MESANGIAL LIPOIDOSIS WITH CHOLESTEROL DEPOSITION – A NEW CASE WITH NEPHROTIC SYNDROME AND RAPIDLY PROGRESSING RENAL FAILURE

R. Robeva[1], T. Todorov[2], V. Dimitrova[1] M. Yordanov[1] and D. Doychinov[1]

[1]Clinic of Internal Disease Therapy, Nephrology, Dialysis and Clinical Pharmacology, Univ. Hospital "Sv . Ivan Rilski"
[2]Department of Pathology, Medical University – Sofia

Summary. More than 140 years ago, first Virchow associated observed lipid abnormalities with the concomitant renal disease. Despite a large body of clinical and laboratory evidence, the precise role of the lipids in the development of the renal disease remains unclear. In 1988, D. Doychinov described a new autosomal dominant hereditary disease leading to cholesterol accumulation within the glomerular mesangium. We report the case of a young man (a member of the affected family) with the same biopsy proven disease but with different clinical abnormalities and course. This patient had an overt nephrotic syndrome from the onset: 5 g/24h proteinuria, hypoproteinemia (52 g/l), hypoalbuminemia (28 g/l), hypercholesterolemia (8.5 mmol/l), edema as well as severe hypertension (180-200/110-120 mm Hg). Five years later he developed renal failure and after another three he was put on hemodialysis

Key words: *mesangial lipoidosis, nephrotic syndrome, renal insufficiency*

More than 140 years ago first Virchow associated observed lipid abnormalities with the concomitant renal disease. Despite a large body of clinical and laboratory evidence, the precise role of the lipids in the development of the renal disease remains unclear. It has been however demonstrated that lipid metabolism abnormalities may promote glomerular injury by an increased intrarenal lipid deposition such as in Fabry`s, Niemann – Pick and Gaucher` diseases, Alagille syndrome, the hereditary serum cholinesterase deficiency, type III hyperlipoproteinemia, lipoprotein glom-

erulopathy [1, 3, 4, 5]. In all of these, systemic signs and symptoms are also present. Disorders of lipid deposition limited to the kidney are rare and are still poorly understood.

In 1988, D. Doychinov described a new autosomal dominant hereditary disease leading to cholesterol accumulation within the glomerular mesangium [2]. This injury was biopsy-proven in another four members of the same family (three men and a woman) and it is probably present in another two older members of the family (refusing biopsy) who developed renal failure at the age of 51and 38 years respectively.

The onset of the disease was in the patient's younger age. 10-20 years after the typical onset with moderate proteinuria and hematuria, severe hypertension and chronic renal failure developed progressively and hemodialysis was indicated. Cholesterol crystal depositions were found in vitro in the glomerular mesangial matrix in all affected patients. No lipid storage in other renal structures or other organs could be established. There were no abnormalities of serum cholesterol and triglycerides [2].

THE CASE REPORT

In 1998, we investigated another member of the affected family (4th generation) aged 17 years who is a son of single affected woman (see Fig. 1). The histological finding from his biopsy was no different from those of the other affected family members (shown on Fig. 2). There were enlargement and lobulation of the mesangial axes by cholesterol deposits, segmental sclerosis of the capillary wall with fibrinoid deposits and peri-glomerular fibrosis in some glomeruli.

The extent of the injury was moderate – 10% sclerotic glomeruli, initial interstitial fibrosis and tubular atrophy were all documented (see Fig. 3).

Unlike his affected family members, this patients had an overt nephrotic syndrome just from the onset: proteinuria – 5 g/24 h, hypoproteinemia – 52 g/l, hypoalbuminemia-28 g/l, hypercholesterolemia – 8.5 mmol/l, edema as well as severe hypertension- 180-200/110-120 mm Hg. His renal function at that time was normal. The patient was treated with heparin, antihypertensive and lipid-lowering drugs. The nephrotic syndrome however persisted; the hypertension was severe and very difficult to treat. In 2003, the condition progressed to chronic renal failure (serum creatinine 250 μmol/l). The follow-up renal biopsy manifested advanced sclerotic changes in the glomeruli (38%), as well as interstitial fibrosis and focal tubular atrophy (see Fig. 4).

The patient was treated again with heparin, antihypertensives and symptomatic medications. Three years later he developed end-stage renal disease and was referred to hemodialysis.

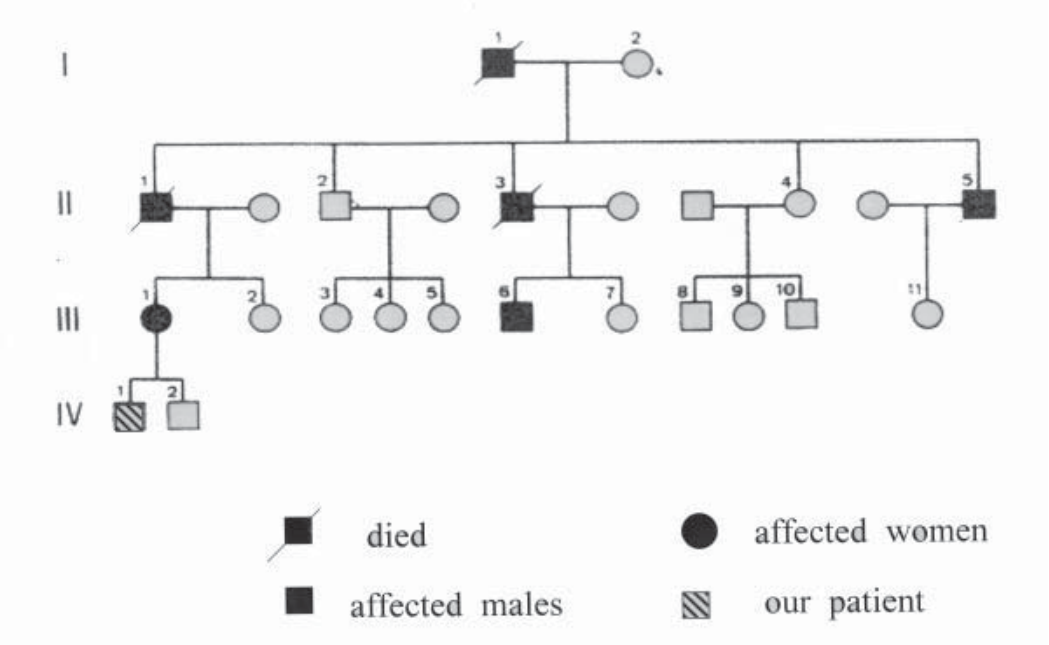

Fig. 1. Genealogy tree of the investigated family

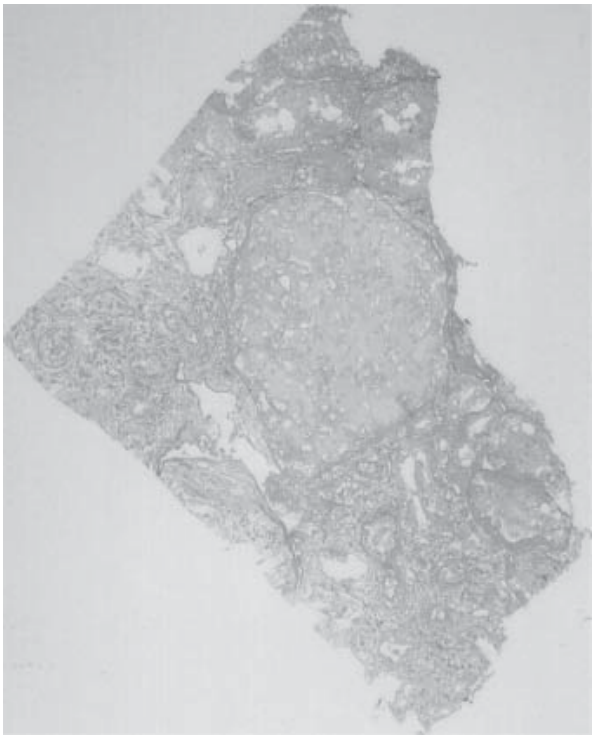

Fig. 2. Histological finding in the first described affected family member (renal biopsy)

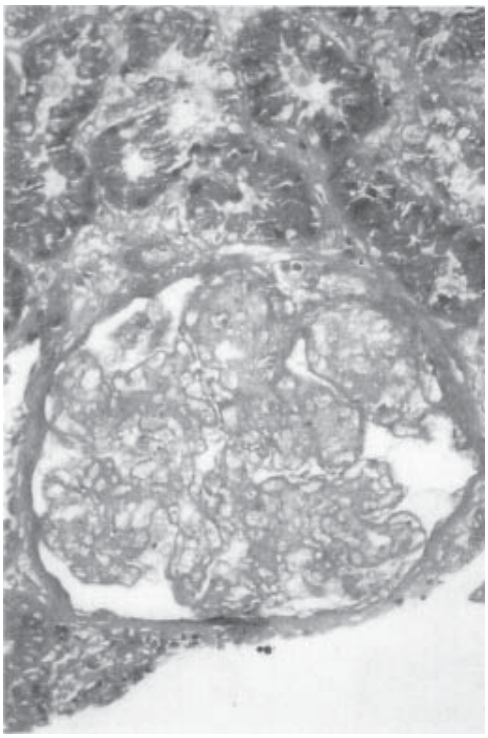

Fig. 3. First biopsy finding of the reported patient (Trichrom Masson x 100)

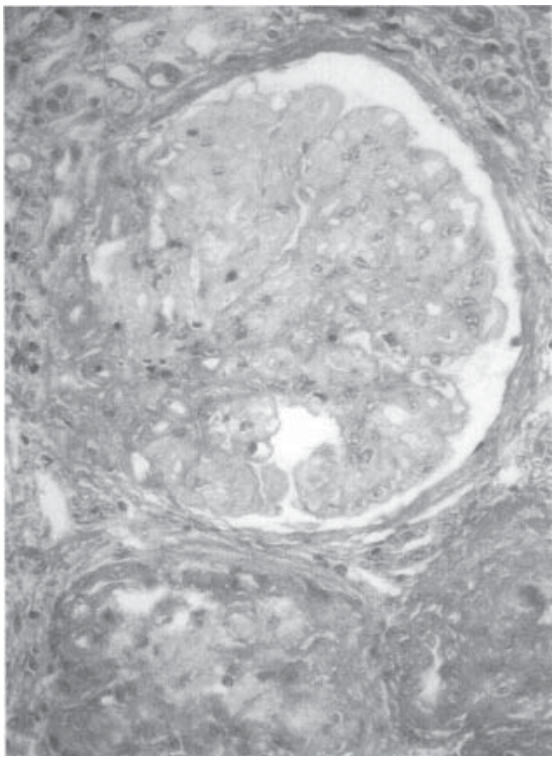

Fig. 4. Follow-up biopsy finding of the same patient

DISCUSSION

Essential lipoidosis with cholesterol deposition is an autosomal dominant hereditary disease. The onset of disease is in the younger age with moderate proteinuria and microscopic hematuria. Our patient however demonstrated that the development of substantial protein losses with subsequent nephrotic syndrome is also possible. In most affected members of this particular family, the hypertension developed progressively, but in our patient the severe hypertension presented early in the course of the disease.

Hypercholesterolemia is not a typical finding, and is probably related to the nephrotic syndrome in our case. The onset of the disease with nephrotic syndrome and hypertension was very abrupt. That is probably due to a faster progression of the chronic renal failure (it takes usually 10- 20 years to develop; in this case – only 5 years).

The patient was treated with heparin as prevention of thrombotic complications of the nephrotic syndrome. There are some observations, that this drug may exert an antisclerotic effect [5].

At the beginning, we were able to influence progression of the disease and to bring the renal deterioration to a steady state. The patient however was non-

compliant and was lost for follow-up. That is why we did not evaluate the long term effect of this treatment. To our knowledge, there is no evidence of an effective treatment of this disease.

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✉ *Address for correspondence:*
Assoc. Prof. R. Robeva, MD
Univ. Hosp. ”St . Ivan Rilski”
Dialysis and Clinical Pharmacology
15, Blvd.” Acad. Ivan Geshov”
1431 Sofia
✆ +35928510846