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NEPHROTIC SYNDROME DUE TO THROMBOSIS OF THE INFERIOR VENA CAVA AND RENAL VEINS

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FIFTY years ago, Rowntree, Fitz and Gerachty (1913) described the proteinuria which occurred in animals following obstruction of the inferior vena cava proximal to the renal veins or of the renal veins themselves. In the same year Shattock (1913) recorded the case of Dr. Rivers Pollock, the obstetric physician to the Westminster Hospital, who sustained a traumatic thrombosis of the inferior vena cava and thereafter had gross albuminuria which persisted until his death 25 years later from streptococcal septicæmia. It was not until 1939 that the first full description of the nephrotic syndrome associated with thrombosis of the renal veins and inferior vena cava appeared (Derow, Schlesinger and Savitz, 1939). Since then other cases have been recorded (Blainey, Hardwicke and Whitfield, 1954; Harrison, Milne and Steiner, 1956; Pollak, Kark, Pirani, Shafter and Meuhrcke, 1956; Hasson, Berkman, Parker and Rifkin, 1957; Blainey, Brewer, Hardwick and Scothill, 1960). This communication describes a further patient observed closely from onset to death from uræmia eight years later and in whom there were many features of particular interest.

Case Report

In April 1955 a previously fit male aged 27 years used a breast drill from the right groin for some hours and the following day he experienced a severe aching pain in this region. Twenty four hours later

the whole of the right leg became swollen and he was admitted to the Royal Salop Infirmary where he was given ten days heparin therapy under which the pain and swelling subsided. Two weeks later œdema of the right leg recurred and he was given anticoagulant therapy with phenindione for seven weeks after which he returned to work and wore an elastic stocking. In December 1955 the left leg became œdematous and he was re-admitted to the Royal Salop Infirmary. Massive albuminuria was found, phenindione therapy was recommenced and on 17th March, 1956 he was transferred to the Queen Elizabeth Hospital, Birmingham. At this time collateral venous channels were evident on the trunk (Fig. 1) and both legs and the lumbo-sacral region of the back were grossly œdematous. The blood pressure was 135/80 mm. Hg. The urinary protein loss fluctuated between 9 and 15 g. daily and the deposit showed 1143 x 10⁶ red blood cells, 15 x 10⁶ white blood cells, 0.2 x 10⁶ hyaline casts and 0.1 x 10⁶ granular casts in twenty-four hours (Fig. 2). The blood urea was 35 mg./100 ml. and the creatinine clearance 119 ml./min. The serum cholesterol was 370 mg./100 ml. and the serum protein 5.3 g./100 ml. of which the albumin was 2.20 g./100 ml. The serum complement fluctuated between 0.8 and 1.0 units/ml. The chest radiograph showed a normal cardiac silhouette and clear lung fields. An intravenous pyelogram revealed no abnormality apart from rather dense renal shadows.

Renal biopsy showed no normal glomeruli. In all there was some degree of hyalinisation patchily distributed within the glomeruli. Glomerular adhesions and periglomerular fibrosis were present in some glomeruli. The tubules were mainly normal.

FIG. 1.—Venous collaterals on the trunk. March 1956.

but there was a slight diffuse increase in interstitial fibrous tissue (Fig. 3); these lesions were classified as “membranous glomerulonephritis”, the glomerular lesion typically associated with renal vein thrombosis (Blainey, Brewer, Hardwicke and Soothill, 1960). Phenindione therapy was continued, cortisone was given in a dose of 100 mg. daily and the patient took a high protein, low salt diet.

Over the course of the next year there was no alteration in the venous collaterals and no diminution in the urinary protein loss and steroid and anti-coagulant therapy were therefore discontinued.

High protein feeding had, however, produced a considerable rise in the serum albumin level (Fig. 2) and oedema was then only minimal and localised to the legs; this was presumed to be due to the inferior vena caval obstruction. The red cell content of the urine diminished progressively to a level of 6×10^6 in twenty four hours in September 1957 by which time, however, a significant fall in creatinine clearance was evident (Fig. 2) and the blood pressure had begun to rise (160/105). Immunochemical protein clearances (Table 1) showed poorly selective proteinuria. During the next five years the patient remained subjectively well and at work but the urinary protein loss continued unabated though the high protein intake produced a progressive rise in the serum albumin level to 3.59 g./100 ml. in September 1959. At this time the creatinine clearance had fallen to 33 ml./min. and the blood urea had risen to 80 mg./100 ml. A rise in the white cell content of the urine to 310×10^6 in twenty-four hours suggested

the possibility of a superimposed pyelonephritic element and over the next eighteen months sulphamethoxypyridazine, tetracycline and sulphamethazine were successively prescribed. This therapy reduced the white cell content of the urine to 10×10^6 in twenty-four hours and appeared to prevent for a time any further rise in the blood urea or blood pressure or fall in the creatinine clearance. In February 1961 an intravenous pyelogram showed kidneys still of normal size and very faint excretory shadows. The urinary protein loss increased to 15-20 g. daily and by August 1962 the blood urea had risen to 140 mg./100 ml., the creatinine clearance had fallen to 11 ml./min., the serum calcium was 8.9 mg./100 ml., the serum phosphorus 7.6 mg./100 ml., the standard bicarbonate 13.8 m. Eq./L and the haemoglobin 57%. During the remaining four months of the patient's life he was given 10 mg. prednisone daily, repeated blood transfusions and a low protein diet. Oral sodium bicarbonate maintained a normal blood pH and standard bicarbonate. Increasing hypertension (to 230/130 mm. Hg.) produced left ventricular hypertrophy, electrocardiographic left ventricular dominance and left ventricular failure and though the blood pressure was controlled with mecamylamine and he was kept fully digitalised. Increasing oedema developed, the blood urea rose (to 372 mg./100 ml.), phosphate retention increased and he died a uræmic death with terminal pericarditis on 28th January, 1963.

Necropsy. At autopsy the kidneys were found to be small and pale and weighed 210 g. The cortex

FIG. 2.—Serum albumin, proteinuria, urine cell count, creatinine clearance and therapy from March 1956 till death in January 1963.

FIG. 3.—Renal biopsy. March 1956.

FIG. 4.—Postmortem appearance of kidney. Thin cortex and poor corticomedullary demarcation.

TABLE 1
IMMUNOCHEMICAL PROTEIN CLEARANCES

	Urine/Plasma Protein Ratio		Serum Concentration (% of Normal)		Clearance Albumin Clearance %		Clearance Siderophilin Clearance %	
	2.10.58	21.8.62	2.10.58	21.8.62	2.10.58	21.8.62	2.10.58	21.8.62
Albumin	1/8	5/16	50	87	100	125		
Siderophilin	1/8	1/4	200	100	100	100		
γ-Globulin	1/16	1/32	100	50	50	87		
Coeruloplasmin	1/8	—	100	—	100	—		
Complement (C ₃)	1/16	1/8	—	87	50	50		
α ₂ -Glycoprotein	1/64	1/128	—	100	12	3		
β-Lipoprotein	0	1/256	150	100	0	1.5		

Albumin Clearance (2.10.58) = 0.225 ml./min.

Siderophilin Clearance (21.8.62)=0.45 ml./min.

FIG. 5.—Postmortem appearances of kidney and inferior vena cava. Kidney surface scarred and pitted. Venous bands and webs in inferior vena cava and right renal vein.

was thin and corticomedullary demarcation poor (Fig. 4). Though the capsule stripped easily, the renal surface was scarred and pitted (Fig. 5). The inferior vena cava contained no recent antemortem thrombi but numerous venous bands and webs formed by organisation and recanalisation of old thrombi were found from a point just above the renal veins to the lowest point in the femoral veins examined in the thigh (Fig. 5). The number of bands was greater the lower the position of the veins and they were most severe and numerous in the veins of the thigh. Venous bands were also present in the right renal vein but the left renal vein appeared completely clear of organised thrombus. The heart showed fibrinous pericarditis, left ventricular hypertrophy and small friable vegetations, 5 mm. in diameter on the anterior and posterior cusps of the mitral valve. The lungs showed congestion, oedema and early bronchopneumonia. The only other abnormalities were small gastric mucosal hæmor-

rhages, cholesterosis of the gall bladder and hypoplastic adrenal glands.

Histology showed, in the kidneys, patchy thickening of the basement membrane, gross in many of the affected glomeruli. Much periglomerular fibroelastosis was evident in many instances obliterating Bowman's capsule. There was widespread shrinkage, fibrosis and hyalinisation of glomeruli with secondary loss of tubules. Considerable accumulations of lymphocytes and some interstitial fibrosis were present and renal arteries showed medial hypertrophy and intimal fibroelastosis (Fig. 6).

Histology of the venous bands in the inferior vena cava and femoral veins showed them to consist of dense fibroelastic tissue indicating that recanalisation was completed a long time ago.

Discussion

There seems no doubt that the patient sustained

FIG. 6.—Histological appearances of kidney at post-mortem.

a traumatic thrombosis of the right femoral vein which spread to involve the inferior vena cava and the renal veins producing a nephrotic syndrome. The histological appearances of the renal biopsy one year after the initial injury showed that gross renal changes had by then developed. The autopsy demonstrated that the inferior vena cava and renal veins had recanalised either naturally or as a result of anticoagulant therapy and the histology of the venous bands suggested that this occurred a long time before death. The clinical course and the postmortem findings indicated that despite this restoration of venous outflow from the kidneys the renal glomerular

lesions had progressed and that renal function became further impaired by pyelonephritis and ischaemic changes secondary to hypertension.

The only therapeutic measures which appeared to have any beneficial effect were the high protein feeding which despite heavy proteinuria restored the serum albumin to levels sufficient to prevent hypoproteinaemic oedema, and sulphonamides and antibiotics which controlled secondary pyelonephritis. As in other patients with nephrotic syndrome associated with renal vein thrombosis which we have treated, steroid therapy failed to diminish urinary protein loss. To what extent anticoagulants were responsible for the recanalisation of the inferior vena cava and the renal veins it is impossible to say but they certainly did not halt the inexorable march of renal destruction.

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HISTIOCYTOSIS X

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THE SUGGESTION that eosinophilic granuloma, Schüller-Christian's disease and Letterer-Siwe's disease are but various expressions of the same illness was advanced by Farber (1941), Green and Farber (1942) and Jaffe and Lichtenstein (1944). The disease entity was called "Histiocytosis X" by Lichtenstein (1953). This integration of the three diseases has not, however, been accepted by everyone (McGavran and Spady, 1960).

The following case is reported because it gives further evidence in support of this unifying concept. Some additional information about this rare condition is also presented.

Case Report

T.Y., a female infant aged 15 months, was admitted to a London hospital on December 20, 1963. She had been in good health until seven weeks before her