picture of iron deficiency from repeated venesections.

In July 1990 a further search for a treatable lesion revealed a large multiloculated fluid collection around the left kidney and a thin rim around the right kidney which were interpreted, following CT scan, as bilateral haematomas and treated conservatively. In March 1991 he developed painful swelling of the right para-umbilical region and loin. Similar pain occurred on the left side after 3 weeks and abdominal ultrasound and CT scan (Figure 1) showed significant increases in the bilateral fluid collections. The swelling increased, necessitating insertion of a percutaneous drain into the right perinephric collection which produced copious clear straw-coloured fluid. Over 14 successive days the volumes drained varied between 4,050 and 1,325 ml. The biochemistry of the fluid showed it to be lymph containing sodium 137–140 mmol/l, potassium 3.9–5.6 mmol/l, urea in the perinephric fluid 10.5–12.8 compared to serum levels of 10.9–14.0 mmol/l, and creatinine 110–190 versus serum 180–260 $\mu\text{mol/l}$. The fluid contained 2 g/l albumin compared with serum, albumin 42 g/l and urine protein 0.35 g/l. Creatinine clearance at the start of drainage was 35 ml/minute. Simultaneous erythropoietin estimation of the fluid and serum showed these to contain levels exceeding 500 mU/ml. Lymph cytology revealed a few leucocytes but no malignant cells or acid-fast bacilli.

Figure 1 CT scan showing bilateral renal lymphocoeles in 1991.

Injection of radiolabelled technetium diethylene triamine pentacetic acid (^{99m}Tc]DPTA) into the drainage catheter showed that the perinephric collections were non-communicating but did not localize a site of lymphatic obstruction.

Blockage of the percutaneous catheter led to treatment by drainage into the peritoneal cavity; at laparotomy both kidneys had a granular appearance with no capsule on the medial wall. Two large windows were created in the mesocolon on each side to allow free communication between the intra- and extraperitoneal spaces. Divided omentum was inserted through the window and sutured to present closure. Postoperative recovery was uneventful.

Wedge renal biopsy showed 30% of glomeruli to be completely sclerosed whilst the remainder showed mild glomerulomegaly owing to mesangial matrix increase and hypercellularity. Blood vessels showed slight wall thickening whilst the interstitium and tubules appeared normal. No interstitial cell hypertrophy, oedema or dilatation of lymphatics was seen. The wall of the perinephric fluid collection consisted of fibrous connective tissue containing chronic inflammatory cells and occasional lymphocytic aggregates, but no epithelial lining.

Abdominal distension has recurred on one occasion coinciding with an increase in polycythaemia but settled on venesection to a normal haematocrit. The patient remains well, with blood pressure 110/70 mmHg, a serum creatinine of 130 $\mu\text{mol/l}$ and renin of 1.9 ng/ml/hour (normal ambulant 4–6 ng/ml/hour).

Discussion

In view of the very high erythropoietin levels in the absence of clinical or radiological evidence of

hepatoma, arteriovenous shunts, chronic lung disease, cirrhosis with development of ascites or renal lesion, we presume that the origin of this patient's secondary polycythaemia was generalized abnormal peritubular endothelial cell hyperfunction. The renal histological abnormalities were similar to those previously described in polycythaemic nephropathy,⁵ glomerular changes predominating.

A recent case report⁶ of massive bilateral pararenal lymphatic cysts in a patient with renin-dependent hypertension has many similarities with our patient, apart from polycythaemia. In their review the authors confirm the rarity of the condition, most reported cases being attributed to enlargement of multiple simple cysts and treated by resection. In our case no cysts were ever identified on repeated radiology despite the long history of erythropoietin hypersecretion. Moreover, chemical analysis of the fluid secreted in massive amounts in both cases (up to 13 l/24 hours) was consistent with lymph being diverted rather than secreted from a cyst.

A possible mechanism based on functional obstruction to lymphatic circulation is suggested. Lymphatics originate at the vascular pole of the glomerulus, and then travel in the perivascular sheath with the afferent arterioles, then lobular and arcuate arteries towards the hilum. Together they form a single functional entity that drains the cortical peritubular interstitium containing the cells secreting erythropoietin, renin and angiotensins allowing free exchange between the vessels in the sheath and contiguous veins. Although lymphatic dilatation was not seen in biopsies, this does not exclude the possibility of obstruction or excessive flow *in vivo* since these vessels collapse in biopsies unless hilar ligation and immediate freezing are undertaken.⁷ The chronically increased blood viscosity in the renal arterioles exacerbated by pressure differences between the afferent and smaller efferent arterioles may have progressively forced more fluid into the interstitium than the lymphatic system was capable of transporting back to the circulation. The lymph may then have exuded into the perirenal space through the cortical surface. The presence of higher levels of erythropoietin in the secreted lymph compared to serum would favour this mechanism. Also recurrence 4 months after laparotomy, of abdominal distension due to ascites coinciding with a rise of haemoglobin and red cell count which resolved following venesection to a normal haematocrit, supports this pathogenesis. Unfortunately, it does not explain the lack of reported cases of renal lymphocoele complicating polycythaemia which can have a protracted course, even in primary cases.

The nearest analogies to our case occur as complications following renal transplantation;

erythrocytosis and lymphocoeles. The former, in about 10–20% of cases and persisting for about 20 months, originates from increased erythropoietin produced by the ischaemic native kidneys³ in association with elevated renin. It resolves following their atrophy or removal.⁸ The levels of erythropoietin found in our patient were far higher than those found in transplant recipients which average 60 U/l and patients with chronic renal failure treated with recombinant erythropoietin who develop hypertension in association with increased angiotensin-II. In fact a recent low renin level and stable creatinine in our patient suggests suppression of the renin–angiotensin axis due to chronic elevation of erythropoietin. The patient's hypertension initially improved following reduction in whole blood viscosity by venesection and has normalized following drainage of lymphocoeles.

The only reported cases of renal lymphocoele which we could find arise following renal transplantation.⁹ These generally are detected within 6 months of operation but in three reported cases developed 5² and 7^{10,11} years after transplantation.

These authors demonstrated a general leakage of lymph from the kidney surface at laparotomy. Renal histology showed interstitial oedema and dilated lymphatics within the kidney. The postulated mechanism supported by isotope studies using [^{99m}Tc]DPTA¹² was lymphatic obstruction from chronic rejection resulting in decapsulation of the kidney.

Management of 'weeping kidney' has included the techniques of peritoneovenous shunting and intracavitary instillation of iodate povidone.¹³ Extraperitoneal marsupialization or windowing¹⁴ was performed in our case in view of the absence of a diagnosis and successfully resolved the massive collections.

Acknowledgements

We thank Mr R.J. Barnard, consultant urologist and, Professor A.M. Heagarty, University Hospital of South Manchester, for advice and Dr P.M. Cotes, Northwick Park Hospital, for erythropoietin estimations.

References

1. Starzl, T.E., Growth, C.G., Putnam, C.W. *et al.* Urologic complications in 216 human recipients of renal transplants. *Ann Surg* 1970, **172**: 1–22.
2. Koene, R.A., Skotnicki, S.H. & Debruyne, F.M. Spontaneous renal decapsulation with excessive fluid leakage after transplantation. *N Engl J Med* 1979, **300**: 1030–1031.
3. Aeberhard, J.M., Schneider, P.A., Vallotton, M.B., Kurtz, A. & Leski, M. Multiple site estimates of erythropoietin and renin in polycythaemic kidney transplant patients. *Transplantation* 1990, **50**: 613–616.
4. Wikre, C.G., Norman, D.J., Bennison, A., Barry, J.M. & Bennet, W.M. Post transplant erythrocytosis: a review of 53 patients. *Kidney Int* 1983, **23**: 731–737.
5. Weidner, N. & Buckalew, V.M., Jr. Sick cell anemia, sickle cell trait, and polycythaemic states. In: Tisher, C.C. & Brenner, B.M. (eds.) *Renal Pathology*, Vol. II. J.B. Lippincott Co., Philadelphia, 1989, pp. 1417–1436.
6. Schwarz, A., Lenz, T., Klaen, R., Offermann, G., Fiedler, U. & Nussberger, J. Hygroma renale: pararenal lymphatic cysts associated with renin-dependent hypertension (Page kidney). Case report on bilateral cysts and successful therapy by marsupialization. *J Urol* 1993, **150**: 953–957.
7. Kriz, W. A periarterial pathway for intrarenal distribution of renin. *Kidney Int* 1987, **31** (Suppl 20): S51–S56.
8. Friman, S., Nyberg, G. & Blohme, I. Erythrocytosis after renal transplantation: treatment by removal of the native kidneys. *Nephrol Dial Transplant* 1990, **5**: 969–973.
9. Schweizer, R.T., Cho, S., Kountz, S.L. & Belzer, F.O. Lymphocoeles following renal transplantation. *Arch Surg* 1972, **104**: 42–45.
10. DeCamp, M. & Tilney, N.L. Late development of intractable lymphocoele after renal transplantation. *Transplant Proc* 1988, **20**: 105–109.
11. Thompson, T.J. & Neale, T. Acute perirenal lymphocoele formation 8 years after renal transplantation. *Aust N Zealand J Surg* 1989, **59**: 583–585.
12. Fortenberry, E.J., Blue, P.W., van-Nostrand, D. & Anderson, J.H. Lymphocoele; the spectrum of scintigraphic findings in lymphocoeles associated with renal transplant. *J Nucl Med* 1990, **31**: 1627–1631.
13. Burgos, F.J., Teruel, J.L., Mayayo, T., Lovaco, F., Berenguer, A. & Orte, L. Diagnosis and management of lymphocoeles after renal transplantation. *Br J Urol* 1988, **61**: 289–293.
14. Buckingham, J.M., Roses, J. & Zincke, H. Internal marsupialisation of lymphocoeles after renal transplantation. *Urology* 1976, **7**: 406–407.