IgA NEPHROPATHY – ONE OF THE POSSIBLE CAUSES OF MALIGNANT HYPERTENSION

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Abstract:

Malignant hypertension (MH) is a state which can rapidly progress to multi-organ failure. It can develop in the course of both primary and secondary type of hypertension. In our study, we present a case of a 36-year-old man diagnosed with renal failure and MH complicated with retinopathy. As the secondary nature of the condition was suspected extensive diagnostics has been conducted. In spite of excluding plenty of pathologies, the underlying cause remained unknown. Eventually, the renal biopsy has been performed, leading to a diagnosis of IgA nephropathy. However, symptoms and course of the disease has not been typical. Nevertheless, IgA nephropathy should be considered as a possible cause of secondary hypertension as well as malignant hypertension. The diagnosis is not easy and a crucial role is played by renal biopsy.

Keywords: IgA nephropathy, malignant hypertension, renal failure, renal biopsy.

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Introduction

Malignant hypertension is the most severe form of hypertension. It is characterized not only by diastolic blood pressure values reaching above 130 mmHg, but also by numerous multi-organ complications including kidney, brain and heart damage [1], Also retinal and vascular impairment can be often observed [2]. MH occurs with an incidence of approximately 2/100,000 cases per year [3]. The most frequently it develops as a result of other problems with health. In young people it almost always indicates that they suffer from some other disease. [4]. What is more, hypertension can be both a cause and a consequence of for example kidney disease. The presence of malignant hypertension in young people is more likely to be an indication for secondary form of hypertension. It may be also a result of: renal artery stenosis, endocrine disease, obstructive sleep apnea as well as glomerulopathy. This case presents an atypical course of IgA nephropathy and diagnostic difficulties that may arise during the search for the cause of malignant hypertension.

Case

A 36-year-old man had been admitted to the Department of Internal Medicine, Nephrology and Dialysotherapy due to very high blood pressure values and newly diagnosed renal failure. The patient hadn't been suffering from chronic diseases nor taking any medications. He has noticed a malaise, nocturnal awakenings due to nycturia and daily headaches since three weeks. A week before admission to the hospital, during an ophthalmologist's appointment,the patient had been diagnosed with retinoschisis. He had received treatment consisting of 25 mg eplerenone, which he took as advised. The day prior to hospitalisation the patient reported to the regional hospital's Emergency Department due to persistent malaise and an episode of vomiting. The physical examination revealed significantly elevated blood pressure reaching values of up to 205/140 mmHg. Abnormal nitrogen retention indices were noted in biochemical tests. Head CT scan did not show any abnormalities. The patient was administered hypotensive drugs – Captopril, Nitredipine, Nitromint and Furosemide, which caused decrease in systolic blood pressure by 10 mmHg only. The patient was transferred to a higher level reference center. Further tests in the Emergency Department were performed and revealedabnormal nitrogen retention: creatinine 7.1 mg/dl, GFR 9 ml/min/1.73m2, urea 139 g/dl. In arterial blood test metabolic acidosis was observed – pH 7.234, pCO2 43.2 mmHg, HCO3 18.3 mmol/l, BE -9.2 mmol/l. In addition, urinalysis showed proteinuria of 300 mg/l, glucose 50 mg/dl and hematuria. Abdominal ultrasound visualised only renal cysts.

The patient was admitted to the Department of Internal Medicine, Nephrology and Dialysotherapy in order that conduct a search to find a cause of renal insufficiency and treatment of arterial hypertension. Upon physical examination no signs of pulmonary congestion, edema, neuro-

logical defects, heart failure or arrhythmia were found. Based on the clinical picture and the results of preformed tests, a preliminary diagnosis of malignant hypertension with renal complications was made.

Additional laboratory tests performed in the clinic revealed secondary hyperparathyroidism. However, no autoantibodies: anti-neutrophil cytoplasmic antibodies associated with systemic vasculitis – pANCA and cANCA and anti-glomerular basement membrane – anti-GBM were found. The complement system markers were also within normal range. During hospitalization, a 24-hour urine collection was performed, which allowed to determine the exact amount of proteinuria, which was 4687 mg/24h. The chest X-ray did not visualise any abnormalities. Echocardiography was performed to exclude aortic coarctation – this examination also did not show any abnormalities.

While searching for possible causes of secondary hypertension, hypotensive therapy was implemented and forced diuresis was maintained. The decision on renal replacement therapy was temporarily postponed. Creatinine, urea, ionogram, arterial blood gases and morphology were regularly monitored. The creatinine concentration, which was 7.2 mg/dl on admission, decreased to 5.9 mg/dl. The patient had three ophthalmological consultations during hospitalization. Hypertensive retinopathy of the left eye was diagnosed and anti-VEGF injections were recommended. After appropriate preparation of the patient abdominal ultrasound was performed. As in the previous examination, bilateral simple renal cysts up to 12 mm in size were described. No renal artery stenosis was found in Doppler ultrasound. Due to proteinuria and hematuria of unclear origin renal biopsy was then performed. The biopsy revealed a picture that was consistent with IgA nephropathy – the mesangium showed IgA deposits. In the glomeruli fibrotic crescents and segmental sclerosis were observed.

Due to the lack of significant improvement in renal function dialysis therapy options was were introduced to the patient. According to his preferences and anatomical conditions, the decision about peritoneal dialysis trial has been made. The patient was discharged with the recommendation to report urgently to the surgical department for Tenckhoff catheter insertion and subsequent treatment.

Discussion

In this case, a diagnostic challenge has been manifested in determining the cause of malignant hypertension and renal failure. In patients under the age of 40 the presence of malignant hypertension, accompanied by renal failure and retinopathy, requires additional diagnostics for secondary causes of hypertension [5, 6]. However, it is very important to remember that hypertension may be both a cause of kidney damage – in the case of poorly controlled primary hypertension – and a symptom of kidney disease – in renal hypertension. Clinical symptoms usually do not suffice for a clear differentiation. The duration of hypertension may be helpful for this assessment, as a long-standing course of the disease, especially if poorly controlled, leads to glomerular sclerosis and the development of hypertensive nephropathy. In hypertension secondary to renal disease, the history of hypertension is often much shorter, and may be more rapid and take the form of malignant or resistant hypertension [6].

In presented case renal artery stenosis, endocrine disorders, aortic coarctation, and systemic diseases that may cause glomerulonephritis, have sequentially been excluded. Renal causes of secondary hypertension include both acute and long-term renal damage. Relatively short history of complaints suggested an acute form of renal failure which, however, is usually associated with oliguria or anuria. In addition, acute or subacute renal damage is also defined by a time criterion, which refers to the progression of changes in renal function. In the described case it couldn't be used due to the lack of previous screening examinations. Chronic kidney disease, according to KDIGO 2012, is defined as abnormalities of kidney structure or function, with health implications, lasting for more than 3 months [7]. However, imaging studies performed in this case did not show renal structural features which could suggest chronic disease. The clinical manifestations of chronic kidney disease depend on its severity. They are initially non-specific – weakness and hypertension, which occurs in up to 90% of patients with chronic kidney disease [8]. Typical abnormalities in laboratory tests are: increased creatinine, urea, uric acid, acid-base imbalance in the form of metabolic acidosis, calcium-phosphate imbalance - hyperphosphatemia, hypo or hypercalcemia, hypernatremia, increased PTH levels, lipid metabolism disorders and anemia.

Described patient, apart from hypertension, did not have typical clinical symptoms of chronic kidney disease. Additional examinations revealed elevated creatinine and urea, lipid metabolism disorders, hyperphosphatemia, as well as elevated PTH levels. Increased PTH indicates secondary hyperparathyroidism, which is a typical feature of chronic kidney disease. The most common causes of chronic kidney disease are diabetes, hypertension and glomerulopathies [9]. The patient had not previously been diagnosed with neither diabetes, nor primary hypertension.

With reference to the described case, worth citing is one of the scientific papers. Chen et al. compared clinical and histopathological features of primary malignant hypertension and malignant hypertension in the course of IgA nephropathy. They showed that patients with malignant hypertension associated with IgA nephropathy more often have proteinuria and hematuria than patients with primary malignant hypertension [4]. Nevertheless, renal parenchymal biopsy is the test that can clearly determine the cause of kidney damage - provide an answer to the question whether glomerulopathy is the cause. The aforementioned study revealed that glomerular changes were more severe in patients with hypertension associated with IgA nephropathy – a higher percentage of glomeruli was affected by sclerotic lesions and formed crescents, due to more intense mesangial proliferation [4]. In the presented case, histopathological examination of the kidney showed features typical of malignant hyperplasia associated with IgA nephropathy, also showing IgA deposits in the mesangium.

IgA nephropathy could be one of the causes of secondary hypertension as well as malignant hypertension [4]. It is the most frequent form of primary glomerulonephritis worldwide [10] and one of the causes of chronic kidney disease. The incidence is approximately 2.5/100,000 people per year [11]. It is characterized by deposition of immune complexes in the glomerular mesangium [12]. The clinical picture of IgA nephropathy varies widely, from asymptomatic microscopic hematuria or gross hematuria to nephritic syndrome. However, the most common manifestation in adults is asymptomatic hematuria with diverse proteinuria [13]. Rarely does IgA nephropathy occurs as macroscopic haematuria associated with upper respiratory tract infection. Described patient denied similar episodes in the past. He hasn't noticed any changes in the appearance of urine. In rare cases, IgA nephropathy may take the form of rapidly progressive glomerulonephritis. Renal biopsy and finding IgA deposits are required to confirm the diagnosis. During the course of the disease, gradual deterioration of kidney function and a decrease in glomerular filtration rate occurs. In most cases, progression of the disease is slow. The risk of end-stage renal disease within 20 years of diagnosis is estimated to be between 13 and 39% [14] and depends mainly on the clinical picture and the severity of histopathological changes. The most important clinical risk factors are persistent proteinuria and hypertension [14, 15]. The histopathological changes considered in the assessment of prognosis are described by the Oxford Classification (MEST score), which evaluates 4 parameters: M –mesangial hypercellularity, E – endocapillary cellularity, S – segmental sclerosis, T – interstitial fibrosis/tubular atrophy [16].

Summary

Malignant hypertension in young patients without previous medical history is an indication to search for secondary causes of hypertension. If renal failure symptoms coexist, special consideration should be given to renal biopsy. This may be crucial in establishing the proper diagnosis. Although IgA nephropathy usually has a slow, long-term course, its progressive nature may lead to end-stage renal failure, which in most cases manifests itself in hypertension, among other symptoms. Chronic kidney disease is associated with increased risk of death, mainly in cosequnce of cardiovascular events. In relation to its progressive nature and number of complications it can cause, early detection and implementation of treatment are crucial for prognosis.

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