Initial psychotic episode in a patient with an inborn error of cobalamin metabolism methylcobalamin type cblG deficiency: A case report

ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY

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PSYCHIATRY RESIDENCY

Background

- Little is known about psychiatric complications of inborn errors of intracellular cobalamin metabolism.
- Patients with these errors can develop seizures, nystagmus, hyperreflexia, and developmental delay.
- Cobalamin G (CbG) deficiency results in elevated homocysteine and intrinsic vitamin B12 deficiency.
- Some patients with CbG deficiency develop psychosis.

Objectives

- Describe the relationship between cobalamin deficiency and psychosis.
- Understand the relationship between transient biomarker elevation and psychosis.
- Assess treatment options for patients with metabolic cobalamin deficiency.

K_i Values (D2)

Name	K_i Value
Amisulpride	1.3
Aripiprazole	0.95
Chlorpromazine	2.0
Clozapine	431
Fluphenazine	0.54
Haloperidol	2
Olanzapine	72
Quetiapine	567
Risperidone	4.9
Ziprasidone	4.0

Adapted from Richtand, N. *et al* (2007).

Case Presentation

23-year-old Caucasian male who presented to the Emergency Department with parents (guardians) in October 2021 with encephalopathy and psychosis. Parents report one month of progressive gait instability accompanied initially by apathy progressing to persecutory delusions, disorganization, and auditory and visual hallucinations. Psychosocial stressors include isolation due to the COVID-19 pandemic and loss of employment.

Patient had no past psychiatric, substance abuse, or family history.

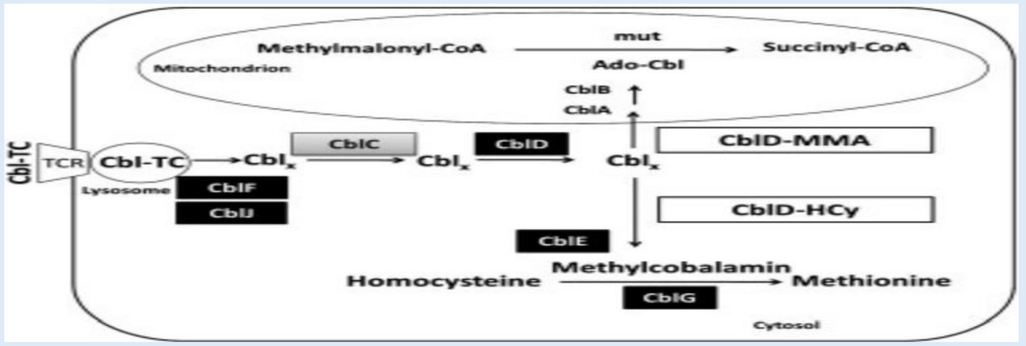
Medical history includes cobalamin G deficiency, seizures, hearing loss, intellectual disability, chronic kidney disease, obstructive sleep apnea on CPAP, hypothyroidism, and hyperlipidemia.

Notable exam findings: Minimally conversational, psychomotor retardation, horizontal nystagmus, oriented, mood neutral, affect flat, disorganized speech with decreased rate and volume, disorganized thought process, persecutory delusions, responding to auditory and visual hallucinations, impaired and poor insight and judgment.

Pertinent Lab Findings	
Creatinine	1.81 ↑
Phosphorus	5.8 ↑
Homocysteine	336 ↑
Vitamin B12	>4000 ↑
5-HIAA (CSF)	28 ↓
Homovanillic Acid (CSF)	95 ↓
3-O-methyldopa (CSF)	154 ↑

Historical Homocysteine Levels	
8/2022	249
5/2022	>250
1/2022	328
10/2021	336
10/2020	233
8/2019	193

Cobalamin Deficiency



From Schiff and Blom (2012).

Treatment Course

- Trial of risperidone 2mg nightly started causing sedation, parents wanted to switch.
- Low-dose olanzapine 2.5mg nightly provided, increased to 7.5mg nightly with partial response.
- Given the importance of high D2 receptor affinity, switched to aripiprazole 10mg nightly.
- Resolution of psychotic symptoms.

Discussion

- Emotional stress could have contributed to elevated homocysteine.
- Elevated homocysteine is observed in neuropsychiatric disorders and correlates with inflammatory markers.
- Aripiprazole and risperidone have been shown to decrease inflammatory biomarkers in patients with psychosis.

Next Steps

- Discussed outcome with advocacy group in which patient is active.
- Coordinated with genetics team to adjust treatment plan to reduce homocysteine.
- Communication with researcher developing protocols to manage patients with cobalamin deficiency.
- Stop antipsychotic due to suspected symptoms resolution with normalizing homocysteine level.

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