MANAGEMENT OF PHARMACOTHERAPY IN A PATIENT WITH ANCA-ASSOCIATED VASCULITIS AND MULTIMORBIDITY, PREVENTION OF POLYPHARMACY – A CASE REPORT

Zarządzanie farmakoterapią u pacjenta z zapaleniem naczyń z przeciwciałami ANCA oraz wielochorobowością, zapobieganie polipragmazji – opis przypadku

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Abstract

Introduction: Multimorbidity is the co-occurrence of two or more chronic diseases. The prevalence of multimorbidity increases with age, although it is not limited to elderly individuals. Polypharmacy, understood as the simultaneous use of five or more medications, is closely linked to multimorbidity and increases the risk of adverse drug reactions. Antineutrophil cytoplasmic antibody-associated vasculitis predisposes patients to both multimorbidity and polypharmacy. Managing comorbid chronic conditions requires particular caution in patients with vasculitis. It is essential to account for drug interactions and balance the risk of adverse effects with the need to control disease activity. **Case report:** This case report describes a 63-year-old patient with vasculitis and multimorbidity admitted to the hospital following a traffic accident. The patient had multiple chronic conditions, including heart failure, coronary artery disease, rheumatoid arthritis, and osteoporosis. Despite treatment, the patient's condition deteriorated, necessitating a 4-month hospitalization during which the patient, due to the development of infectious complications, including sepsis, required multiple courses of antibiotic therapy and was qualified for chronic haemodialysis due to progressive renal failure. **Conclusion:** Managing multimorbidity and polypharmacy presents a significant challenge in everyday clinical practice, particularly among older patients, due to the increased risk of adverse drug reactions. An evidence-based therapeutic approach is crucial for treating complex medical conditions.

Streszczenie

Wstęp: Wielochorobowość definiuje się jako współwystępowanie co najmniej dwóch chorób przewlekłych. Częstość jej wzrasta z wiekiem, jednak jej występowanie nie ogranicza się wyłącznie do osób starszych. Polipragmazja, rozumiana jako jednoczesne stosowanie co najmniej pięciu leków, jest ściśle związana z wielochorobowością i zwiększa ryzyko wystąpienia działań niepożądanych farmaceutyków. Zapalenie naczyń związane z przeciwciałami przeciwko cytoplazmie neutrofilów predysponuje do wystąpienia zarówno wielochorobowości jak i polipragmazji. Leczenie współistniejących schorzeń przewlekłych u pacjentów z zapaleniem naczyń wymaga szczególnej ostrożności. Należy uwzględniać interakcje między lekami oraz równoważyć ryzyko działań niepożądanych z kontrolą aktywności choroby. **Opis przypadku:** W pracy przedstawiono przypadek 63-letniego pacjenta z zapaleniem naczyń i wielochorobowością, przyjętego do szpitala po wypadku komunikacyjnym. Chory był obciążony m.in. niewydolnością serca, chorobą wieńcową, reumatoidalnym zapaleniem stawów oraz osteoporozą. Pomimo leczenia jego stan pogarszał się i konieczna była 4-miesięczna hospitalizacja, podczas której z powodu rozwijających się powikłań infekcyjnych, w tym sepsy, wymagał kilkukrotnej antybiotykoterapii oraz względu na postępującą niewydolność nerek został zakwalifikowany do leczenia przewlekłymi hemodializami. **Wnioski:** Zarządzanie wielochorobowością i polipragmazją stanowi poważne wyzwanie w codziennej praktyce klinicznej, szczególnie u pacjentów starszych, ze względu na zwiększone ryzyko działań niepożądanych. Kluczowe w leczeniu złożonych schorzeń jest właściwe podejście terapeutyczne, oparte na najlepszych dostępnych dowodach naukowych.

Keywords: adverse drug reactions; multimorbidity; polypharmacy; ANCA antibody-positive vasculitis

Słowa kluczowe: działania niepożądane leków; wielochorobowość; polipragmazja; zapalenie naczyń z przeciwciałami ANCA

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Introduction

Multimorbidity is defined as the co-occurrence of at least two independent chronic conditions [1]. These may include metabolic, cardiovascular, and musculoskeletal diseases, as well as mental disorders, chronic pain, and substance abuse [2]. It should be distinguished from comorbidity, defined as the simultaneous presence of two or more disease entities that mutually influence prognosis [3]. Although the incidence of multimorbidity and comorbidity increases with age, younger populations may also be affected. As reported by Bandosz et al., the prevalence of multimorbidity was 69.3% among individuals aged 60–64 years, rising to 91% in those over 85 years, with a slight decrease after the age of 90 years [4]. Furthermore, more than 60% of patients over 80 years of age presented with at least four chronic conditions [4].

Inappropriate polypharmacy, defined as the concurrent use of five or more medications, is closely associated with multimorbidity. It increases the risk of non-compliance (non-adherence), pharmacotherapeutic errors, and adverse drug events (proportional to the number of medications used), as well as a higher incidence of hospital admissions, falls, and disability [5]. Appropriate polypharmacy, i.e., the use of multiple medications tailored to the patient's health condition, differs from inappropriate polypharmacy in that it aims to provide a broad therapeutic effect without increasing the risk of adverse effects [6]. Both appropriate and inappropriate types of polypharmacy are frequently observed among the elderly. Payne et al. [7] showed that 56% of individuals aged ≥85 years used five or more medications as compared to 9% in the 45–54 age group.

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) are a group of disorders involving severe, systemic, small-vessel vasculitis characterized by the presence of autoantibodies against proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA). AAV is classified into three types: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Although AAV can affect almost any organ, the upper and lower respiratory tract and the kidneys are most commonly and severely affected [8]. By causing vascular damage, the disease affects multiple systems and organs, contributing to dysfunction and the development of comorbidities [9].

Cao et al. [10] have shown that AAV patients experience significant polypharmacy, with over 80% taking five or more medications and more than 40% taking ten or more. Furthermore, older patients and those with additional chronic diseases were more likely to receive multidrug therapy. When multiple chronic conditions coexist, precise therapy selection is crucial. Drug interactions should be considered, and the risk of adverse reactions must be weighed against the need to control disease activity [11]. In this paper, we present a case of a patient with AAV and analyse the relationships between comorbidity, multimorbidity, and both appropriate and inappropriate polypharmacy.

The management of patients with multiple conditions should focus on optimizing pharmacotherapy and clearly defining therapeutic goals. In selected cases, de-escalating treatment may lead to more favourable clinical outcomes and a better quality of life compared with introducing modern, complex therapies.

Case report

A 63-year-old patient was transferred to a specialist hospital due to the failure of previous treatment at a lower-referral facility. Severe oedema and dyspnoea were the main reasons for admission. The man was in moderate clinical condition, with stable circulation. However, he presented with respiratory failure on admission to the Department of Internal Medicine and Nephrology. His vital signs were as follows: blood pressure 142/88 mmHg, heart rate 76 bpm, oxygen saturation 90% on room air, and 96% on passive oxygen therapy via a nasal cannula at 5 L/min. On auscultation, wheezing, isolated crackles, and decreased vesicular sounds were noted at the bases of both lungs. Massive oedema of the upper and lower extremities, sacrum, and genital area was observed. A stage 2 pressure ulcer was found over the sacrum.

The patient had been involved in a road traffic accident resulting in fractures of the third through eighth ribs on the right side a few days before admission. He had a history of multiple cardiovascular events, including two non-ST-elevation myocardial infarctions (NSTEMIs), both managed with angioplasty.

The patient had a history of multiple chronic conditions, including chronic obstructive pulmonary disease (COPD), mild aortic stenosis, hypertension (HT),

atherosclerosis, rheumatoid arthritis (RA), mixed hyperlipidaemia, reflux oesophagitis, benign prostatic hyperplasia, and mild erythematous gastropathy. He also had a history of osteoporotic Th5 and Th7 compression fractures. Additionally, alcohol dependence syndrome, nicotine dependence (40 pack-years), and colonization with multidrug-resistant microorganisms, including vancomycin-resistant *Enterococcus faecium* (VRE) and metallo-β-lactamase-producing *Klebsiella pneumoniae* were noted. He was diagnosed with pANCA-associated vasculitis coexisting with nephrotic syndrome in 2022. Renal biopsy revealed two coexisting types of glomerulopathy: necrotizing glomerulitis with crescents in some glomeruli, associated with ANCA, and membranous glomerulopathy (grade III/IV) without detectable anti-phospholipase A2 receptor (anti-PLA2R) antigen in the glomeruli.

The patient had been previously treated with 13 medications: prednisone, torasemide, acetylsalicylic acid, clopidogrel, pantoprazole, atorvastatin, bisoprolol, lercanidipine, ramipril, tamsulosin, ipratropium bromide, salmeterol, and pregabalin. He also received iron, calcium, vitamin D, and vitamin B supplements.

Laboratory tests revealed normocytic anaemia, hypoalbuminemia, elevated renal function parameters, and increased inflammatory markers; pANCA antibodies were negative on admission.

The patient was hospitalized for 4 months. After excluding acute coronary syndrome, intensive antibiotic therapy with piperacillin/tazobactam and metronidazole was initiated due to worsening dyspnoea, pain, deterioration of his general clinical condition, and elevated inflammatory markers. Blood and urine cultures were sterile.

During the subsequent days of hospital stay, the patient developed *Clostridioides difficile*-induced diarrhoea, which was treated with oral vancomycin. Transfusion of 11 units of packed red blood cells was performed due to progressive anaemia. Renal replacement therapy with haemodialysis was initiated due to worsening hypervolemia and nephrotic syndrome refractory to immunosuppressive therapy (no response to cyclosporine). Peripheral oedema decreased and respiratory function improved. However, two weeks later, the patient's condition deteriorated rapidly, with septic shock requiring catecholamine infusion. The patient was started on empirical antibiotic therapy with meropenem and vancomycin. Blood and urine cultures were sterile, but the central-line tip was positive for vancomycin-sensitive *Staphylococcus haemolyticus* (MRS, MLS_BK). Once pharmacotherapy was modified, inflammatory markers decreased, but respiratory failure persisted. Chest X-ray revealed significant right-sided pleural effusion. Purulent fluid drained from the pleura gave a positive culture for *Serratia marcescens*. Based on these findings, vancomycin was discontinued, and sulfamethoxazole/trimethoprim was added. Following a thoracic surgery consultation, continuous pleural drainage was maintained. An attempt to discontinue haemodialysis due to gradual improvement in diuresis was unsuccessful, and the patient was therefore started on chronic haemodialysis.

As a result of treatment, the patient's condition improved, with reduced oedema and dyspnoea. Persistent respiratory failure required continued supplemental oxygen therapy. The patient was discharged with a referral to a hospice.

Considering the patient's overall clinical picture and health status, the following therapeutic regimen was prescribed : home oxygen therapy, trimethoprim/sulfamethoxazole, prednisone, bisoprolol, furosemide, acetylsalicylic acid, atorvastatin, omeprazole, ipratropium bromide, salmeterol, pregabalin, acetylcysteine, and epoetin. Additionally, iron, calcium, and vitamin D supplements were prescribed. Diagnoses and treatments are summarised in Table 1.

Discussion

The presented patient faced multiple chronic conditions. During hospital stay, antibiotic therapy, blood product transfusions and pleural drainage were performed , and dialysis was started. Managing therapy in a patient with ANCA-positive vasculitis, coexisting

Table 1. Pharmacotherapy at discharge and indications

Pharmacotherapy at discharge	Indications
Prednisone	p-ANCA-associated vasculitis, membranous glomerulopathy, rheumatoid arthritis
Dialysis therapy	End-stage renal disease
Furosemide, bisoprolol , ASA	Hypertension, history of NSTEMI , heart failure
Atorvastatin	Generalized atherosclerosis, mixed hyperlipidemia
Acetylcysteine, ipratropium bromide, salmeterol	COPD
Home oxygen therapy	Chronic respiratory failure
Trimethoprim/sulfamethoxazole	Pleural empyema
Omeprazole	Erythematous gastropathy, reflux esophagitis
Epoetin, iron preparations	Anaemia
Ca2+, vitamin D supplementation	Osteoporosis
Pregabalin	Anxiety disorders, chronic pain
ANCA – anti-neutrophil cytoplasmic antibody; ASA – acetylsalicylic acid; NSTEMI – non-ST-elevation myocardial infarction; COPD – chronic obstructive pulmonary disease	

chronic conditions, and polypharmacy is a major clinical challenge due to the elevated risk of complications in this population [9]. Despite a prolonged hospital stay and numerous therapeutic challenges, optimal causal and symptomatic treatment was tailored to the patient's individual needs, resulting in clinical stabilization.

Multimorbidity and polypharmacy present significant challenges in everyday medical practice, particularly in older patients. Adding further medications in patients who are already receiving multiple drugs may not yield proportional therapeutic benefits, while the risk of adverse reactions increases with the number of treatments used. The rates of adverse effects are 4% for five, 10% for 6–10, 28% for 11–15, and up to 54% for more than 15 drugs [12]. It should be emphasized, however, that not all cases of polypharmacy are inappropriate. Implementing optimal therapy based on the best available scientific evidence is the appropriate approach for complex conditions. Neither advanced age nor the number of medications should be a barrier to effective treatment [13]. Key aspects of managing elderly patients with multimorbidity and polypharmacy include early identification of those with multiple conditions, assessment of their vulnerability to additional health problems, and shared, individualized therapeutic decisions focused on the patient's needs [14, 15]. In the described case, despite the use of twelve medications, guideline-based therapy accounting for multiple comorbidities and potential drug interactions (Tab. 1) led to an improvement in the patient's overall condition.

The patient was admitted to the hospital one year after his AAV diagnosis. Studies have shown that, compared to the general population, patients with microscopic polyangiitis face increased risks for other conditions, especially within the first two years after diagnosis. These individuals develop chronic inflammation, which contributes to vascular damage and, consequently, kidney failure, a significant risk factor. Multidrug therapy, which is associated with an increased risk of adverse effects, is an additional burden. For instance, glucocorticoids increase the risk of osteoporosis and metabolic disorders, while their concurrent use with acetylsalicylic acid promotes the development of gastric and duodenal ulcers.

A study found that 23% of patients developed multimorbidity within one year of AAV diagnosis, a rate that increased to 37% after 10 years. Patients with AAV and multimorbidity incur significantly higher healthcare costs, particularly those with three or more comorbidities [9].

Since AAV treatments may interact with other medications, the risk of interactions should be carefully assessed before introducing further treatments. For this purpose, clinicians may consider using available online tools for identifying potential risks associated with planned pharmacotherapy. When discharging a patient to hospice, it is important to prioritize maintaining the best possible quality of life. Therapy should be symptomatic, focusing on the relief of dyspnoea, pain, oedema, and anxiety.

Conclusions

Patients with AAV face an increased risk of inappropriate polypharmacy and multimorbidity due to the underlying disease and the use of multiple medications. Key elements of care for this population include accurate identification of comorbidities and optimization of therapy, taking into account the patient's individual therapeutic goals.

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