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Case Report

CASE REPORT

Development of geriatric syndromes after taking countermeasures for polypharmacy: an overlooked issue of quitting semiregular single-dose medicine

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Abstract

We report a case of an elderly woman on polypharmacy who developed appetite loss, general fatigue and muscle weakness mainly from secondary adrenal insufficiency caused by quitting one semiregular single-dose medicine. Because the degree of insufficiency was mild, her symptoms were eliminated after some time without additional treatment. The present case includes important lessons related to medication management in elderly patients. Additionally, the present case also warns us to be cautious while diagnosing geriatric syndromes as a part of the physiological aging process or additional disease symptoms. Drug-induced geriatric syndrome from quitting semiregular-use drugs should be investigated in future studies.

INTRODUCTION

Adverse drug reactions (ADRs) in elderly patients can be mistaken as part of physiological aging or an additional disease symptom (1). The differentiation of ADRs from physiological aging or disease symptoms requires utmost care, particularly when the ADRs are caused by reducing the number of drugs (2). This becomes difficult if a patient is taking semiregular-use drugs.

CASE REPORT

At the end of July 2015, a 78-year-old woman visited a general hospital for appetite loss, general fatigue and muscle weakness. Because she was taking several drugs, her doctor stopped some medications, including antidiabetics (metformin 500 mg/day and vildagliptin 100 mg/day), antihypertensive agents (amlodipine 5 mg/day, candesartan 8 mg/day and doxazocine 1 mg/day) and statins (pitavastatin calcium 1 mg/day), as these could cause ADRs. She was also directed to stop all over-the-counter and semiregular-use drugs. However, her symptoms did not improve. Over 2 months, her weight reduced by ∼2.0–50.7 kg (body mass index: 23.2 kg/m^2). By the end of September, she developed mild fever and was admitted to our hospital, accompanied by her granddaughter. Her children took turns with her hospital visits, except when she was temporarily admitted to a nearby clinic.

She had some concomitant disease, including hypertension, type II diabetes mellitus, osteoporosis, osteoarthritis, insomnia, bronchial asthma and skin rash, resulting in regular hospital visits. She regularly took more than 10 oral medications (includ-

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ing diabetic drugs, antihypertensive drugs, benzodiazepine and proton pump inhibitors). Besides hearing difficulties, she was diagnosed with mild cognitive impairment 1 year before admission. Her daughter-in-law helped her manage regular drugs. She had good adherence to regular medicines.

Although she had right knee osteoarthritis, she could walk independently. Pretibial and pedal edema was observed in both legs. She had a rash, a mild headache with no neck stiffness and a body temperature of ~37.5°C. She had no diarrhea, vomiting or abdominal pain, and she defecated every other day without laxatives. There were no signs of upper respiratory tract infections. Her muscle strength was not sufficient to open a bottle cap. Pyramidal/extra-pyramidal signs and ataxia was not observed. She had no significant family history of disease.

In blood tests, inflammation was negative (white blood cell count: 6.3×10^3/μL; C-reactive protein: 0.2 mg/dL). Eosinophilia (16.6% [1046/μL]) and hypokalemia (2.8 mmol/L) with normal serum sodium level (144 mmol/L) were observed with indications of malnutrition (albumin: 3.0 g/dL; total cholesterol: 139 mg/dL; total lymphocyte count: 29.0% [1827/μL]). Procalcitonin level was 0.08 ng/mL. Total serum calcium corrected for albumin level was 11.0 mg/dL. Zinc deficiency was not observed. Thyroid hormones were within normal range (FT3: 4.72 pg/mL; FT4: 1.63 ng/dL; human thyroid-stimulating hormone: 0.646 μIU/mL). Hemoglobin A1c, fasting blood glucose, blood urea nitrogen and creatinine levels were 6.4%, 105 mg/dL, 5.0 mg/dL and 0.60 mg/dL, respectively, with normal transaminase and biliary enzyme activity. Autoantibodies were negative, and urine was clear. Occult blood was not detected in her stool.

Chest x-ray was normal. Electrocardiogram showed sinus arrhythmia (75 bpm). Abdominal ultrasonography, computed tomography and upper gastrointestinal tract endoscopy showed no significant abnormalities.

Her mini mental state examination score was 24/30, and immediate recall failure was observed. Her geriatric depression scale score was 6/15. Magnetic resonance imaging of brain showed only bilateral hippocampal atrophy.

Immediately after admission, we stopped donepezil 5 mg/day as it was found to be prescribed for 2 months. However, improvement was negligible to alleviate malnutrition. There were no other potentially inappropriate medications (PIMs) or risky combinations in her regular drugs (3–5).

As fever was sustained at ~37.5°C, and we performed lumbar puncture; cerebrospinal fluid and laboratory tests were normal. One month after the patient's admission, her granddaughter informed that the patient sometime visited a clinic and obtained ointments and medicines to relieve itching, which she managed herself. Based on doctor's instruction, in July 2015, the family had taken these drugs away. Shortly afterwards, she developed mild fever. We asked the concerned doctor what types of medicines he had prescribed. We found she had been taking an antihistamine (d-crolefeniraminmarein acid) containing a steroid (betametazone 0.25 mg/tablet) almost every other week for 10 years, without anybody's knowledge. There seemed to be no non-adherence to the drug.

Based on the information provided, we speculated that her symptoms were related to adrenal insufficiency, derived from quitting semiregular use of this steroid-containing agent. One month after admission, we performed the adrenocorticotropic hormone (ACTH) loading test. Peak cortisol level was 16.0 μg/dL after 90 min, which was slightly lower than standard, indicating mild adrenal insufficiency. Fortunately, her appetite and pyrexia began to recover when the test was performed. Two months after admission, fever lysis was achieved without the initiation of steroid medications. Eosinophilia and hypokalemia gradually improved toward the date of discharge. On her visit to our outpatient clinic after discharge, we found that muscle strength and cognition had recovered, even though we did not restart cholinesterase inhibitors. Likewise, it was unnecessary to restart medications for diabetes mellitus and dyslipidemia. We restarted olmesartan 10 mg/day a few days after admission, during the hospital stay and after discharge. No additional antihypertensive drugs were required.

Based on her symptoms, clinical course and recovery without additional treatment, infectious, malignant and autoimmune diseases were unlikely. The ACTH test results indicated that secondary adrenal insufficiency occurred from quitting semiregular use of a steroid-containing antihistamine agent. We conclude that appetite loss, which was caused by multiple factors (i.e. hot climate, initiation of cholinesterase inhibitor), and subsequent cessation of steroid-containing agent has triggered mild secondary adrenal insufficiency. We asked her family to fix a person in charge of her health and warned them to consult a specialist when symptomatic treatment is not effective.

DISCUSSION

We described an elderly woman on polypharmacy who developed appetite loss, muscle weakness and general fatigue from multiple factors, mainly secondary adrenal insufficiency caused by quitting one semiregular single-dose medicine. Reducing polypharmacy, even semiregular-use drugs, should be performed carefully (6, 7), especially when multiple prescribers are present.

The detection of ADRs becomes difficult if symptoms are like those of geriatric syndrome (1). Distinction becomes even more difficult if the symptoms are derived from semiregular-use medicines and if stopping the prescription is the cause. Adrenal insufficiency manifests symptoms that can be confused with geriatric syndrome or multimorbidity (8). Several reports of secondary adrenal insufficiency from the steroid-containing antihistamine exist in Japan. The present case report adds an important lesson for the management of PIMs.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

This study did not receive any external funding.

ETHICAL APPROVAL

As this is a case report, we did not obtain any ethical approval. Written informed consent was obtained.

CONSENT

Written permission was granted by the patient and the primary caregiver of the patient.

GUARANTOR

Naoki Tomita.

AUTHOR CONTRIBUTIONS

.T. is responsible for patient diagnosis and care and manuscript preparation; A.I., S.O. and K.F. also helped with patient diagnosis and gave advice on the manuscript; and H.A. contributed with intellectual inputs, patient diagnosis and gave advice on the manuscript. All authors read the final version of the manuscript.

REFERENCES

1. Shah BM, Hajjar ER. Polypharmacy, adverse drug reactions, and geriatric syndromes. *Clin Geriatr Med* 2012;**28**: 173–86.
2. Mishima E, Nishimiya K, Fujiwara Y, Nishizawa M, Kiyomoto H, Ito S. Serious hypocalcemia after withdrawal of vitamin D analog in bedridden nonagenarians with previous thyroidectomy: a report of two cases. *J Am Geriatr Soc* 2016; **64**:1374–6.
3. American Geriatric Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2015;**63**:2227–46.
4. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Aging* 2015;**44**:213–8.
5. Kojima T, Mizukami K, Tomita N, Arai H, Ohrui T, Eto M, *et al*. Screening tool for older persons' appropriate prescriptions for Japanese: report of the Japan Geriatrics Society Working Group on "guidelines for medical treatment and its safety in the elderly". *Geriatr Gerontol Int* 2017;**17**:363.
6. Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, *et al*. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med* 2015;**175**:827–34.
7. Sergi G, De Rui M, Sarti S, Manzato E. Polypharmacy in the elderly: can comprehensive geriatric assessment reduce inappropriate medication use? *Drugs Aging* 2011;**28**:509–18.
8. Kojima G, Laurel P, Inaba M, Tanabe M. Unveiling adrenal insufficiency can make a difference in elderly adults. *J Am Geriatr Soc* 2014;**62**:2456–7.