Features of kidney damage in a patient type 2 diabetes mellitus

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Abstract: Diabetic nephropathy refers to late complications of diabetes mellitus (DM), which develops, as a rule, in patients with its long decompensated course. Diabetic nephropathy is characterized by a special form of glomerular lesion with diabetic glomerulosclerosis. The most common is its nodular (or nodular) form, which until recently was considered pathognomonic for DM.

Keywords: diabetes mellitus, diabetic nephropathy, renal pathology

Diabetic nephropathy is a late complication of diabetes mellitus (DM), which usually develops in patients with its long decompensated course [1]. Diabetic nephropathy is characterized by a special form of glomerular lesions - diabetic glomerulosclerosis. The most common is its nodular (or nodular) form, which until recently was considered pathognomonic for DM. Recently, however, nodular glomerulosclerosis has been identified in non-diabetic patients. The spectrum of diseases in which nodular glomerulosclerosis has been described is quite wide and, in addition to diabetic nephropathy, includes various types of glomerulonephritis (type I mesangicapillary, cryoglobulinemic, fibrillar, and immunotactoid), amyloidosis, non-amyloid deposition of immunoglobulin light chains in the kidneys, and the so-called idiopathic nodular glomerulosclerosis associated with a long history of smoking and arterial hypertension [2, 3, 4, 5].

Particular difficulties in the interpretation of nodular glomerulosclerosis arise in patients with a combination of several of its causes, which is demonstrated by the given clinical observation. The patient, 45 years old, a nurse, belongs to the category of "heavy smokers" (smoking index is 29 pack/years). Since childhood, livedo has been determined on the skin of the lower extremities. In the obstetric anamnesis - a miscarriage at a short gestational age. For more than ten years he has been suffering from Raynaud’s syndrome. In 2001, chronic obstructive pulmonary disease was diagnosed, which was regarded as the result of prolonged smoking. During this period, the examination of the pathology of the kidneys was not revealed.

In 2006, for the first time, the appearance of edema of the legs and face was noted. Since March 2007 - moderate arterial hypertension, at the same time for the first time detected: proteinuria more than 4 g/l, microhematuria, a moderate increase in creatinine levels (up to 1.6 mg/dl). Didn’t receive therapy. In July 2007, she was examined for

the first time in the clinic. EAT. Tareeva. Arterial hypertension with a maximum rise in blood pressure up to 180/110 mm Hg, moderately pronounced nephrotic syndrome (proteinuria 2.5 g/day, albumin 31 g/l), and minimal erythrocyturia were revealed. The blood creatinine level remained normal, but the glomerular filtration rate was 49 ml/min. At the same time, on the basis of the first discovered hyperglycemia (blood glucose level of 20 mmol/l), DM2 was diagnosed. The nature of kidney damage was unclear. The possibility of developing diabetic nephropathy seemed unlikely due to a short history of diabetes.

The combination of acute nephritic and nephrotic syndromes was more likely to substantiate the diagnosis of chronic glomerulonephritis, for confirmation of which a kidney biopsy was planned. However, due to the decompensation of DM and the exacerbation of broncho-pulmonary infection that developed in the clinic, nephrobiopsy was postponed. For the same reasons, it was decided to refrain from active immunosuppressive therapy. In addition, taking into account a aggravated obstetric (miscarriage at a short gestational age) history, including family history (eclampsia with a fatal outcome in a sister), hereditary burden of vascular accidents (myocardial infarction in a father at a young age), the presence of livedo and syndrome Raynaud, primary antiphospholipid syndrome (APS) was suspected. The detection of a five-fold increase in the level of antibodies to cardiolipin allowed us to confirm this assumption. Anticoagulants were not prescribed due to the absence of thrombosis and identified erosive lesions of the stomach.

Over the next six months, as a result of treatment with gliclazide, a significant decrease in the level of glycemia was achieved. Conducted nephroprotective therapy with ACE inhibitors, calcium channel blockers, which allowed to stabilize blood pressure at 140/80 mm Hg. By the time of re-hospitalization in January 2008, the nephrotic syndrome had regressed, microhematuria had disappeared, and glycosylated hemoglobin remained within normal limits. However, despite a clear improvement in the condition, there was a tendency to increase the level of creatinine. Taking into account the persistent impairment of kidney function with a decrease in proteinuria and normalization of blood pressure in a patient with APS, it has been suggested that the development of thrombotic microangiopathy (TMA) as a manifestation of APS-associated nephropathy.

On the other hand, taking into account pronounced coagulation disorders (increased levels of D-dimer, soluble fibrin-monomer complexes) in the absence of arterial and venous thrombosis, aggravated family history, the possibility of combining APS with a genetic form of thrombophilia was discussed. A molecular genetic study revealed heterozygous mutations in the fibrinogen β-chain (genotype GA) and plasminogen activator-1 inhibitor (genotype 4G5G) genes, which confirmed the presence of multigene thrombophilia, which could also contribute to the development

of renal TMA. For the final verification of the diagnosis, the patient underwent a biopsy.

In the kidney biopsy, light microscopy revealed signs characteristic of diabetic glomerulosclerosis. All six or seven glomeruli are in a state of partial or total glomerulosclerosis. In the glomeruli, there is a thickening of the BMC, an expansion of the mesangium with the formation of lobules, sclerosis of vascular loops with the formation of lobules, and multiple synechiae with a sclerosed outer leaflet of the capsule. The epithelium of the convoluted tubules is in a state of protein dystrophy and atrophy, the lumen is enlarged, contains protein cylinders. Diffuse sclerosis of the stroma - with focal lymphoid infiltrates. Arteriosclerosis. Electron microscopy, which confirmed the presence of diabetic nephropathy, also revealed blood clots in the lumen of the glomerular capillaries, which made it possible to diagnose TMA.

The results of a kidney biopsy gave grounds to exclude the diagnosis of chronic glomerulonephritis, which seemed the most probable, and to avoid the appointment of prednisolone and cytostatics, which was planned at the initial stage of the examination. Continued hypoglycemic and antihypertensive therapy. Clexane treatment was started, and after a month and a half of therapy, normalization of serum creatinine levels and a decrease in proteinuria were noted. Subsequently, two courses of sulodexide were carried out. So far, the kidney function is stable, blood creatinine does not exceed 100 μmol/l, proteinuria is less than 0.3 g/s.

Discussion

Thus, kidney damage in a patient with DM and primary APS with identified polymorphism of the genes of a number of blood coagulation factors (heterozygous carriage of the G allele of the fibrinogen β-chain and the 4G PAI-1 allele) was represented by a combination of diabetic nephropathy and TMA. It can be assumed that relapses of intraglomerular thrombosis, characteristic of APS-associated nephropathy (APSN), could accelerate the development of diabetic glomerulosclerosis in a patient with a short history of DM. The important role of glomerular capillary thrombosis in the induction of glomerulosclerosis in various thrombotic microangiopathies, including in patients with primary APS and secondary AFSN in lupus nephritis, has been demonstrated by many researchers [6, 7, 8]. The exact mechanism of the profibrogenic effect of TMA has not been established, but it can be assumed that it is due to renal ischemia due to widespread microthrombosis, which accelerates the development of sclerotic processes in the glomeruli, extraglomerular vessels, and interstitium.

The multigenic thrombophilia present in the presented patient should apparently be considered a factor contributing to the recurrence of thrombosis in the microvasculature of the kidneys, which in turn can lead to the progression of diabetic glomerulosclerosis, as was found in patients with IgA nephropathy, membranous

nephritis, lupus nephritis. Another factor that contributed to the accelerated development of glomerulosclerosis, apparently, is persistent smoking, which is now considered as an independent risk factor for renal failure in diabetic nephropathy in patients with type 1 and type 2 diabetes [4, 12]. In addition, it turned out that the development of nodular glomerulosclerosis in individuals who do not suffer from DM was associated with smoking [3, 4]. The effects of smoking on the kidneys are diverse and affect all structures of the renal parenchyma, including glomeruli, tubules, interstitium, and vessels. Long-term smoking induces the development of nephrosclerosis even in individuals who do not suffer from arterial hypertension and DM, and, as it turned out, can be the only cause of impaired renal function in the absence of other renal diseases [4].

The main target of the toxic components of tobacco smoke, apparently, are the endothelial cells of the capillaries of the glomeruli and intrarenal vessels of a larger caliber (interlobular arteries and arterioles), the damage of which in smokers has been established in a number of studies [4, 12, 14]. Ultimately, smoking causes proliferation of endothelial and mesangial glomerular cells, myointimal proliferation and hyperplasia of arterial walls, and accumulation of extracellular matrix. In addition, smoking induces increased platelet aggregation, which, in combination with damage to endothelial cells, can cause activation of intraglomerular blood coagulation with the development of microthrombosis.

Thus, changes in kidney tissue found in heavy smokers, to which the present patient belongs, are nonspecific and may resemble histological signs of other nephropathies, one way or another associated with endothelial damage, including diabetic glomerulosclerosis and thrombotic microangiopathy. The development of nodular and global glomerulosclerosis, tubulointerstitial fibrosis and arteriosclerosis in the observed patient with a relatively short (about one and a half years) history of nephropathy, apparently, can be explained by a combination of several factors acting in the same direction (DM, prothrombotic state due to a combination of acquired and hereditary thrombophilia, persistent smoking), and it is extremely difficult to single out the main one in this situation.

References

1. Nephrology: Textbook for postgraduate education / Ed. EAT. Shilov. – M.: GEOTAR-MED. – 2007. – 683 p.

2. Alsaad K.O., Herzenberg A.M. Distinguishing diabetic nephropathy from other causes of glomerulosclerosis: an update // J. Clin. Pathol. – 2007. – 60. – P. 18–26.

3. Markowitz G.S., Lin J., Valeri A.M. et al. Idiopathic nodular glomerulosclerosis is a distinct clinicopathologic entity linked to hypertension and smoking // Hum. Pathol. – 2002. – 33. – P. 826–835.

4. Liang K., Greene E., Oei L., et al. Nodular glomerulosclerosis: Renal lesions in chronic smokers mimic chronic thrombotic microangiopathy and hypertensive lesions // Am. J .Kidney. Dis. – 2007. – 49. – P. 552– 559.

5. Suneja M., Khan A., Katz D., et al. Nodular Glomerulosclerosis in a Kidney Transplant Recipient Who Smokes // Am. J. Kidney. Dis. – 2007. – 50. – P. 830–833.

6. Kant K.S., Pollak V.E., Weiss M.A. et al. Glomerular thrombosis in systemic lupus erythematosus: prevalence and significance. //Medicine. – 1981. – 60(7). – P. 71–85.

7. Nochy D., Daugas E., Droz D. et al. The intrarenal vascular lesions associated with primary antiphospholipid syndrome // J. Am. Soc. Nephrol. – 1999. – 10. – P. 507–518.

8. Козловская Н.Л., Шилов Е.М., Метелева Н.А. Клинико-морфологические особенности нефропатии при первичном и вторичном антифосфолипидном синдроме. //Тер. Архив. – 2007. – № 6. – С. 16–25.