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## REFERENCES

1. Handke M, Harloff A, Bode C et al. Patent foramen ovale and cryptogenic stroke: A matter of age? *Semin Thromb Hemost* 2009;35:505-514.
2. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: An autopsy study of 965 normal hearts. *Mayo Clin Proc* 1984;59:17-20.
3. Overell JR, Bone I, Lees KR. Interatrial septal abnormalities and stroke: A meta-analysis of case-control studies. *Neurology* 2000;55:1172-1179.
4. Cabanes L, Mas JL, Cohen A et al. Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age. A study using transesophageal echocardiography. *Stroke* 1993;24:1865-1873.
5. Adams HP Jr., del Zoppo G, Alberts MJ et al. Guidelines for the early management of adults with ischemic stroke. A Guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups. *Stroke* 2007;38:1655-1711.
6. Wu LA, Malouf JF, Dearani JA et al. Patent foramen ovale in cryptogenic stroke. Current understanding and management options. *Arch Intern Med* 2004;164:950-956.
7. Lethen H, Flachskampf FA, Schneider R et al. Frequency of deep vein thrombosis in patients with patent foramen ovale and ischemic stroke or transient ischemic attack. *Am J Cardiol* 1997;80:1066-1099.
8. Caputi L, Carriero MR, Falcone C et al. Transcranial Doppler and transesophageal echocardiography: Comparison of both techniques and prospective clinical relevance of transcranial Doppler in patent foramen ovale detection. *J Stroke Cerebrovasc Dis* 2009;18:343-348.
9. Kefer J, Sluysmans T, Hermans C et al. Percutaneous transcatheter closure of interatrial septal defect in adults: Procedural outcome and long term results. *Catheter Cardiovasc Interv* 2011 Apr 26. doi: 10.1002/ccd.23119. [Epub ahead of print].

## A CASE OF PHYSICAL AND MENTAL ADVERSE DRUG REACTIONS ASSOCIATED WITH LEVETIRACETAM IN POST-STROKE EPILEPSY

*To the Editor:* A 72-year-old man was admitted with a seizure in March 2011. He had suffered a right total anterior circulation stroke in September 2010 with left hemiparesis, facial palsy, and dysphasia. Subsequent successful rehabilitation saw him discharged home, walking independently with a cane. His GP had started him on low-dose citalopram for reactive depression secondary to his stroke, but he was cognitively unimpaired.

Admission medications were amitriptyline 25 mg, citalopram 20 mg, indapamide 2.5 mg, digoxin 125 µg, simvastatin 40 mg, and codeine 30 mg. (Warfarin had been commenced for atrial fibrillation but discontinued after a fall and subdural hematoma.) Initially, he was postictal but examination and baseline investigations were normal other than mild left-sided weakness. A computed tomography (CT) scan showed the old infarction and chronic subdural hematoma. After discussion with neurology, he was

started on levetiracetam 250 mg twice daily with the intention of uptitrating to a treatment dose of 1,500 mg. Baseline function was quickly regained, and his discharge was planned.

## THE CASE

Over 7 days, he deteriorated, becoming drowsy and incontinent and displaying reduced mobility. Neurological examination showed increased weakness on the left side and an Abbreviated Mental Test Score (AMTS) of 6 out of 10, which had been 10 out of 10 previously. Blood tests were performed and were unremarkable, with no evidence of sepsis. A repeat CT scan excluded further bleeding or other pathology, but his AMTS dropped further to 4 out of 10, and power on neurological examination was now scored 0 out of 5 on the left side. He developed significant signs of depression, including reduced eye contact and interaction and a slow monotonous voice, followed by frank psychotic symptoms (persecutory delusions and hallucinations). A psychiatry review was requested and concluded that he had depression and acute delirium. After further neurological review, lamotrigine 25 mg was substituted for levetiracetam.

Four days after stopping levetiracetam, he had significantly improved and was orientated to time and place, his paranoia had resolved, and he was walking with his cane and following instructions. His AMTS had returned to 10 out of 10, and power was 3 out of 5 on the Medical Research Council scale on the left side, and he was discharged home.

## DISCUSSION

Levetiracetam can cause dizziness, fatigue, headache, somnolence, and rarely psychiatric disorders.<sup>1</sup> It is believed that these adverse reactions are not related to the speed of introduction of the drug.<sup>2</sup> Having reviewed the current published literature, reactions in terms of depression and psychosis such as in this case are well described in adults and children. There are case reports of psychosis in adolescence<sup>3</sup> and childhood.<sup>4</sup> Both of these reports showed the symptoms appearing and resolving over a period of time similar to that in the current case. Small studies in 2003 reported psychiatric side effects with the use of levetiracetam;<sup>5</sup> 10.1% of 517 participants experienced psychiatric side effects. This was again documented in 2007,<sup>6</sup> with a positive association with previous personal and psychiatric history.

Fewer data were found on psychiatric side effects in older adults. A few case reports that described delirium and depression were found<sup>7,8</sup> but no significant evidence or study data. Also, in the current case, the physical deterioration preceded delirium, which appeared the following week. This has not been previously reported as a side effect of levetiracetam.

The deteriorations in physical and subsequently mental health all followed commencement of the drug. If this is assessed as a reaction using the Naranjo criteria,<sup>9</sup> the score is 6 out of 10, indicating a probable adverse drug reaction. There is no competing explanation for this individual's deterioration and rapid recovery. The symptoms

started to develop just days after he started levetiracetam and resolved within 5 days of cessation.

The reduction in mobility and the psychotic symptoms were most likely due to levetiracetam. Given that there is not sufficient literature on such side effects involving older adults and the unique feature of reduced mobility, it was felt that this warranted highlighting.

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## REFERENCES

1. Wilmore LJ, Wheless JW, Pellock JM. Adverse effects of anti-epileptic drugs. In: Pellock JM, Dodson WE, Bourgeois BF. *Pediatric Epilepsy*. New York: Demos. 2001, pp 343–355.
2. Cereghino JJ, Biton V, Abon-khalil B et al. Levetiracetam for partial seizures. *Neurology* 2000;55:236–242.
3. Kossoff EH, Bergey GK, Freeman JM et al. Levetiracetam psychosis in children as epilepsy. *Epilepsia* 2001;42:1611–1613.
4. Youroukos S, Lazopoulou D, Michelakou D et al. Acute psychosis associated with levetiracetam. *Epileptic Disord* 2003;2:117–119.
5. Mula M, Trimble MR, Yuen A et al. Psychiatric adverse events during levetiracetam therapy. *Neurology* 2003;61:704–706.
6. Mula M, Trimble MR, Sander JW. Are Psychiatric adverse events of antiepileptic drugs unique entity? A study on topiramate and levetiracetam. *Epilepsia* 2007;48:2322–2326.
7. Foley KT, Bugg KS. Separate episodes of delirium associated with levetiracetam and amiodarone treatment in an elderly woman. *Am J Geriatr Pharmacother* 2010;8:170–174.
8. VandeGriend JP, Linnebur SA, Bainbridge JL. Probable Levetiracetam associated depression in the elderly: Two case reports. *Am J Geriatr Pharmacother* 2009;7:281–284.
9. Naranjo CA, Busto U, Sellers EM et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–245.

## AN UNUSUAL CASE OF CHOLECYSTITIS AND LIVER ABSCESES IN AN OLDER ADULT

*To the Editor:* A 76-year-old man was admitted to the emergency department (ED) for anorexia, weight loss of 5 kg in 2 months, fatigue, and anhedonia after his sole sister's death. He had no other complaints: no abdominal pain, transit abnormalities, fever, or chills. He had a history of type 2 diabetes mellitus, severe chronic kidney failure, peripheral neuropathy, hypertension, stage 2 lower extremity vascular disease, hypothyroidism, and atrial fibrillation. His regular medication consisted of acetylsalicylic acid, venlafaxine, hydrochlorothiazide, torasemide, levothyroxine, atenolol, and insulin.



Figure 1. Abdominal computed tomography scan showing acute cholecystitis.

Upon admission, he was awake and responsive but weak and appeared depressed. Temperature, blood pressure, and heart rate were normal. Abdominal examination showed active bowel sounds, no tenderness or rebound tenderness, and no masses. Lower liver border was not palpable, and Murphy maneuver was negative.

Initial laboratory values showed normocytic anemia (hemoglobin 10.0 g/dL), leukocytosis with no left shift (white blood cell count 14,000 cells/ $\mu$ L) and C-reactive protein (CRP) of 246 mg/dL. Electrolytes were normal despite severe chronic renal failure (calculated creatinine clearance of 21 mL/min according to the Cockcroft formula). Liver enzymes were normal except for a slightly high gamma-glutamyltranspeptidase (76 IU/L, normal <40 IU/L) and bilirubin (1.75 mg/dL, normal <1.46 mg/dL).

Because of suspected depression, he was referred to a specialized geriatric ward where a combined follow-up by geriatricians and psychiatrists is provided. During the following days, he developed no new symptoms but still refused any food. Biological inflammatory markers remained high. Liver enzymes remained unchanged except for normalization of bilirubin values. Chest X-ray was normal. Urine and blood cultures were negative. The dose of venlafaxine was doubled at admission to 75 mg/d and thereafter remained unchanged.

Because of persistent inflammation, he underwent a thoracoabdominal computed tomography scan without contrast injection. The imaging revealed a dilated gallbladder (9.6  $\times$  5.3 cm in the axial cross-section) with thickened walls, compatible with acute cholecystitis, and multiple hypodense lesions of liver segments V and VIII, suggestive of liver abscesses (Figure 1).

Cholecystectomy and surgical drainage were performed. Cultures grew *Escherichia coli*. He was prescribed ceftriaxone for 3 weeks. He was discharged 2 months later, after a normal abdominal ultrasound and major mood improvement. Signs and symptoms consistent with normal grieving remained.

## DISCUSSION

We present the case of an older adult with acute cholecystitis and multiple liver abscesses, with no suggestive symptoms except for anorexia and biological signs of inflammation. Atypical presentation of acute cholecystitis is frequent in older adults, with 5–25% presenting without