RENAL VEIN THROMBOSIS AND THE NEPHROTIC SYNDROME

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SUMMARY

A 31 year old Chinese man developed the nephrotic syndrome, and was found to have some of the clinical features of renal vein thrombosis such as a rapid deterioration in renal function and great variability in proteinuria. Radiological studies confirmed the diagnosis of bilateral renal vein thrombosis. The clinical features and pathogenesis of renal vein thrombosis are discussed.

INTRODUCTION

Renal vein thrombosis (RVT) was first described by Rayer on the basis of autopsy findings in seven patients [1] and prior to 1956, the diagnosis of this disorder was made at postmortem. [2] With the development of newer radiological techniques, the antemortem recognition of RVT was made possible and subsequently more information became available on this entity.

Clinical findings of RVT includes the nephrotic syndrome (NS), great variability in proteinuria and glomerular filtration rate, pulmonary embolization, sterile pyuria, haematuria, hyperchloremic acidosis, decreased renal tubular threshold for glucose and increased fibrin degradation products. [3] However the experience of Llach *et al.* indicate that RVT usually occurs without overt clinical signs or symptoms [4] but can be detected by selective renal venography.

We describe a case of NS with some clinical features of RVT which was subsequently confirmed by selective renal venography.

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CASE REPORT

A 31 year old Chinese male presented with retrosternal chest pain of 1½ years duration. During the preceding one month he had epigastric pain which was relieved by antacids. He also complained of anorexia, weight loss and nocturia of one month's duration. Two days before admission, he developed dyspnoea on exertion, orthopnoea and paroxysmal nocturnal dyspnoea. He had no previous history of renal disease, diabetes, heart disease, rheumatic fever, rash, arthralgias, insect bites and was not on any medication.

Physical examination revealed pallor with a sallow complexion, anasarca and dyspnoea. His blood pressure was 185/125 mm of Hg. He had bilateral basal crepitations.

Laboratory studies revealed a Haemoglobin of 5.5 g/dl, urea of 18.4 mmol/l, creatine of 332 umol/l, bicarbonate of 18 mmol/l, uric acid of 957 umol/l, albumin of 18 g/l, globulin of 29 g/l, VDRL was non reactive, Hbs Ag was not detected, ANF was positive 1 in 5 dilution, rheumatoid factor was negative and serum lipids were normal. 24 hour urine for proteins on three different occasions were 14.6 g, 18.0 g and 8.0 g. Whilst in the ward, over a period of few weeks his blood urea rose to 40.8 mmol/1 and his creatinine to 516 umol/l.

Plain abdominal radiography revealed bilaterally enlarged kidneys. Intravenous

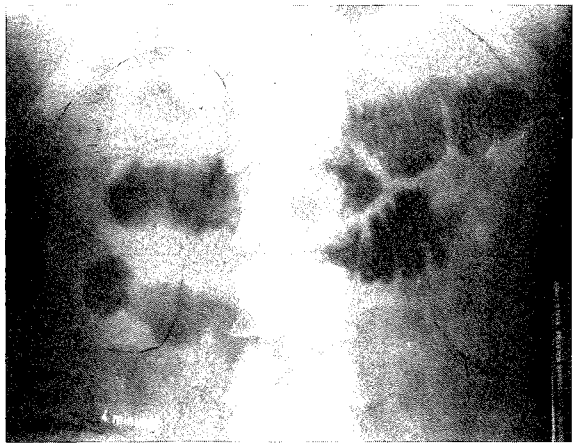

Fig. 1 IVU showing a faint nephrogram with bilaterally enlarged kidneys.

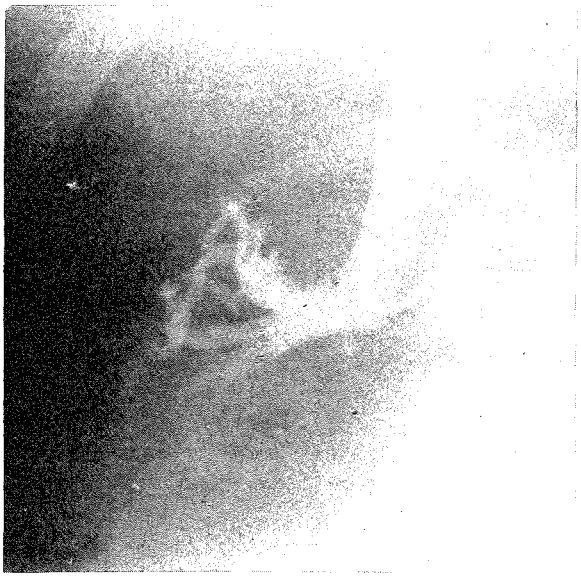

Fig. 2 Selective right renal venogram showing normal upper pole veins and thrombosis of the lower pole veins.

urography (Fig. 1) disclosed a faint bilateral nephrogram throughout the period of examination. The kidneys were enlarged and smooth in outline, the right kidney measuring 14.5 cm and the left kidney measuring 15.0 cm.

The inferior venacavogram appeared normal. Retrograde filling of both proximal renal veins was noted during the valsalva phase.

Selective renal venogram showed normal right upper pole renal veins and thrombosis of the lower pole veins (Fig. 2). There is no filling of the tributaries of the renal vein on the left side (Fig. 3).

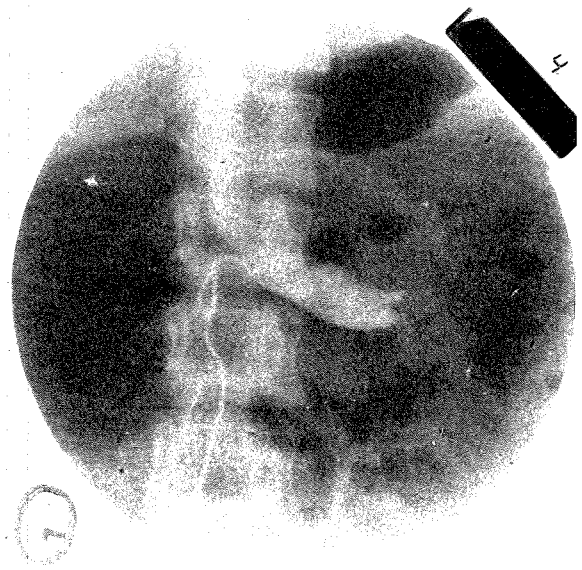

Fig. 3 Selective left renal venogram showing absence of filling of tributaries.

The testicular veins are also not seen on the left. The findings were suggestive of left renal vein thrombosis and right lower renal vein thrombosis.

Renal biopsy samples were examined with light microscopy and immunofluorescence. They showed a crescentic nephritis with an underlying membranous glomerulonephritis (Fig. 4). Silver stains showed typical 'spikes' (Fig. 5) and immunoflourescence showed IgG, IgA, and C3 deposits along the capillary walls. There was associated marked tubular atrophy with a lymphocytic-histiocytic infiltrate and interstitial fibrosis.

DISCUSSION

Although proteinuria varies from day to day in most patients with renal disease, in RVT this variation tends to be very marked. This variability in proteinuria and in creatinine clearance is probably due to varying degrees of venous obstruction which occurs as a result of alternate recanalization and recurrent thrombus formation in the renal vein. [3] Formation of collateral channels and their subsequent thrombosis is a second possible cause of variable proteinuria and glomerular filtration rates. A third possible cause is the occurrence of pulmonary embolization.

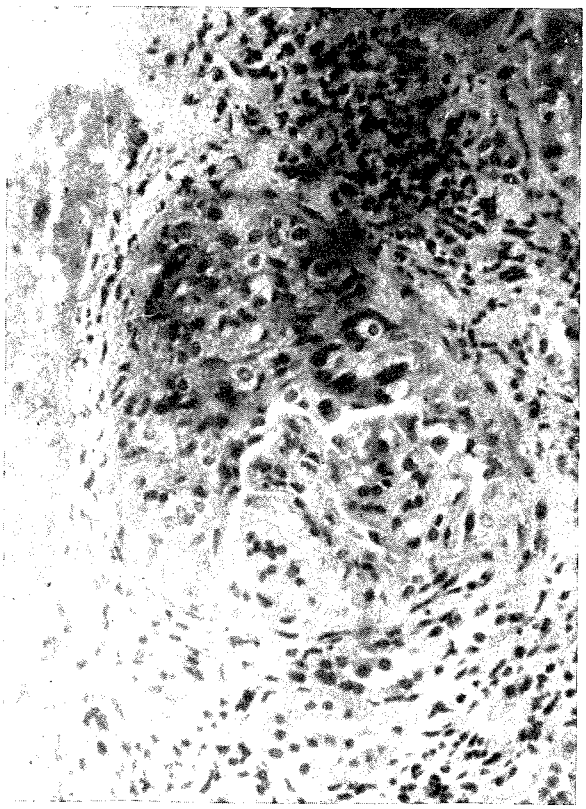

Fig. 4 Glomerulus showing thickened, eosinophilic capillary walls with a large crescent. There is surrounding tubular atrophy with a lymphocytic - histiocytic infiltrate (H & E x 800).

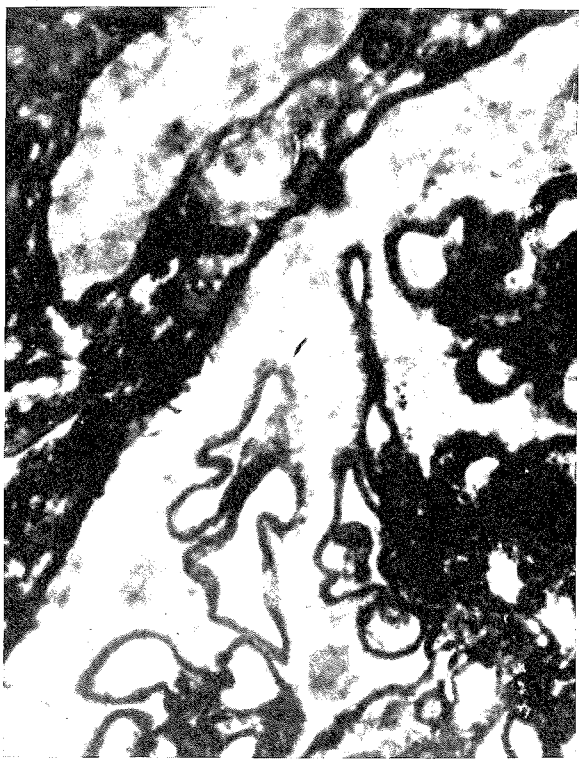

Fig. 5 Part of the glomerula tuft showing typical 'spikes' (Jones' methenamine silver x3200).

The occurrence of pulmonary embolism in a patient with NS is a strong indication of the presence of RVT.

Sterile pyuria is a finding in RVT. The occurrence of "marginated" granulocytes in the glomerulus gives added importance to this finding.

Renal tubular functional abnormalities such as glycosuria and hyperchloremic acidosis have been noted to occur in RVT. [3] This proximal tubular defect may be due to increased venous pressure, damage caused by fibrin or its breakdown products or interference of metabolism of proximal tubular cells by interstitial oedema and fibrosis.

Fibrin degradation products have also been found to be increased both in peripheral and in renal venous blood in RVT.

Other clinical features include flank pain and haematuria.

In intravenous urography, the kidney will appear large, with masses of oedematous renal parenchyma distorting the calyces and causing stretching and narrowing of the infandibula. This appearance is frequently confused with polycystic kidney disease. Compression of the renal pelvis with filling defects (blood clots) may also be seen. Ureteral notching due to dilated collateral veins may be present.

Inferior venocavography may demonstrate filling defects opposite the renal vein and lack of "streaming" of unopacified blood from the renal vein. [5] Selective renal venography may be performed if no filling defects are demonstrated on the inferior venacavogram and may reveal slow washout.

Chest radiographs and pulmonary scans may show evidence of thromboembolism which may be present in up to 75 percent of cases. [5]

Renal pathology commonly demonstrated margination of leukocytes in the glomerular capillaries and interstitial oedema in primary RVT.

In our patient, the only clinical features of RVT was the variability of proteinuria. Whilst the rapid

deterioration in renal function that occurred in this patient could be due to RVT, it could also have been due to his rapidly progressive glomerulonephritis.

Various studies demonstrate a high incidence of RVT in patients with the NS due to membranous glomerulonephritis (MGN) or membranoproliferative glomerulonephritis (MPGN). In a study of 98 patients with NS by Llach *et al.* the incidence of RVT in patients with NS due to MGN or MPGN was 41 percent. [4] Other studies quote figures that range between 33 and 50 percent. RVT has also been reported in the NS due to lupus nephritis and diabetic nephropathy but this is rare.Controversy exists on whether RVT is a cause or a consequence of the NS. The balance of evidence according to Llach *et al.* [4] now suggests that RVT is usually an effect and not a cause of NS. Four main reasons are advanced for these views. Firstly many patients with RVT and/or thrombosis of the inferior vena cava above the renal veins do not have NS. Secondly patients with NS without RVT as evidenced by normal renal venography on follow up subsequently developed RVT documented by a second renal venography performed 1 - 3 years after the initial study. Thirdly there is evidence for the presence of a hypercoagulable state in patients with NS. This increased tendency for hypercoagulation is probably a major factor in the causation of RVT and in the increased incidence of thromboembolic episodes in patients with NS. Fourthly as mentioned earlier RVT occurs more frequently in patients with NS due to MGN or MPGN, suggesting that the disease process underlying the NS may play a paramount role in the genesis of RVT.

The prognosis of untreated RVT is poor, with mortality rates as high as 60 percent largely attributable to thromboembolic phenomena than to renal failure. Early diagnosis, is hence imperative. In patients with the NS, strong consideration should be given to inferior venacavography when any of the following factors are present : history of flank trauma, rapid deterioration of renal function, malignancy, sickle cell anaemia, suggestive features on the intravenous urogram, leukocyte margination on biopsy specimens and venous thromboembolism.

Therapy of RVT is anticoagulation. The duration of therapy is difficult to determine and it has been suggested that a case can be made for indefinite anticoagulation. [6] There is no convincing evidence that thrombectomy is any better than anticoagulant treatment alone. [6] The value of steroid treatment for the NS associated with RVT is not established. Anticoagulants remain the mainstay of therapy, reducing the incidence of thromboembolic events and possibly preventing the aggravation of any renal insufficiency that might otherwise have resulted from RVT.

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