Lamotrigine in the treatment of psychotic depression associated with hereditary coproporphyria – Case report and a brief review of the literature

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Objective: We report a successful treatment with lamotrigine of a patient with hereditary coproporphyria presenting with affective and psychotic symptoms. **Case report:** M.F., a 38-year-old, single woman was admitted to an acute psychiatric ward because of suddenly emerging psychosis. Ms F's hereditary coproporphyria was diagnosed 9 years before the current admission. While on treatment with olanzapine (20mg/day) the psychotic symptoms have gradually disappeared. In view of her significant mood fluctuations predominantly with depressed phases, lamotrigine was started and titrated up to 125 mg/day. Ms F's mood gradually became euthymic, suicidal ideations and anxiety disappeared. At 5-month follow-up, while still on lamotrigine, her porphyria was asymptomatic. **Conclusion:** To the best of our knowledge, this is the first report about the safe administration of lamotrigine in hereditary coproporphyria. Lamotrigine did not trigger an acute porphyric attack as confirmed by clinical and laboratory findings.

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Keywords: lamotrigine; hereditary coproporphyria; psychotic depression

Porphyrias are inherited metabolic disorders of the hem biosynthesis (Stölzel et al. 2010). Each porphyria type is originated from the decreased function of one of the enzymes of the hem biosynthesis pathway resulting in increased secretion of porphyrins and porphyrin precursors (van Serooskerken et al. 2010). From a practical point of view, the most appropriate classification of porphyrias is based on the clinical presentation distinguishing acute and non-acute porphyrias (van Tuyll et al. 2010). Acute porphyrias can be triggered by endogenous factors (puberty, pre-menstruation and pregnancy) and physical or psychological stress such as starvation, infections or porfirinogenous drugs (Tasnádi et al. 2003). An acute attack can be manifested with abdominal cramps, constipation, vomiting, muscle weakness, tachycardia, hypertension and red-colored urine. Acute porphyrias are commonly associated with neuropsychiatric syndromes such as anxiety, depression, delirium and psychosis (Millward et al. 2005, Burgovne et al. 1995).

The prevalence of porphyria in psychiatric patients is 0.21-0.48% higher than in the general population (Burgovne et al. 1995, Tishler et al. 1985). The list of psychotropic drugs deemed to be safe in porphyrias i.e. not provoking acute porphyric attacks include mirtazapine, mianserine, fluoxetine, citalopram, clozapine, haloperidol, olanzapine, fluphenazine, perphenazine, sulpiride, amisulpride, lithium, clonazepam, and zopiclone (American Porphyria Foundation. Drug Database, http://www.porphyria-europe.com, http://www.cardiff-porphyria.org, The Norwegian Porphyria Centre (NAPOS). The Drug Database for Acute Porphyria). The management of psychiatric symptoms in patients with porphyria is challenging, because there are no sufficient data about the use of novel psychiatric drugs in this patient population

(Ghosh et al. 2006). Case reports suggest that clomipramine, clonazepam, chlorpromazine, dothiapine, olanzapine, sertraline, risperidone, venlafaxine, clozapine, buspirone, trazodone and lorazepam are safe in porphyria while imipramine worsens porphyria (Holroyd et al. 1999)

The mood-stabilizing effect of lamotrigine and its role in preventing depressive episodes is well documented (Fountoulakis et al. 2012) but there are limited data about its use in acute porphyrias. Only the Porphyria Association of the United Kingdom considers lamotrigine safe (http://www.cardiff-porphyria.org) while in the Norwegian Porphyria Centre (NAPOS) database lamotrigine appears in the "probably not porphyrinogen" group. This database has a registry of 6 patients who received lamotrigine without adverse effects. Gregersen (Gregersen et al. 1996) described a patient with acute porphyric attack, multi-organ failure, and disseminated intravascular coagulation while on lamotrigine and considered this as a rare side-effect of the lamotrigine. He rated the risk of provoking an acute porphyric attack with lamotrigine as low. Lamotrigine caused porphyrin accumulation in chicken hepatic cells therefore lamotrigine was not recommended in porphyria (Hahn et al. 1997). In one of the three cases, reported by Winkler et al. (Winkler et al. 2005) seizure activity of a patient with acute intermittent porphyria worsened after introducing lamotrigine, while lamotrigine improved the neurological symptoms in patient with variegate porphyria.

We report a successful and uncomplicated treatment with lamotrigine of a patient with HCP presenting with affective and psychotic symptoms.

CASE REPORT

M.F., a 38-year-old single woman was admitted to an acute psychiatric ward because of suddenly emerging psychosis. On admission she responded to questions circumstantially and displayed loose associations to the point of incoherence. She was overwhelmed by anxiety and felt that she was the centre of the world. She heard malicious voices of accusatory and commanding nature.

A few months before the current admission, Ms F. became depressed. She also reported fluctuating mood over the last few years having one manic and several depressive episodes. While manic, she felt capable of everything; she wore colorful dresses, engaged in irresponsible sexual relationships and had difficulties in reality testing. The depressive and manic symptoms resolved spontaneously.

Ms F's hereditary coproporphyria was diagnosed 9 years before the current admission. She had two acute phases, with increased coproporphyrin excretion, tremor, palpitation and dyspnea. She denied using alcohol or other substances.

Ms F's father had alcohol dependence and her mother also had porphyria. On admission Ms F's somatic and neurological status was negative. Routine laboratory tests and urine drug screen were negative and so was a brain CT scan. Psychological tests confirmed delusional thinking and severe depression (Beck Depression Inventory: 27 points). Differential diagnoses according to ICD-10 (World Health Organisation 1992) included "Organic affective disorder" (F.06.30), "Bipolar disorder–psychotic depression" (F31.50), and "Schizoaffective disorder–depressed type" (F25.10).

After introduction of olanzapine, (20 mg/day) the psychotic symptoms have gradually disappeared. In view of her significant mood fluctuations with predominance of depressed phases that persisted despite adequate treatment with olanzapine for adequate time, lamotrigine was started and titrated up to 125 mg/day. Ms F's mood gradually became euthymic, the suicidal ideations and anxiety disappeared and after 63 days in the hospital, she was discharged.

Ms F's pharmacotherapy was monitored by the National Porphyria Centre, where she had been treated for her porphyria. At 5-month follow-up, while still on lamotrigine, her porphyria was asymptomatic. A 24-hour urine collection showed that her coproporphyrin, uroporphyrin, porfobilinogen and delta – aminolevulin acid levels were within normal limits.

CONCLUSION

Psychopharmacotherapy for patients with porphyria requires a cautious approach. Available guidelines do not provide unequivocal assistance concerning the use of psychotropic drugs. As for lamotrigine, at this juncture there are not enough data supporting its safety despite claims to the contrary (http://www.cardiff-porphyria.org).

To the best of our knowledge, this is the first report about the safe administration of lamotrigine in hereditary coproporphyria. Lamotrigine did not trigger an acute porphyric attack as confirmed by clinical and laboratory findings. The clinical picture was stable on lamotrigine at the 5-month follow-up.

Further case reports and case series are needed to reach a firm conclusion about lamotrigine's safety in porphyria.

Conflict of interest: The authors report no conflict of interest.

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A lamotrigin szerepe a herediter koproporfíriához társuló pszichotikus depresszió kezelésében – esettenulmány és rövid irodalmi áttekintés

Célkitűzés: Tanulmányunkban egy herediter koproporfíriában szenvedő, affektív és pszichotikus tünetek miatt akut pszichiátriai osztályra felvett beteg lamotriginnel történt sikeres kezelését ismertetjük. **Esetleírás:** F. M. 38 éves nőbeteg, aktuális, első pszichiátriai osztályos felvételére sürgősséggel került sor pszichotikus állapot miatt. Herediter koproporfíriáját 9 évvel az aktuális felvételt megelőzően diagnosztizálták. 20 mg olanzapin beállítása után a beteg pszichotikus tünetei háttérbe szorultak. Figyelembe véve a hangulati fluktuációra vonatkozó anamnesztikus adatokat és főként depresszív epizódok jelentkezését, lamotrigin alkalmazását kezdtük el. 125mg/nap lamotrigin alkalmazása mellett a beteg hangulata eutímmé vált, öngyilkossági gondolatai és szorongása megszűnt. A lamotrigin beállítását követő ötödik hónapban a lamotrigin alkalmazása mellett végzett kontrollvizsgálat a porfíriát inaktívnak mutatta. **Megbeszélés:** Lamotrigin sikeres és komplikációmentes alkalmazásáról porfíriában tudomásunk szerint jelen beszámoló az első az irodalomban. A fent leírt esetben akut porfíriás rohamra utaló klinikai vagy laboratóriumi eltérések a gyógyszer alkalmazása mellett nem jelentkeztek.

Kulcsszavak: lamotrigin, herediter koproporfíria, pszichotikus depresszió