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Acute kidney injury and thrombotic microangiopathy caused by malignant hypertension in a 21-year-old patient

Ostre uszkodzenie nerek i mikroangiopatia zakrzepowa spowodowane nadciśnieniem złośliwym u 21-letniego pacjenta

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Abstract

The authors present a case of a severe cardiovascular emergency in a 21-year-old patient — malignant hypertension complicated by acute kidney injury and thrombotic microangiopathy.

Key words: malignant hypertension, hypertensive crisis, acute kidney injury, thrombotic microangiopathy; emergency

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Introduction

Malignant hypertension (MH) is an emergency defined as severe hypertension with fundoscopic changes, that can be accompanied by acute deterioration in real function, encephalopathy or acute heart failure [1]. Its prevalence is estimated at 2–10/100,000/year [2, 3]. MH most commonly appears in patients with essential hypertension, but it may also be caused by renal, endocrine, vascular or rheumatoid diseases, as well as juxtaglomerular area neoplasms [4–6]. The 5-year survival rate in patients who underwent MH ranges from <5% (if the episode was left untreated) to 90% [3, 7]. Up to 35% of patients require haemodialysis or a kidney transplant. MH-associated mortality is estimated at 2.6/ 100 patient-years (whereas essential hypertension — 0.5/100 patient-years) and renal failure is the most common cause of death [6, 7]. This unfavourable outcome constitutes an important clinical issue.

Case report

A 21-year-old, previously untreated, obese man was admitted to the Intensive Cardiological Care Unit with MH [blood pressure (BP) 250/150 mm Hg] and first symptoms of pulmonary oedema. Features of overhydration and basal crackles were noted. Anamnesis revealed high values of BP in the past 3 years (up to 180/100 mm Hg) and headaches. Deterioration of exercise tolerance, dyspnoea and oedema of the lower limbs have been observed over the last 2–3 weeks.

Electrocardiography showed sinus tachyarrhythmia (115/min). Echocardiography revealed concentric hypertrophy of the left ventricle [(LV) 60/31 mm) and left atrium enlargement (51 mm) with mild decreased LV ejection fraction [(LVEF); 50%] and diastolic dysfunction. Laboratory tests revealed impaired renal function and anaemia (Table 1). Abdominal ultrasound showed bilateral thickening of renal parenchyma up to 20 mm and increased echogenicity. Due to the deterioration of renal function, the patient was transferred to the Nephrology Clinic on the next day. Laboratory tests showed acute kidney injury (AKI). Mild hypokalaemia was present. Blood tests revealed haemolytic anaemia and thrombocytopenia, suggesting thrombotic microangiopathy (TMA) (Table 1).

Due to suspicion of rapidly progressive glomerulonephritis, antibody panel [extractable nuclear antigen (ENA), anti-glomerular basement membrane (anti-GBM), anti-neutrophil cytoplasmic antibodies (ANCA)] was conducted, but the results were negative. Endocrine causes of MH were excluded. Haemolytic activity of complement elements was within normal limits (168.10 UEq/mL; N: 79.0–187.0 UEq/mL).

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Table 1. Laboratory test values

Parameter	Intensive Cardiological Care Unit	Nephrology Clinic			Normal range
		On admission	After therapy	Follow-up laboratory tests	
Bilirubin [mg/dL]	1,40	1,60	–	0,53	0,10–1,30
Bilirubin free	–	1,28	–	–	
BNP [pg/mL]	2603,0	–	–	–	0,0–100,0
Calcium total [mEq/L]	–	–	–	4,80	4,50–5,50
CK-MB [U/l]	22	–	–	–	0–39
Creatinine [mg/dL]	4,47	4,98	4,60	3,38	0,70–1,30
Creatinine clearence (MDRD) [mL/min]	18,2	–	–	–	75,0–110,0
CRP [mg/L]	–	19,58	–	0,43	0,10–5,00
D-dimer [µg/L]	1672,0	–	–	–	0,0–500,0
Kalium [mEq/L]	3,20	3,20	5,00	5,70	3,50–5,20
Total protein [g/dL]	5,50	–	–	–	6,00–8,00
hs-troponin T [Ng/L]	92,8	–	–	–	0,0–14,1
Urine total protein [g/L]	4,11	1,35	0,51	0,35	0,05–0,08
Urea [mg/dL]	93	165	167	104	20–45
Uric acid [mg/dL]	8,50	–	–	–	3,40–7,00
RBC [M/µL]	3,01	2,76	3,41	3,0	3,90–5,70
Hb [g/dL]	9,3	8,4	10,9	9,3	13,0–17,2
Hct [%]	25,5	23,7	31,1	25,9	37–49,5
MCV [fL]	84,7	85,9	91,1	86,4	80,0–97,0
PLT [K/µL]	140	127	263	206	140,0–440,0
Reticulocytes [‰]	–	57	–	10	5–15
Phosphor [mg/dL]	–	–	7,20	4,60	2,50–4,80
Ferritine [mg/mL]	–	–	678	710	20–300
LDH [U/L]	–	782	488	142	120–230
PTH [pg/mL]	–	–	174	39	15–65
Proteinogram					
Albumin [g/dL]	3,31	–	–	–	4,02–4,76
Gamma [g/dL]	0,53	–	–	–	0,80–1,35
$Alpha_1$ [g/dL]	0,44	–	–	–	0,21–0,35

BNP — B-type natriuretic peptide, CK-MB — creatine kinase myocardial bound; MDRD — Modification of Diet in Renal Diseas; CRP — C-reactive protein; hs — high-sensitive; RBC — red blood cells; Hb — hemoglobin; Hct — hematocrit; MCV — mean corpuscular volume; PLT — platelets; LDH — lactate dehydrogenase; PTH — parathormone

After BP was stabilized, a renal biopsy was performed. It revealed chronic nephropathy with focal glomerular sclerosis, stromal fibrosis and tubular atrophy. No deposits of immunoglobulins or complement elements were found. Full obliteration of arterioles' lumen was observed, most likely due to MH.

Within the next days, the normalization of haemolysis parameters was observed, but renal function was not retrieved. Normalization of BP values and improvement of platelet count was achieved. The patient was discharged with the recommendation of ambulatory care and one-month follow-up. Amlodipine, ramipril, and methyldopa were ordered.

Follow-up laboratory tests revealed elevated creatinine and urea levels, as well as anaemia (Table 1). BP was stabilized at an optimal level (120/90 mm Hg). The patient

was referred to a nephrological and cardiological outpatient clinic. Qualification for erythropoietin treatment was recommended if anaemia persisted. Antihypertensive therapy was maintained.

Discussion

The exact cause of MH in this patient is unknown. Endocrine and rheumatoid causes have been excluded. The patient might have suffered from essential hypertension, which caused chronic nephropathy and, left untreated, lead to MH or he might have developed renal pathology first that caused secondary hypertension resulting in progression of kidney injury. The results of the kidney biopsy remained inconclusive. Although some findings of the patient's kidney biopsy were consistent with typical features of MH (narrowing of arterioles' lumen) [6], others (focal glomerular sclerosis, stromal fibrosis, tubular atrophy) were non-specific and indicated that the renal pathology was chronic. However, the biopsy was not representative, as only 5 glomeruli were sampled.

AKI is frequent in MH, as 55% of patients may present with it and the only proteinuria may be present in 10% of patients [3]. MH may cause progression of kidney function deterioration, even up to end-stage renal disease [3, 6], which is why the patient was ordered long-term nephrological follow-up. The degree of kidney injury seems to have a bigger impact on MH prognosis than the values of BP [2]. However, well-controlled BP in a long period can decrease the risk of further renal impairment [6]. Observed hypokalaemia (in contrast to hyperkalaemia, typically observed in AKI) is caused by renal TMA, in which activated renin causes secondary hyperaldosteronism resulting in potassium excretion through kidneys.

Haematologic abnormalities in the course of MH require sensible approach, as it is important to distinguish between TMA and thrombotic thrombocytopenic purpura (TTP), since they may manifest similarly but their treatment is significantly different- in TTP plasmapheresis is recommended, whereas patients suffering from MH-induced TMA respond well to hypertensive therapy [8]. Based on the lack of fever, relatively modest thrombocytopenia and the degree of kidney injury, the diagnosis of TMA was made and proper hypertensive treatment lead to improvement of haematologic parameters. Although MH-induced TMA is associated with epithelial damage, its exact pathogenesis remains unknown [8]. Some studies suggest the role of complement (especially alternative pathway) dysregulation [9], however, complement abnormalities were excluded in this case [3].

In summary, MH is a serious cardiovascular event of potential long-term complications that can occur also in young patients.

Streszczenie

Przedstawiono opis przypadku zagrażającego życiu stanu nagłego u 21-letniego pacjenta, jakim jest nadciśnienie złośliwe powikłane ostrym uszkodzeniem nerek i mikroangiopatią zakrzepową.

Słowa kluczowe: nadciśnienie złośliwe, przełom nadciśnieniowy, ostre uszkodzenie nerek, mikroangiopatia zakrzepowa, stany nagłe

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