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THE ASSOCIATION OF NEPHROTIC SYNDROME AND RENAL VEIN THROMBOSIS: A CLINICOPATHOLOGICAL ANALYSIS OF EIGHT PEDIATRIC PATIENTS*

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Renal vein thrombosis (RVT) occurs in two forms in childhood: one, the most common life-threatening condition seen in infancy which often presents as acute renal failure usually causing hemorrhagic infarctions of the kidney, and the other, seen in association with the nephrotic syndrome (NS) mainly in older children and rarely in congenital NS cases that are not necessarily associated with infarction of the kidney[1,2]. There has been continual controversy regarding the etiology of the relationship of the nephrotic state to renal venous thrombosis that is, as to whether RVT is a cause or complication of it[3-5].

The incidence of the association of RVT in adult nephrotics is higher in membranous glomerulonephritis (MGN) or membranoproliferative glomerulonephritis (MPGN), ranging from 38 to 50 percent, and is lower in lipoid nephrosis (minimal lesion disease), focal glomerulosclerosis, rapidly progressive glomerulonephritis, amyloidosis, and lupus nephritis[3-7]. The overall incidence of thromboembolism (excluding RVT) is approximately 20 percent in adults and includes the pulmonary embolism, the most common severe type which accounts for eight percent of the cases[6].

When compared to adults, the occurrence of RVT in nephrotic children is rare. The present study evaluates eight pediatric nephrotic cases associated with tissue-diagnosed renal venous thrombosis. Clinical and laboratory findings suggestive of RVT in nephrotic patients are emphasized, and in addition, the association of various types of glomerulonephritis in nephrotic children with RVT and the pathogenesis of this association is discussed.

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Material and Methods

Cases with a pathological diagnosis of RVT associated with NS were studied retrospectively for clinicopathological evaluation. There was a total 23 RVT cases in two thousand complete and/or partial consecutive pediatric necropsies including two cases of unilateral surgical nephrectomies, eight of which were nephrotic patients. All of the material had been investigated at Hacettepe University Children's Hospital over a nineteen-year period, from 1966 to 1985.

The renal tissues were fixed both in formalin and Dubosque Brasil solution. The sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS), trichrome and Jone's silver reagent. Phosphotungstic acid hematoxylin (PTAH) stain for fibrin was applied when indicated. Gross and microscopical findings of some of the cases are shown in Figs. 1-7. Clinical and pathological findings of the eight cases are briefly summarized as follows.

Cases Reports

Case 1

A four-day-old female baby was admitted to the hospital because of generalized body swelling since birth. She was the product of a 24-year-old, gravida-4 mother, following a spontaneous vaginal delivery. The placenta was enlarged and had a foul odor. A past history revealed a first-degree consanguineous marriage, and two siblings who had died with generalized edema before the age of two months.

Some of the pertinent clinical and laboratory findings revealed a weight of 3000 g; blood pressure of 85/50 mmHg; the liver three cm and the spleen one cm palpable below the costal margin. Bilateral pretibial pitting edema was present. Urinalysis showed (+++) proteinuria and microscopic hematuria. The hemoglobin level was 19.9 g/dl and white blood cell count 9400/mm^3; blood biochemistry revealed total protein 4.3 g/dl, albumin 2 g/dl, total lipids 1500 mg/dl, cholesterol 370 mg/dl, calcium 6 mg/dl; Na^+ 165 mEq/lt, K^+ 5 mEq/lt, Cl^- 114 mEq/lt and BUN 20 mg/dl. IVP was within normal limits except for double ureters and double renal pelvises.

During the clinical course twitching of the upper extremities developed. On the tenth day of admission bronchopneumonia, and on the twenty-sixth day, diarrhea and sepsis developed. In spite of the administration of appropriate antibiotics and fresh plasma, the baby died on the forty-fifth day of admission.

Case 2

A 21-day-old female baby was admitted to the hospital with complaints of diarrhea, failure-to-thrive, and body swelling since birth. The baby's and the family's past histories were unremarkable including pregnancies and deliveries.

There was no parental consanguinity. The pertinent clinical and laboratory findings revealed a weight of 3400 g, blood pressure of 80/60 mmHg, and generalized edema with marked ascites. Urinalysis revealed (+++) proteinuria and hematuria. The hemoglobin level was 7.8 g/dl, white blood cell count 12,800/mm^3, peripheral blood smear showed 58% neutrophils with toxic granulation and the disappearance of platelets once during the clinical course; blood biochemistry revealed total protein 3.2 g/dl, albumin 1.6 g/dl, total lipids 21800 mg/dl, cholesterol 1355 mg/dl, creatinine 8 gm/dl, BUN 16 mg/dl, VDRL and dye-test both were negative, and IVP was within normal limits.

During the clinical course in addition to nephrotic state, sepsis complicated by disseminated intravascular coagulation (DIC) had developed. The patient was administered human albumin, antibiotics and dexamethasone. She expired on the eighteenth day of admission, at the age of 39 days.

Case 3

A three-month-old male baby was admitted to the hospital with complaints of fever and cough. He was born after an unremarkable pregnancy and there was neither a history of parental consanguinity nor familial disease. He had a healthy one-and-a-half year-old sister.

Physical examination revealed a weight of 4000 g and blood pressure of 90/70 mmHg. He was unconscious, dehydrated, febrile and had tachycardia and tachypnea. There were prominent intercostal retractions and crepitant rales. Only the liver was palpable 1.5 cm below the costal margin. Some of the pathological findings were trace proteinuria and microscopic hematuria; hemoglobin level of 11.79 g/dl decreasing to 8.30 g/dl in two days during which time the white blood cells rose from 8600/mm^3 to 15,600/mm^3, blood biochemistry revealed BUN 82 mg/dl, CO_2 content 8.25 mEq/lt, Na^+ 150 mEq/lt, K^+ 3.8-8.8 mEq/lt, and Cl^- 116-102 mEq/lt.

During the clinical course septicemia associated with bronchopneumonia, gastroenteritis and dehydration developed. Parenteral fluid, intravenous antibiotics and a transfusion of fresh blood were administered. The patient expired on the fourth day of admission.

Case 4

A two-and-a-half-year-old boy was admitted to the hospital with generalized edema and fever of one month's duration. Physical examination revealed a height of 82 cm and weight 13.5 kg. He had edema of the eyelids and lower extremities. Urinalysis showed (+++) proteinuria and microscopic hematuria along with clusters of neutrophils. The hemoglobin level was 13.26 g/dl and white blood cell count 11,600/mm^3; blood biochemistry revealed BUN 12 mg/dl, serum total protein

4.1 g/dl, albumin 2.5 g/dl, total lipids 1480 mg/dl, cholesterol 560 mg/dl. IVP was within normal limits. While in the hospital in addition to the nephrotic syndrome tonsillitis, bronchopneumonia and urinary tract infection were diagnosed for which diuretics and appropriate antibiotic therapy were administered. A renal biopsy was performed and the diagnosis was that of membranoproliferative glomerulonephritis for which prednisolone 2 mg/kg/day and cyclophosphamide 5 mg/kg/day were started. On the twenty-first day of admission abdominal pain, vomiting, diarrhea, hypotension, dyspnea, and 5 cm hepatomegaly developed which resulted in his death on the thirty-eighth day of admission.

A stool culture taken prior to his death, and a postmortem blood culture taken after his death yielded *Salmonella paratyphi-B.*

Case 5

A 10-year-old-girl was admitted to the hospital with edema, abdominal distention and frequent but diminished urination for the last 15 days. Physical examination revealed a weight of 34 kg, blood pressure of 130/90 mmHg, marked pitting edema of the lower extremities, ascites and hydrothorax.

The relevant laboratory findings were microscopic hematuria; a daily urinary loss of protein of 1.2 g/m^2; hemoglobin level of 15 g/dl; white blood cell count 5800/mm^3. Blood biochemistry showed BUN 15 mg/dl; creatinine 0.6 mg/dl, total protein 4.4 g/dl, albumin 1.6 g/dl, total lipids 2300 mg/dl, cholesterol 640 mg/dl, Na^+ 115 mEq/lt, K^+ 4 mEq/lt, Cl^- 95 mEq/lt, and IVP was normal except for duplication of the collecting system of the right side.

Prednisolone in a dose of 2 mg/kg/day along with diuretics and salt-free human albumin infusion were given. No clinical response was observed and the patient died on the thirty-eighth day of admission.

Case 6

An 11-year-old girl was admitted to the hospital with edema of the eyelids of 18-months' duration along with generalized edema for two months. There was marked swelling of the right leg for one week and anuria for two days. Physical examination revealed a blood pressure of 100/60 mmHg and pitting edema of the lower extremities.

Laboratory investigations revealed (+++) proteinuria, the presence of pyuria and bacteriuria; hemoglobin level of 8.55 g/dl, and white blood cell count 12.000/mm^3. Blood chemistry showed Na^+ 125 mEq/lt, K^+ 2-9 mEq/lt, Cl^- 106 mEq/lt, CO_2 content 9.32 mEq/lt; BUN 53 mg/dl, creatinine 6.5 mg/dl, total lipids 530 mg/dl, cholesterol 112 mg/dl, calcium 7.2 mg/dl, phosphate 7 mg/dl, creatinine clearance 0.8 ml/min/1.73 m^3. Urine culture grew 10^5 *coloni E. coli.* Plane X-ray examination of the abdomen showed enlarged kidneys. During the clinical course, inspite of

appropriate fluid, plasma, and electrolyte therapy, diuresis did not occur so that peritoneal dialysis was performed.

Due to hypotension, and hematochezia, salt-free human albumin was given. No clinical response was observed, and the patient expired on the sixteenth day of admission.

Case 7

A 13-year-old girl had a nine-year history of back pain, swelling of the lower extremities which began six months ago, diarrhea, vomiting and tachypnea of one month's duration for which she was hospitalized. Her mother and father were first cousins, and two of their four previous children had died; one at age five months and the other at age one. The other two remaining children were healthy as were the parents.

Clinical and laboratory findings revealed a blood pressure of 90/40 mmHg and pulse rate of 110/min. The patient's general condition was poor; she was dehydrated and had flank pain. Urinalysis showed (+++) proteinuria, pyuria and leukocyte casts. The daily urinary protein loss was 4-5 g/m^2; blood biochemistry showed Na^+ 126 mEq/lt, K^+ 2-3 mEq/lt; Cl^- 110 mEq/lt, CO_2 content 9 mEq/lt, BUN 100 mg/dl, creatinine 7.1 mg/dl, total protein 3.5 g/dl, albumin 1.2 g/dl, total lipids 920 mg/dl, cholesterol 213 mg/dl, uric acid 10.6 mg/dl, calcium 8.2 mg/dl, phosphate 6.7 mg/dl, and creatinine clearance 2.4 ml/min/1.73 m^2. The chest X-ray was normal; but abdominal ultrasonography revealed bilaterally enlarged kidneys.

During the clinical course the general condition of the patient was poor. Appropriate fluid and electrolyte therapy was administered. She was given a blood transfusion because hematemesis and melena had developed. Peritoneal dialysis was performed because of uremic pericarditis. Her general condition worsened and she died on the tenth day of admission.

Case 8

A 10-year-old girl presented with swelling and pain in her joints of a three-year duration along with generalized edema of six months and anuria lasting for four days for which she was hospitalized. Peritoneal dialysis was performed because of chronic renal failure for the last two months. Physical examination revealed a blood pressure of 90/75 mmHg and a pulse rate of 80/min. She had generalized edema. The patient's general condition was very poor. Laboratory findings revealed a hemoglobin level of 3.48 g/dl, white blood cell count 11,000/mm^3; blood biochemistry showed Na^+ 137 mEq/lt, K^+ 5.5 mEq/lt, Cl^- 95 mEq/lt, CO_2 content 11.7 mEq/lt, BUN 120 mg/dl, creatinine 3.8 mg/dl, calcium 5.5 mg/dl, phosphate 13.6 mg/dl, total protein 5.2 g/dl, and albumin 2.6 g/dl. No urine sample could be obtained.

Immediately following admission peritoneal dialysis was performed because of a high BUN level and hematemesis. A blood transfusion, appropriate fluid and electrolyte therapy and antibiotics were administered. The patient died on the fourth day of admission.

Results

In our pathological material consisting of 2000 consecutive pediatric necropsies approximately 1 percent were RVT cases while 0.4 percent were nephrotic patients associated with RVT. In other words, 34 percent of all RVT cases were nephrotic.

The glomerulopathies of these RVT plus NS patients consisted of three cases of Finnish-type congenital NS (FCNS), three cases of renal amyloidosis, and two cases of MPGN. In all the nephrotic patients, a diagnosis of RVT was not made prior to postmortem examination. Four cases in our RVT plus NS series (Case Nos. 1, 2, 3 and 5) showed no distinctive clinical features when compared to the RVT cases without NS (Tables I and II). In Case No. 4, the rapid deterioration of the clinical course could have been related to either complicated salmonellosis or RVT. The common findings during the clinical course of the three renal amyloidosis cases (Case Nos. 6, 7 and 8) were that of rapid deterioration of renal function with the presence of anuria, azotemia and acidosis, and the development of hypotension. Additionally, one of these three cases (Case No. 7) revealed flank pain (Table III).

Discussion

The association of the nephrotic syndrome and renal vein thrombosis was first recognized in 1840[8]. Before 1956, most cases were diagnosed at postmortem examination. Since then, with the development and application of more advanced radiographic techniques and selective catheterization, intravitam diagnosis of more cases of RVT has been made[7].

The significance of RVT in NS has been a subject of controversy for many years. It was thought that RVT was a cause of NS in 17.7 percent of adult patients[9]. Recent evidence, however, shows that RVT is a complication of NS rather than its cause.

In a prospective study of patients with NS who underwent venography, the incidence of renal vein thrombosis was reported to be 30 percent[1].

There have been many studies showing the hypercoagulable state in nephrotic patients[6,10-12]. It has been shown that patients with NS have an increase in the platelet count and platelet aggregation, fibrinogen, and factors,V, VII, IX and X[2,5,6,11]. Some evidence suggests that fibrinolytic activity is impaired in these

TABLE I: Some of the Clinical and Pathological Findings of Three Cases of Congenital NS Associated with RVT

Case No.	Age Sex	Clinical diagnosis	Type of pathological study	Final pathological diagnosis	Location of thrombus: Main renal artery	Location of thrombus: Other	Infarct	Extrarenal thrombus
1	45 days F	Congenital NS Septicemia	Necropsy	– Finnish-type congenital NS (FCNS) – Septicemia – DIC – RVT – Double renal pelvis and ureter	–	Interlobar vein	Microscopic	– Pulmonary vein
2	39 days F	Congenital NS Septicemia	Necropsy	– FCNS – Septicemia – DIC – CMV – RVT (UL) (gross)	–	Interlobar Interlobular and arcuate veins	Microscopic	– Inferior vena cava (gross) – Portal vein (gross) – Pulmonary vein (gross, mic) – Intrahepatic vein (mic) – Adrenal vein
3	3 months M	Septicemia	Necropsy	– FCNS – Septicemia – RVT (gross) (UL)	+	–	Microscopic	– absent

DIC : Disseminated intravascular coagulation
RVT : Renal venous thrombosis
FCNS : Finnish-type congenital nephrotic syndrome
mic Microscopic
CMV cytomegalovirus infection

TABLE II: Some of the Clinical and Pathological Findings of Two Cases of MPGN Associated with RVT

Case No.	Age Sex	Clinical diagnosis	Type of pathological study	Final pathological diagnosis	Location of thrombus: Main renal artery	Location of thrombus: Other	Infarct	Extrarenal thrombus
4	2.5 years M	– NS – Bronchopneumonia Urinary tract infection	– Necropsy	– MPGN – Septicemia – RVT (mic)	–	– Interlobular veins	–	lung heart spleen
5	10 years F	– NS – MPGN – % Amyloidosis	Necropsy (partial)	– MPGN – RVT (gross) (UL)	–	– Arcuate and interlobar veins	–	not investigated

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MPGN : membranoproli ferative glomerulonephritis
RVT : Renal venous thrombosis
NS : Nephrotic syndrome
UL : Unilateral
mic : Microscopic

TABLE III: Some of the Clinical and Pathological Findings of Three Cases of Amyloidosis Associated with RVT

Case No.	Age Sex	Clinical diagnosis	Type of pathological study	Final pathological diagnosis	Location of thrombus: Main renal artery	Location of thrombus: Other	Infarct
4	11 years F	– NS – Amyloidosis – Acute renal failure	Needle Necropsy Maternal	– Renal amyloidosis – RVT (mic)	–	– Interlobular vein	Microscopic
7	13 years F	– NS – Amyloidosis – Gastroenteritis – Acute renal failure – flank pain	Necropsy (partial)	– Renal amyloidosis – RVT – Amyloidosis in liver	+	– Interlobar and arcuate veins (gross)	none
8	10 years F	– Amyloidosis – Chronic renal failure – Chronic pyelonephritis	Postmortem Nephrectomy	– Renal Amyloidosis – RVT (mic) – Renal scarring (gross and mic) (pyelonephritic type)	–	– Interlobular and arcuate veins (gross)	none

RVT Renal venous thrombosis
NS Nephrotic syndrome
mic Microscopic

patients; inhibitors of fibrinolysis and impaired production of plasminogen activator have been observed[11]. Activated clotting factors are inhibited by naturally occurring coagulation inhibitors. Antithrombin III (AT III) is the most important of these coagulation inhibitors. It has been demonstrated that the serum AT III level in nephrotic patients is decreased and that there is a significant negative correlation between serum AT III concentration and urine protein excretion[6,11,12].

These alterations in the coagulation mechanism in nephrotic patients are reflected clinically in a widespread tendency towards intravascular coagulation, RVT formation or the occurrence of other extrarenal thromboembolic phenomena. It has been reported that in nephrotic patients, the incidence of RVT is about 35 percent while the incidence of extrarenal thromboembolic phenomena is about 20 percent[6]. Spontaneous thrombosis of femoral, mesenteric and pulmonary arteries and axillary, subclavian and leg veins have been observed[1,2]. The most common severe type of thromboembolic phenomena is the pulmonary embolism[2,6].

It has been observed that spontaneous RVT occurred in approximately 20 percent of rats with Heymann nephritis which was an experimental model of MGN[13]. This observation also supports the fact that RVT is a consequence of NS.

It has been argued that RVT causes NS by inducing an alteration in the permeability of the glomerular capillary wall which could result from two possible mechanisms[1,2]. The first is an elevation in venous pressure following thrombosis of the renal vein, causing alterations in glomerular permeability[1,2]. However unilateral renal vein ligation in a dog (rabbit or cat) does not cause nephrotic range proteinuria unless the contralateral kidney is removed[14]. Increased renal vein pressure due to thrombosis of the renal vein, constrictive pericarditis, occlusion of the vena cava above the renal veins, extreme obesity, and tricupsid valve disease may lead to disturbance of glomerular-capillary wall function in NS[1,2]. However, in many of the reported cases of NS, association of congestive failure or constrictive pericarditis, and injections of mercurial diuretics, are known causes of NS. In addition, there have been many cases reported of RVT with venal caval obstruction that were not associated with NS[1,2]. Thus, the relationship between increased renal venous pressure and the development of NS in man is debatable.

The second mechanism is that RVT may cause an immune-complex mediated type of glomurulonephritis by releasing renal tubular antigens which may induce glomerulopathy and associated NS. However, there is little evidence available supporting this theory[15-17]. The multiple factors leading to a hypercoagulable state and RVT are shown in Fig. 8.

There have been no reports in the literature concerning the incidence of RVT associated with NS in childhood in which a large group of patients have been

studied[1-4,7]. Our study, even though not large enough, also showed that RVT in childhood, when compared to its incidence in adults, is rare. But despite this fact, an incidence of nearly 34 percent of RVT was found to be associated with nephrotic children in the presented small series. This suggests the importance of thromboembolic events in children having glomerulopathy as has been shown in adults. Contrary to our findings, none of the 115 children with RVT which have been reported by the European Society of Pediatric Nephrology[1] nor the 50 children with RVT studied by Arneil et al[18] in Glasgow had associated NS. In our postmortem studies concerning RVT, a total of eight cases of nephrotic patients plus RVT were found: three cases with FCNS, three cases with amyloidosis, and two with MPGN.

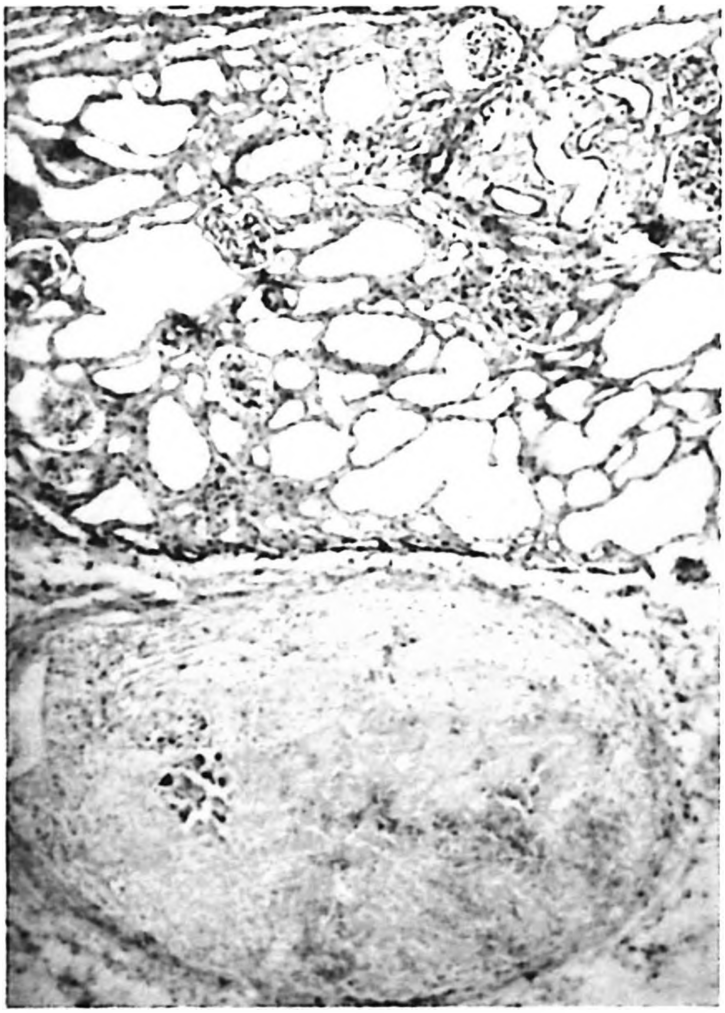

Fig. 1: Microscopical section of Finnish-type congenital NS showing a large, almost completely thrombosed vein (interlobar renal vein). The thrombus reveals areas of calcification (black dots), and cleft-like spaces (recanalization), fibrin depositions and fibrosis. Renal parenchyma reveals a rather characteristic appearance of microcystic dilatation of the convoluted tubules of FCNS (H.E stain X 75).

Renal venous thrombosis may occur in congenital NS but it is more likely a consequence rather than its cause. In the Finnish-type congenital NS, which is an autosomal recessive disorder, proteinuria is usually present at birth and or shortly after birth. This is one of the evidences which indicates that proteinuria can start in intrauterine life. Thromboembolic events can be seen in some congenital NS cases[19]. In addition to the coagulation abnormalities seen in nephrotic patients, infections and DIC observed frequently in these cases may lead to thrombosis[19-21]. Thus RVT occurs as a consequence of congenital NS.

In our series the three Finnish-type congenital NS cases revealed associated sepsis and/or DIC as was demonstrated histopathologically, in addition to RVT (Table I). The demonstration of the extrarenal venous thrombi in two of the congenital NS cases by macroscopic and microscopic examination supports the fact that sepsis and DIC lead to thromboembolic phenomena although specific studies were not performed. In addition, the hypercoagulable state occurring in

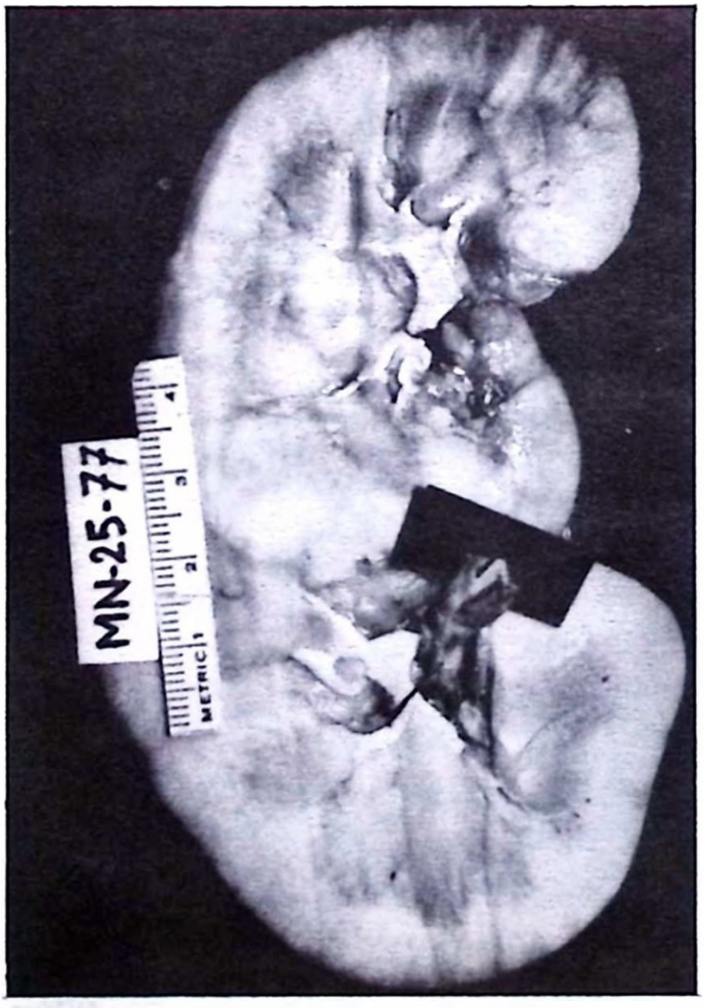

Fig. 2: Hemisected kidney of a case of MPGN shows a large bulging thrombosed branch of the main renal vein approximately 2 cm in length extending into the lower pole of the kidney (above the black rectangle).

nephrotic patients may play a role in the formation of RVT, as mentioned in the literature.

The ages of these patients ranged between 45 days and three months. The clinical signs and symptoms of NS had been present since their birth. Furthermore, microscopically and macroscopically the venous thrombi revealed organization, recanalization, and calcification (Figs. 2, 3). The findings in these cases suggest that the thrombi were two or three weeks old. It is concluded, therefore, that RVT occurred after the onset of NS. According to the data, it was agreed that the thrombosis in these three congenital NS cases occurred as a complication of the nephrotic state.

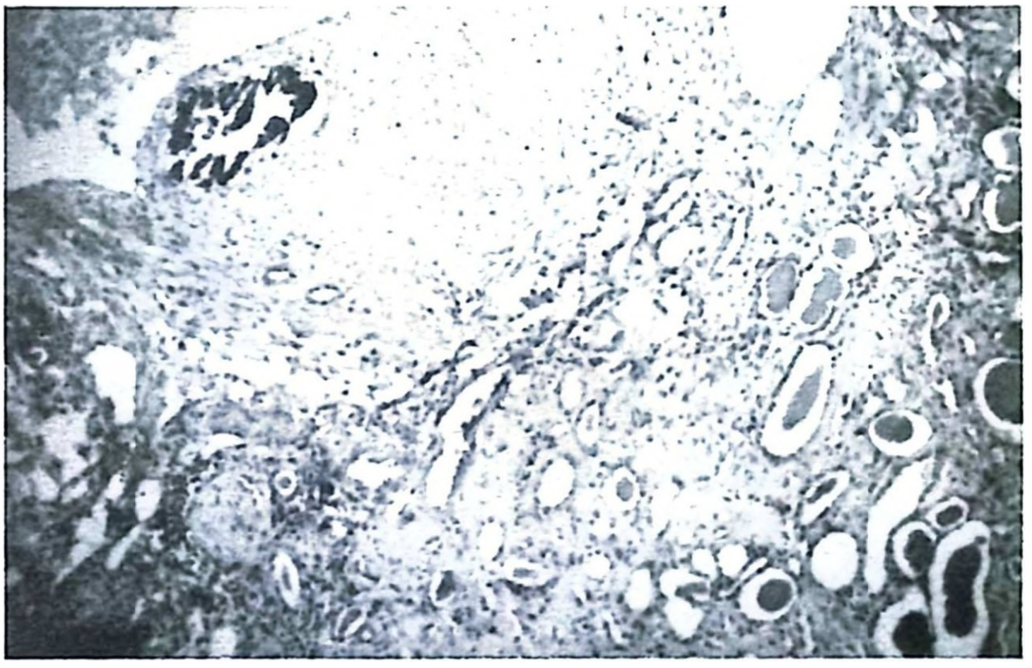

Fig. 3: Microscopical section of one of the renal amyloidosis cases showing a large vein near one corner of the picture which is completely thrombosed. The thrombus contains rather large areas of calcification (black dots) with clefts. Renal parenchyma shows an easily recognizable glomerulus which is completely obliterated due to amyloid deposition. There are homogenous tubular casts, varying in size, and the increased interstitial tissue is rather less cellular (amyloid deposition) (H.E. stain × 75).

The incidence of RVT in adult patients with MPGN or MGN has been reported to be between 38-41 percent[3,4,6,22]. In our study, only two of eight cases had MPGN, and sepsis was demonstrated in one of them (Fig. 4; Table II). After NS was diagnosed in these cases, cortisone, endoxan, diuretic and antibiotic therapy was given for approximately 35 days. It is known that cortisone, diuretics and also sepsis may precipitate thromboembolic events[2,6]. We believe that the hypercoagulable state in nephrotic patients, as reported in the literature, the therapy administered and the sepsis which was demonstrated in one case, may have led

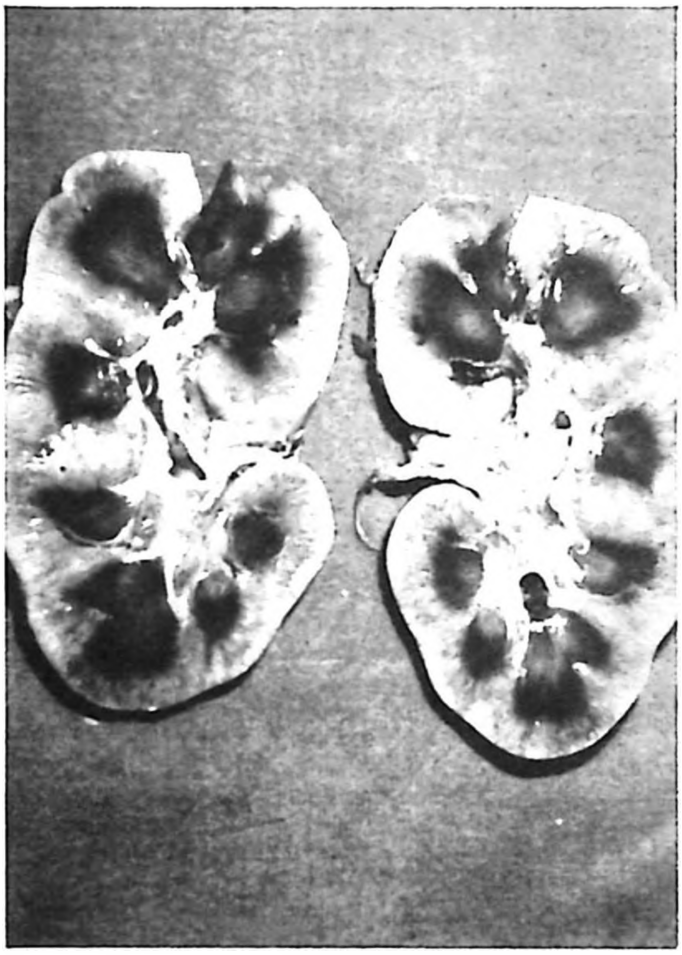

Fig. 4: Cut surfaces of a kidney of another case of renal amyloidosis showing dark areas corresponding to the infarct mainly located in the medullary of the pyramids. On the right side, close to the hilus, there appeared to be the presence of a lobar and/or arcuate vein. Dark discoloration of the renal pelvis is evidence of macroscopic hematuria.

to thrombosis in our patients. Due to fresh thrombi in the MPGN cases, it is presumed that the thrombi had occurred after the onset of MPGN (Fig. 2).

The last three cases in our study had RVT associated with amyloidosis (Figs. 5-7). The edema present in these patients lasted for six months (Case Nos. 6 and 7) and 18 months (Case No. 8). Acute deterioration in renal function supports the fact that RVT occurred after the development of the nephrotic state (Table III).

It should be stressed that in order to make an antemortem diagnosis of RVT, a good physical examination must be performed to detect the possible existence of RVT in nephrotic patients. If acute flank pain, marked costa-vertebral angle tenderness, macroscopic or microscopic hematuria, an increase in proteinuria, acute deterioration of renal function, an intravenous pyelogram revealing abnormalities with unilateral kidney enlargement and pelvocalyceal irregularities

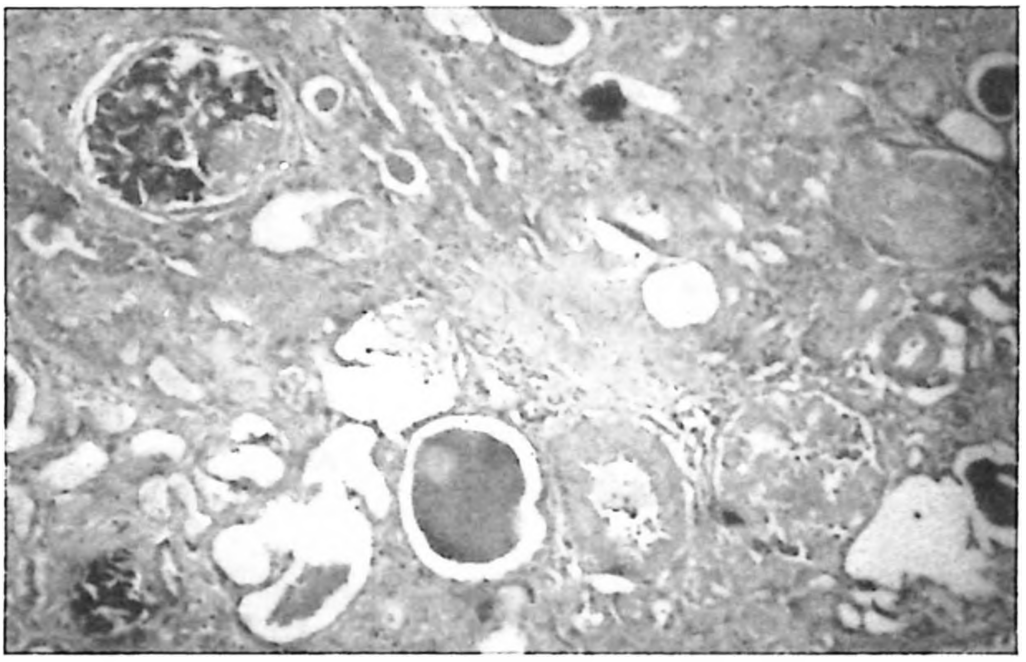

Fig. 5: Microscopical appearance of another case of renal amyloidosis showing amyloid deposition in the glomeruli. Additionally, there are calcifications in the glomeruli (dark-stained areas), tubular atrophy, tubular casts and widening of the interstitial tissue (H.E stain X 125); (This case shows renal venous thrombosis with calcification in the arcuate and lobar veins without renal infarction but these changes are not represented in this figure).

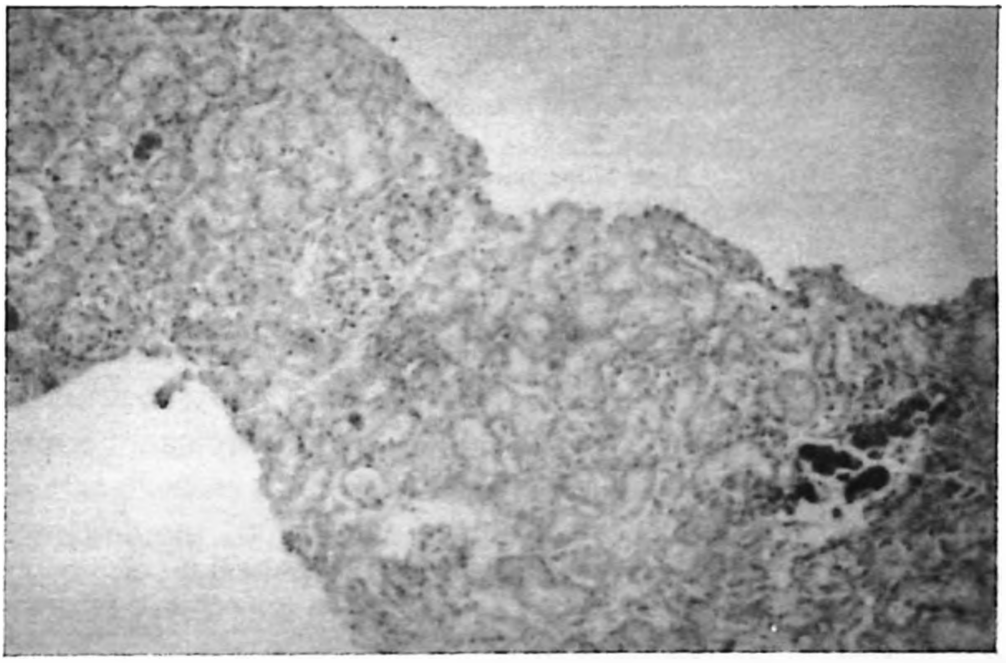

Fig. 6: Microscopic appearance of a needle renal biopsy (case in addendum) under medium power magnification in a case of mesangioproliferative glomerulonephritis. Note the dark-stained areas representing early thrombi in the arcuate and interlobular veins (H.E. stain X 75).

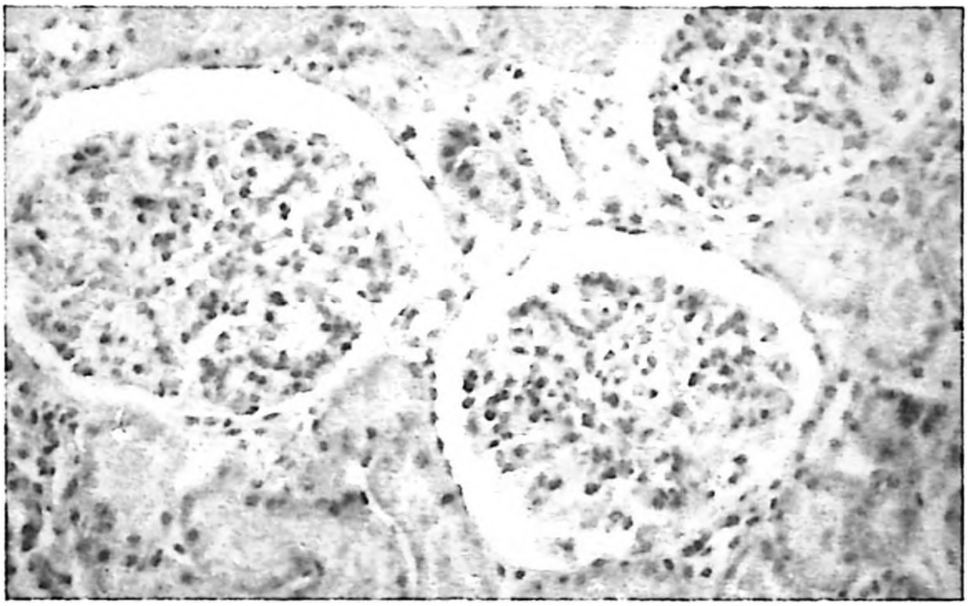

Fig. 7: Appearance of the glomeruli under higher magnification of case represented in Fig. 6 (H.E stain).

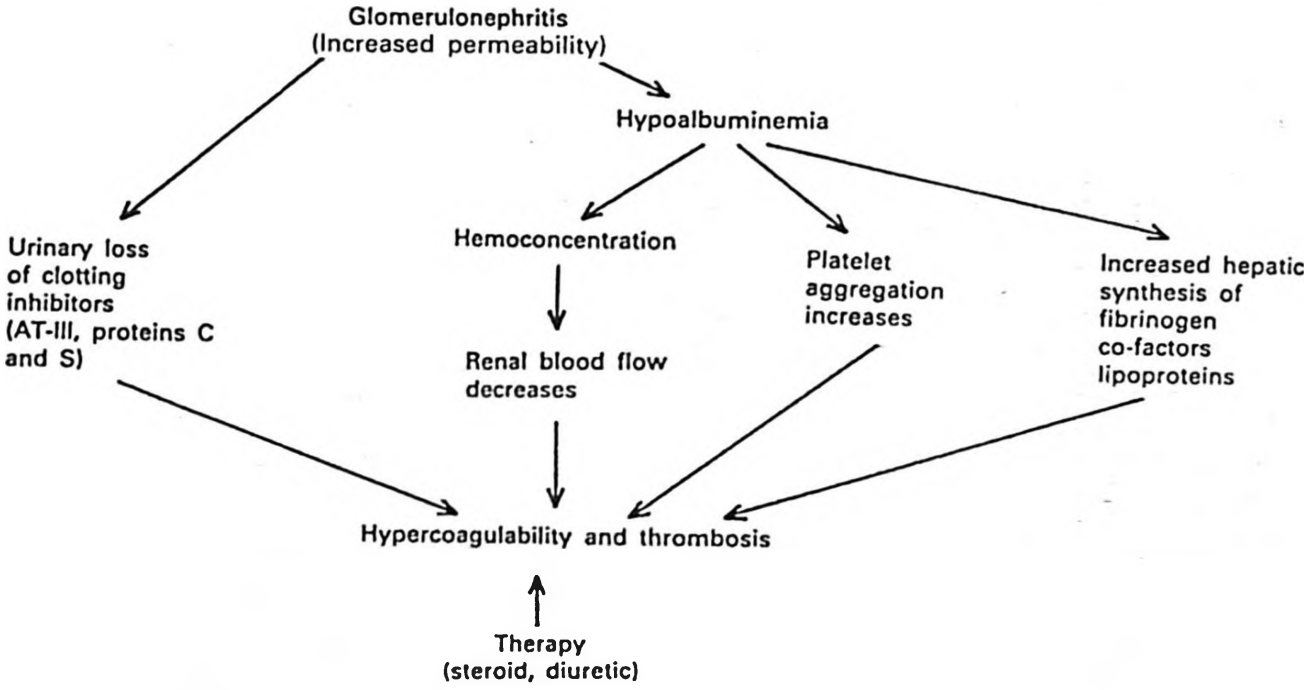

Fig. 8: A simple schema of etiopathogenic factors causing hypercoagulability, thromboembolic events and renal vein thrombosis in nephrotic syndrome.

are present, then RVT should be considered and the necessary investigations for a definite diagnosis should be made. After a diagnosis of RVT is made, a good prognosis depends largely on whether anticoagulant therapy is given to the patient to prevent hypercoagulability and thromboembolic events, along with specific therapy used to treat NS and a successful follow-up[1,2-4,17].

Summary

Cases with a pathological diagnosis of renal venous thrombosis (RVT) associated with nephrotic syndrome (NS) were studied retrospectively for clinicopathological evaluation. The material consisted of 21 RVT cases which were diagnosed in 2000 consecutive pediatric necropsies, with an overall incidence of about one percent. Eight of the 21 RVT cases were associated with nephrotic syndrome (34%), and this group formed 0.4 percent of the total necropsies in our pediatric center. The glomerulopathies of these nephrotic patients consisted of three cases of Finnish-type congenital NS (FCNS), three cases of renal amyloidosis secondary to familial Mediterranean fever, and two cases of membranoproliferative glomerulonephritis (MPGN). The presence of sepsis associated with disseminated intravascular coagulation, and the morphological age of the thrombi suggested that the RVT was secondary to sepsis in the FCNS cases.

In the MPGN and secondary renal amyloidosis cases, the long duration of both the nephrotic state and the administration of diuretics along with glucocorticoid treatment and also the newly formed thrombi without infarction are strong evidences, although not definite, that the RVT developed as a complication of the glomerulopathy.

Even though there were no definite clinical criteria for the diagnosis of most of the RVT cases, we would like to emphasize the importance of flank pain, the rapid deterioration of renal functions in a stable nephrotic patient, as well as the hypercoagulable state in the consideration of the development of RVT which indicate the need for approriate radiological studies for confirmation of this condition during life.

Addendum

After completing this manuscript, we encountered RVT involving arcuate and interlobular veins without infarction in a needle renal biopsy of a nine-year-old boy having corticosteriod resistant nephrotic syndrome. The glomerulopathy was that of diffuse mesangial proliferation with negative immunohistological findings which was classified as a variant of the idiopathic type of NS. This is the only case in our approximately 700 needle renal biopsy material, in a twelve-year period, which we diagnosed histologically during life. Even though hematuria could associate in cases of idiopathic NS, the presence of it in this particular patient might be a clue for the consideration of the development of RVT along with the other afore-mentioned findings.

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