CHALLENGES IN THE DIAGNOSIS AND TREATMENT OF NEPHROTIC SYNDROME IN AN ELDERLY PATIENT

Trudności diagnostyczne i terapeutyczne zespołu nerczycowego u pacjenta w wieku podeszłym

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Abstract

Nephrotic syndrome is a set of symptoms primarily characterized by daily protein loss in the urine exceeding 3.5 grams, which can be caused by a range of underlying conditions. The presented case of an 88-year-old patient with nephrotic syndrome illustrates the challenges associated with the diagnostic process and treatment of this disorder in the presence of multiple comorbidities and advanced age. Despite contraindications for biopsy and, consequently, the lack of histological findings, treatment was initiated, resulting in significant partial remission, marked by a substantial reduction in proteinuria, decreased creatinine levels, and a satisfactory eGFR. This case highlights the importance of treating nephrotic syndrome in elderly patients and demonstrates the possibility of effective therapy despite diagnostic difficulties arising from contraindications for renal biopsy.

Streszczenie

Zespół nerczycowy to zespół objawów, charakteryzujący się przede wszystkim dobową utratą białka z moczem powyżej 3,5 grama, który może być wywołany przez szereg jednostek chorobowych. Przedstawiony przypadek 88-letniego pacjenta z zespołem nerczycowym obrazuje wyzwania związane z procesem diagnostycznym oraz leczeniem tego zespołu przy licznych obciążeniach i zaawansowanym wieku pacjenta. Mimo przeciwwskazań do wykonania biopsji nerki i braku jej wyniku, wdrożono leczenie, które pozwoliło na uzyskanie niepełnej, lecz znaczącej remisji w postaci istotnego zmniejszenia białkomoczu, obniżenia stężenia kreatyniny i uzyskania wartości przesączania kłębuszkowego na satysfakcjonującym poziomie. Opisany przypadek podkreśla konieczność leczenia zespołu nerczycowego u pacjentów w bardzo zaawansowanym wieku oraz pokazuje, że skuteczna terapia jest możliwa pomimo trudności diagnostycznych wynikających z przeciwwskazań do wykonania biopsji nerki.

Keywords: elderly patient; diagnostic challenges; nephrotic syndrome

Słowa kluczowe: pacjent geriatryczny; trudności diagnostyczne; zespół nerczycowy

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Introduction

Nephrotic syndrome (NS) is a clinical condition characterized by proteinuria >3.5 grams/day, hypoalbuminaemia, lipiduria, hyperlipidaemia, severe oedema, and transudation into body cavities [1]. It may be primary, arising from glomerulopathies, or it may develop secondary to systemic conditions such as diabetes mellitus, amyloidosis, or lupus erythematosus. Nephrotic proteinuria arises from damage to the glomerular filtration membrane caused by the disease process, specifically affecting the basement membrane and podocytes, particularly their foot processes. As a result, in addition to mechanical damage, the electrostatic barrier is lost, leading to increased permeability to proteins, primarily albumin [2].

Oedema is often the first clinical manifestation noticed by the patient. Other symptoms may include generalised

asthenia, abdominal pain, headache, nausea, vomiting, loss of appetite, malnutrition, and transudation of fluids into body cavities.

The diagnosis of NS patients has three main objectives: to identify the underlying disease, to assess complications, and to determine the histological type of glomerular changes [3]. Diagnostic workup should consider the most common causes of NS within the patient's age group, as well as individual factors such as medication history and prior infections. Importantly, elderly patients should be screened for neoplastic aetiology.

The third diagnostic goal, i.e. determining the exact aetiology, often requires percutaneous renal biopsy. The obtained biopsy is then analysed using light, fluorescence, and electron microscopy – the gold standard for diagnosing renal parenchymal diseases [4].

Treatment of NS is challenging due to the lack of clear guidelines supported by scientific evidence [3]. Current recommendations, based on expert consensus, offer only a few general guidelines [5]. Once the aetiology is established, causal treatment should be initiated. The therapy additionally incorporates dietary recommendations (sodium and fluid restriction), oedema reduction, proteinuria control, as well as prevention and management of complications.

Acute kidney injury (AKI), chronic kidney disease (CKD), infections, and venous thrombosis are the most common complications of NS. Systematic reviews do not support routine antithrombotic or anti-infective prophylaxis; however, it is important to monitor serum albumin and, if it drops below 2.5 g/dL, low-molecular-weight heparins should be administered [6, 7].

As with many other diseases, the patient's advanced age is an additional factor complicating the diagnosis and treatment of NS. Elderly individuals often present with multiple comorbidities, which can obscure symptoms and reduce vigilance, especially in the patient. Elderly patients require special consideration, as invasive or aggressive procedures are not always applicable in this group, further complicating the therapeutic process.

Case report

An 88-year-old man was admitted to the Department of Internal Medicine, Nephrology, and Dialysis at the Military Institute of Medicine – National Research Institute after being brought to the Emergency Department following a fainting episode. The patient had been hospitalized four times in various departments over the past six months. The current admission was a continuation of the diagnostic process initiated during two previous stays at the Department of Nephrology, Transplantology and Internal Diseases at the University Clinical Center of the Medical University of Gdańsk.

Nephrotic syndrome in the course of CKD, stage G3aA3, was the primary diagnosis and the reason for hospital stay on admission. Additionally, the patient presented with multiple chronic diseases, including hypertension, chronic coronary syndrome treated with coronary angioplasty with drug-eluting stent implantation in the circumflex branch of the left coronary artery (15 years ago), sick sinus syndrome with bradycardia, axonopathic sensorimotor polyneuropathy, multilevel degenerative and discopathic changes involving the lumbar-sacral spine, a history of L1 body compression fracture, benign prostatic hyperplasia, post-inflammatory cystic changes in the pancreas and one intraductal papillary mucinous neoplasm (IPMN), peptic ulcer disease of the stomach and duodenum, gastric atrophy, depression, bilateral hearing loss, a history of stroke with left-sided facial-brachial paresis, vascular changes of the white matter and generalized cortical-subcortical atrophy.

Due to the above-mentioned comorbidities, the patient received combination therapy. Until admission, CKD was managed with glucocorticoids (GCs), initially administered intravenously and then orally. Additionally, prednisone, omeprazole, acetylsalicylic acid, valsartan, amlodipine, sertraline, rosuvastatin, tamsulosin, finasteride, allopurinol, and pregabalin were used for other comorbidities.

On admission, the patient was in relatively good general condition, alert, and oriented. Physical examination revealed lower leg oedema and signs of stasis at the base of the lungs. Laboratory workup showed impaired renal function: creatinine 1.5 mg/dL, estimated glomerular filtration rate (eGFR) 47 mL/min/1.73 m², and urea 76 mg/dL. Urinalysis showed decreased specific gravity, significant proteinuria (>3 g/L), and haematuria of 17.1/µL (normal: up to 13.6/µL).

Renal biopsy was not performed due to contraindications. Further diagnosis focused on less invasive investigations, with an emphasis on symptom management. Secondary glomerulopathies were excluded in the first place. Normal blood glucose and glycated haemoglobin (HbA_{1c}) ruled out diabetic nephropathy. Additionally, low serum amyloid A and absence of echocardiographic features of amyloid deposition excluded amyloidosis.

Due to significantly increased serum gamma globulin fraction, plasma-cell dyscrasia was initially suspected. However, it was ruled out based on normal free light chain index and the absence of monoclonal protein in serum and urine immunofixation. Given the patient's age, paraneoplastic syndrome was also considered; however, extensive imaging, including gastroscopy, ultrasonography, computed tomography, and magnetic resonance imaging of the abdomen and pelvis, revealed no suspicious findings, except for a stable IPMN in the pancreas.

An immunological panel was also performed, including the assessment of ANCA, c-ANCA, ANA, anti-dsDNA, and anti-PLA2R antibodies, as well as C3 and C4 complement components. The results obtained allowed for the exclusion of several autoimmune diseases, including membranous nephropathy, the only primary glomerulopathy that can be diagnosed without renal biopsy. The presence of haematuria, which is not typical of this condition, further excluded the diagnosis.

Ultimately, primary glomerulopathy was considered the most likely aetiology, although a more specific diagno-

sis could not be reached. It was decided to intensify the treatment, adding oral tacrolimus to GCs. The patient was placed under further observation, waiting for the expected clinical response.

Partial, yet clinically meaningful, remission was achieved during the six-month follow-up. Urine protein, which had peaked at 6.59 g/L, dropped to 0.58 g/L, corresponding to a daily protein loss of up to 1.5 g. Creatinine decreased from >1.5 mg/dL to 1.1 mg/dL, while eGFR improved from 47 mL/min/1.73 m² to 64 mL/min/1.73 m². Once partial remission was achieved, GCs were discontinued, and the patient was maintained on tacrolimus monotherapy. Clinical and laboratory parameters remained stable over one-year follow-up at the Nephrology Clinic.

Discussion

The presented case highlights the therapeutic challenges associated with managing multiple comorbidities in an elderly patient. Determining the aetiology of NS without a kidney biopsy was the primary challenge. Histological verification provides the most reliable basis for diagnosis and, consequently, the implementation of effective treatment. In the case discussed, the diagnostic approach relied on a series of less invasive investigations and a stepwise exclusion of the most epidemiologically likely conditions.

After excluding autoimmune-related glomerulopathies, as well as plasma-cell dyscrasias or paraneoplastic syndrome, it was considered that the disease most likely belongs to the group of primary glomerulopathies. Primary causes are the most common aetiology of NS in the adult population, whereas secondary factors, often related to long-term chronic diseases, tend to predominate among the elderly [8]. Hence the importance of broad differential diagnosis, which should include screening for signs of new disorders, e.g. by performing echocardiography for amyloid deposition, as well as assessment of chronic disease control, e.g. by measuring HbA_{1c}.

As already mentioned, an accurate diagnosis requires histological evaluation; however, biopsy should be carefully considered even in the absence of contraindications as the patient's age also influences the expected treatment outcomes. Renal biopsy would probably be performed without hesitation in a younger patient's case to enable prompt initiation of aggressive and effective treatment to ensure long-term survival. In the case described, the patient was 88 years old and, although in relatively good condition for this age, his life expectancy was limited. This permits a slightly greater tolerance for residual symptoms, the long-term effects of which may not become clinically significant within his remaining lifespan. Furthermore, while the expected eGFR exceeds 90 mL/min/1.73 m² in young individuals, it begins to decline by approximately 1 mL/min/1.73 m² per year beginning from the third decade of life [9]. For this reason, eGFR of 64 mL/min/1.73 m² obtained after six months was entirely satisfactory in the described patient. It is also worth noting that the patient, initially classified as having CKD stage G3aA3, was reclassified as G2A3, further reflecting the success of the implemented therapy.

The patient's treatment initially involved high-dose GC pulses, followed by continued oral administration. In the six months that followed, an oral calcineurin inhibitor, tacrolimus, was introduced. Once partial remission was achieved, therapy was de-escalated and GCs were discontinued due to their widespread systemic effects and the risk of multiple complications associated with prolonged use. Satisfactory outcomes were maintained after one year of follow-up on tacrolimus monotherapy. If the patient's condition deteriorates, careful assessment of the potential benefits and risks of further treatment, including the possible reintroduction of GCs, should be conducted. At the same time, the focus should remain on providing the most effective therapy possible.

The partial remission achieved underscores the key conclusion of this case: nephrotic syndrome requires active treatment regardless of advanced age. Since proteinuria is the primary prognostic factor for the progression of CKD, its effective control reduces the risk of advancing to more severe disease stages [10, 11]. This is particularly important considering the number of medications taken by the patient, many of which may required dose adjustments or discontinuation. Such changes carry the risk of disrupting the fragile homeostatic balance in this 88-year-old patient [12].

Conclusions

Immunosuppressive treatment of nephrotic syndrome is crucial and can be effective even in elderly patients. Diagnostic challenges posed by the lack of possibility to perform a kidney biopsy should prompt a thorough differential diagnosis. This approach often allows for selecting effective therapy.

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Introduction