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Case Report: Vitamin B12 deficiency in an adolescent female with Polycystic Ovarian Syndrome

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Dear editor

We describe for the first time a case of vitamin B12 deficiency associated with metformin use in an adolescent girl with PCOS. Polycystic ovarian syndrome in adolescent girls is associated with hyperandrogenism, irregular menses, metabolic syndrome and insulin resistance. [1] Metformin ameliorates insulin resistance and can restore regular menses. Metformin use has been linked to vitamin B12 deficiency in adult patients with type 2 diabetes but not in women with PCOS.[2] B12 body stores take years to deplete and therefore it is uncommon to find B12 deficiency in adolescents. [3, 4]{Rasmussen, 2001 #832} A 15 1/2 year old girl presented to NIH for further management for PCOS. After menarche at the age of 11 years, her menses were always irregular. She was obese since the age of three years and she was not vegetarian. Her past medical history was significant for atypical Asperger's syndrome and depression, for which she was treated with several psychotropic medications. She had no family history of PCOS or Type 2 Diabetes. She met the NIH criteria for PCOS. For her underlying PCOS, the patient was treated with regular metformin 1000mg once daily for approximately one year and then the dose was increased to 2000mg once daily for a second year. When first evaluated at the NIH, serum vitamin B12, homocysteine, methylmalonic acid, and folate concentrations were measured (Table 1). Other causes of vitamin B12 deficiency such as atrophic gastritis and folate deficiency were ruled out based on finding no measurable intrinsic factor or parietal cell antibodies, normal pepsinogen, gastrin and folate concentrations and she wasn't taking proton pump inhibitor medications. Treatment with oral cyanocobalamin was initiated at a dose of 1000 µg daily. Repeat assessment after one month's treatment showed a normal B12. The family reported improvement of her psychiatric symptoms after serum vitamin B12 normalization. Vitamin B12 supplementation was discontinued and the patient returned 5 months later. Her serum B12 concentration had decreased, but remained normal. Due to the lack of available large studies in adolescent girls with PCOS it is premature to suggest universal screening for vitamin B12 deficiency in adolescent girls with PCOS. Clinicians should nonetheless consider assessing vitamin B12 status in adolescent girls treated with metformin who also have other risk factors for B12 deficiency such as obesity.

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Table 1

Labs at presentation and after treatment

Laboratory Assessment	First presentation at NIH	After 1 month of treatment	After 5 months of treatment
Vitamin B12 (normal 193 – 982 pg/mL)	177	532	263
Homocysteine (normal 0–15 umol/L)	10	6	8
Methylmalonic acid (normal <0.40 nmol/mL)	0.71	0.14	0.41
Folate (normal 3–17 ng/mL)	16	20.8	19
Hemoglobin (g/dL)	12.5		
Hematocrit (%)	37.5		
MCV (normal 79.4–94.8 fL)	94.2		
Androstenedione (normal 17–175 ng/dL)	328	273	
Testosterone ng/dL	49.5	24.7	
Fasting glucose mg/dL	101	100	
Fasting insulin uIU/mL	19.8	13.9	