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Case Report: Oseltamivir – Induced Nephropathy and Encephalopathy in an Elderly Patient with Multiple Comorbidities

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ABSTRACT

An 84- year- old man with longstanding COPD, chronic kidney disease - stage 3B, type 2 diabetes, mild pulmonary artery hypertension and benign prostatic hypertrophy presented with abruptly altered mental status one day after finishing a 15-day course of Oseltamivir for lower respiratory tract infection. He was admitted to the hospital due to unresolving lower respiratory tract infection, insufficient oral intake, leading to acute kidney injury superimposed on chronic kidney disease, and ECG incidentally revealed a recent anterolateral ST- elevated myocardial infarction. He recovered completely with multimodal supportive care, without being exposed to Oseltamivir again. This was rated as probable (score: 6) on Naranjo adverse drug response probability scale, demonstrating uncommon but dangerous dual renal and neurologic toxicity of Oseltamivir, in susceptible elderly individuals with renal impairment who need dosage modification.

Keywords: Oseltamivir, Acute kidney injury, Encephalopathy, Adverse drug reaction, Elderly.

INTRODUCTION

Oseltamivir is the first-line treatment for influenza, but in individuals with chronic kidney illness, its active metabolite oseltamivir carboxylate accumulates dangerously due to primary renal excretion. Although 1-2% of users experience neuropsychiatric adverse effects such as delirium, hallucinations or abnormal behavior, these risks greatly increase in the elderly and those with renal impairment. Acute tubular necrosis is one of the less frequently described effects of renal toxicity, which have been shown in both animal models and human case series, especially with extended or incorrect doses. Although off-label prolonged courses for non-influenza respiratory infections increase exposure hazards, the standard treatment duration is 5 days. We highlight the vital necessity for renal dosage modifications and careful monitoring by presenting a convincing case of coupled nephropathy and encephalopathy in a multimorbid elderly patient.

CASE REPORT

An 84- year- old man with uncontrolled type 2 diabetes mellitus - HbA1c of 8.5, who was also diagnosed

with COPD, stage 3b chronic kidney disease, benign prostatic hypertrophy, mild pulmonary artery hypertension, and systemic hypertension, showed up at the emergency department, with one day history of acute decrease in responsiveness. Two weeks prior, he was treated for respiratory tract infection at a local facility with oral Oseltamivir for 15 days (dose unspecified) and symptoms began immediately after completion of therapy. He did not have any known drug allergies, dysuria, angina, palpitations, loose stools, or breathlessness. There was no bleeding or infarct visible on an urgent CT scan of Brain

On admission, he had no pallor, icterus, cyanosis, clubbing, lymphadenopathy or pedal oedema, but he was sleepy and confused about time, place and people. Heart rate was 95bpm, blood pressure was 120/90 mm hg, respiratory rate was 20 breaths/min and SpO2 89 % on room air. The cardiovascular and abdominal exams were unremarkable, the respiratory exam revealed bibasilar crackles and wheezes. The CNS exam revealed a GCS score of E3 V3 M5 on admission, he was moving all extremities, there was no cranial nerve palsies, pupils were equal and reacting to light, plantar reflex was flexor response and meningeal signs were absent.

Radiological and Cardiac investigations

Chest X -ray (02/12/2025) Prominent calcific aortic knuckle: bilateral scattered non homogenous opacities suggestive of LRTI. (PIC)

ECG (03/12/2025) ST elevation in levels I, aVL; Q waves in V1-V3 (fresh anterolateral STEMI) (PIC)

USG Abdomen/Pelvis (03/12/2025) Bilateral increased renal cortical echogenicity, mild gall bladder sludge, prostate inadequately visualized.

Laboratory Findings on Admission

CBC / LFT- normal; CRP – 139.9 mg/L, Serum creatinine – 2.9 mg/dL, urea- 106.1 mg/dL, Ca-8 mg/dL, Na- 138 m Eq/L, K+ - 5.83 m Eq/L (later resolved), and negative blood/urine/ sputum cultures. Trop i- 1.0 ng/ml (later resolved).

Primary Diagnosis: Oseltamivir – induced nephropathy/encephalopathy, fresh anterolateral STEMI, COPD with acute exacerbation as LRTI, mild PAH, systemic hypertension, type 2 DM, AKI on CKD stage 3b and BPH.

Treatment and Hospital Course

The patient was admitted under General Medicine due to poor oral intake and altered sensorium, a nasogastric tube was placed for feeding. Intravenous ceftriaxone was started empirically after collecting cultures for the respiratory tract infection, in addition to IV fluids and supportive measures. After optimal fluid resuscitation, his renal parameters reverted to baseline. Conservative treatment was recommended after consulting a cardiologist for STEMI.A decrease in haemoglobin led to an anaemia workup (low serum iron), which was treated with oral iron supplements; stool tests came out negative. As his oral tolerance returned and his level of consciousness improved, the NG tube was taken out. Through-out, he maintained hemodynamic stability

After 7 days of observation in the ward, he became fully conscious. Fluid intake matched urine output. He was mobilized out of bed by the physiotherapists, chest signs cleared, and all tubes were removed, including Foley's catheter. ECG and Lab readings returned to normal.

DISCUSSION:

Oseltamivir dosing requires adjustment in renal impairment (e.g. 75 mg every other day for CrCl 10-30mL/min); as unmonitored use leads to carboxylate accumulation, proximal tubular toxicity and osmotic nephrosis. Neurologically, the parent compound crosses the blood-brain barrier and inhibits nicotinic

receptors and monoamine oxidase-A, causing encephalopathy, particularly delayed onset in the elderly following extended exposure. Temporal association (+2), dechallenge improvement (+2), objective evidence (+1), no other causes (+1), dose response relationship (+) and prior literature (+1) are all reflected in this patient's Naranjo score of 6 (probable causality). Geriatric CKD presentations, in contrast to acute paediatric instances, frequently show subtle delirium that quickly goes away after withdrawal.

A number of patient – specific risk factors matched the body of research on Oseltamivir toxicity. He was 84-years-old, he fell into the high -risk- age group >65 years where neuropsychiatric odds ratios reach 1.9. Additionally, he had chronic kidney disease at baseline, with creatinine rising to 2.9 mg/dL, which is similar to 0.67% AKI incidence from accumulation in prophylactic trials. His numerous comorbidities (COPD, diabetes, hypertension, PAH and BPH) increased CNS vulnerability, through polypharmacy and decreased physiologic reserve and the unusual 15-day course exceeded standard 5-day therapy, resulting in dose-dependent toxicity as reported in extended-use cases. The ECG changes on admission may have been an incidental finding, though acute H1N1 like viral infections produce myocarditis, this patient presented after 15 days of illness, however, Oseltamivir is known to produce bradycardia and QT prolongation. (Ref -10)

Multidisciplinary involvement was crucial; rechallenge was not possible due to ethical limits. Limitations include a lack of drug levels and an unclear specific dosage of oseltamivir, despite a robust clinical-radiologic connection.

CONCLUSION:

This case clearly demonstrates the often-overlooked combined nephrotoxic and neurotoxic risks of Oseltamivir in elderly patients with chronic kidney disease (CKD) who have not had their dosage adjusted. During extended treatment, healthcare providers need to calculate the creatinine clearance (CrCl), adhere to renal dosing guidelines, and monitor serum creatinine levels along with mental health status. In patients with multiple comorbidities, early identification and discontinuation of the medication typically lead to full recovery and help prevent longer hospital admissions

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