

## An Infant Refugee with Anemia and Low Serum Vitamin B<sub>12</sub>

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### CASE DESCRIPTION

An infant with a history of hypotonia, developmental delay, and inadequate nutrition was evaluated. The patient was the offspring of a consanguineous (first cousin) Syrian couple, born at term in Syria after an unremarkable pregnancy. His neonatal course was unremarkable. At the age of 7 months he presented with intermittent diarrhea, fever, and poor feeding. His symptoms progressed, and at 11 months (upon migration to Canada) he was admitted to the hospital for weight loss, decreased urine output, fever, and the loss of skills such as babbling, rolling over, or sitting without support. At the time of admission, he was only taking maternal breast milk.

On physical examination, he was pale and irritable. There were no dysmorphic features. He had limited antigravity movements, hepatomegaly, and a systolic ejection murmur. His initial chemistry and hematology evaluation included hemoglobin level of 45 g/L (reference interval, 100–140 g/L), with moderate microcytosis and macrocytosis, mild polychromasia, and schistocytes. His reticulocyte count was  $168 \times 10^9/L$  (reference interval, 10–100  $\times 10^9/L$ ). Plasma vitamin B<sub>12</sub> was <62 pmol/L (reference interval, 119–1164 pmol/L), and plasma folate was 33.9  $\mu\text{mol}/L$  (reference interval, >23  $\mu\text{mol}/L$ ). A nasopharyngeal swab was positive for rhinovirus.

Metabolic studies were obtained (Table 1). The total and free carnitine concentrations were normal. Urine organic acids identified an increased methylmalonate peak of >200 mmol/mol creatinine (reference interval, 0.58–3.56 mmol/mol creatinine), and his acylcarnitine profile included increased propionylcarnitine of 2.26  $\mu\text{mol}/L$  (reference interval, <1.08  $\mu\text{mol}/L$ ). The total plasma homocysteine (Hcy) was increased at 239  $\mu\text{mol}/L$  (reference interval, 2.9–10  $\mu\text{mol}/L$ ). Methionine concentration in plasma was normal at 25  $\mu\text{mol}/L$  (reference interval, 3–29  $\mu\text{mol}/L$ ), and the cystine concentration was 1  $\mu\text{mol}/L$  (reference interval, 23–68  $\mu\text{mol}/L$ ).

He was treated with packed red blood cells, iron supplementation, fortified formula through nasogastric feeds, and an intramuscular injection of cyanocobalamin (1000  $\mu\text{g}$ ).

Forty-eight hours after B<sub>12</sub> administration and transfusion, his urine methylmalonate had normalized (Table 1). The methionine was now greatly increased at 781  $\mu\text{mol}/L$ . His acylcarnitine profile had normalized. His total Hcy remained high at 146.1  $\mu\text{mol}/L$ . He was started on vitamin B<sub>6</sub> 50 mg twice daily, and blood testing was repeated. These studies showed a sustained increase in total Hcy of 119  $\mu\text{mol}/L$  and a high methionine concentration of 917  $\mu\text{mol}/L$ .

Table 1. Patient values and patterns seen typically with select disorders.						
Analyte	Admission	2 days post-B <sub>12</sub>	2 days post-B <sub>6</sub>	B <sub>12</sub> deficient	Methionine synthase	CBS
Homocysteine, $\mu\text{mol/L}$ ; reference interval, 2.9–10 $\mu\text{mol/L}$	239	146	119	↑	↑↑	↑↑
Methionine, $\mu\text{mol/L}$ ; reference interval, 3–29 $\mu\text{mol/L}$	25	781	917	↓ or nl <sup>a</sup>	↓↓	↑↑
Methylmalonate, mmol/mol Cr; reference interval, 0.58–3.56 mmol/mol	200	<20	0	↑↑	nl	nl
Propionylcarnitine (C3), $\mu\text{mol/L}$ ; reference interval, <1.08 $\mu\text{mol/L}$	2.26	1.08	<1	↑	nl	nl
Cystine, $\mu\text{mol/L}$ ; reference interval, 23–68 $\mu\text{mol/L}$	1	17	16	nl	nl	↓

<sup>a</sup> Normal.

#### QUESTIONS TO CONSIDER

- What potential disorders are suggested by the increases in serum methylmalonate and plasma homocysteine concentrations?
- What is the most likely diagnosis given the increased methionine and plasma homocysteine concentrations after vitamin B12 administration?
- What testing could be done to confirm the patient's diagnosis?

#### Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the November 2018 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol64/issue11> and follow the link to the Clinical Case Study and Commentaries.

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