Methylmalonic Acidemia in Mainland China

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Methylmalonic acidemia (MMA, OMIM 251000), an autosomal recessive disorder of protein metabolism, results from a deficiency of methylmalonic-CoA mutase or enzyme defects in cobalamin (vitamin B₁₂) metabolism. MMA was first described in mainland China in 2000, but the incidence of this disorder in the Chinese population is unknown. Screening of inborn errors of metabolism was conducted in 8,611 sick Chinese infants by tandem mass spectrometry and gas chromatography/mass spectrometry. In this sample, 652 cases of inborn errors of metabolism were identified. Almost one fourth of these cases (24.54%) were suffering from MMA [1–3]. To date, 400,000 babies have been screened for MMA in Beijing and Shanghai. Of these, 15 patients were diagnosed with the disease. Based on this date, our estimated incidence in mainland China is 1 in 26,000 infants.

Further reports have identified a total of 354 patients with MMA in mainland China since the initial report in 2000. Of those, 149 were found to have combined MMA and homocystinemia while 205 cases had isolated MMA. Few of our patients had a family history (7.91%), and none was diagnosed prenatally. In treatment, 272 (76.84%) were found to be vitamin B₁₂-responsive while 56 cases were vitamin B₁₂-nonresponsive. Some of our patients (n = 17) presented with secondary MMA due to maternal vitamin B₁₂ deficiency. Clinical symptoms were variable and ranged from 2 h to 34 years. Some became symptomatic in the neonatal period (12.71%) but most patients developed symptoms before their first birthday (61%). Initial presentation included recurrent vomiting (98 patients) and hypoglycemia (56 patients).

Ninety-six patients in our sample developed renal injury and 211 presented with delayed physical development and mental retardation. MRI/CT demonstrated an abnormal signal in 111 cases (31.36%). Most of our patients were treated with hydrocobalamin injections (81.64%) and carnitine via injection or oral administration at a dose of 50–100 mg/kg/day (78%). Thirty-four patients (9.6%) died, some as a result of their parents' decision to stop treatment. Of those whom we continue to follow, 187 have done well after discharge from hospital. These families were advised to feed their children a metabolic formula and a low-protein diet, and to return to the hospital every 2 or 3 months for laboratory testing.

It is unfortunate that few of these patients have had genetic analysis. Testing is not available in most parts of China and the cost of sending DNA out of the country is prohibitive. Thus, most (79.94%) of these patients were diagnosed by gas chromatography/mass spectrometry and 20.05% were diagnosed by gas chromatography/mass spectrometry and tandem mass spectrometry. In a clinical study [4], mutations of MUT gene were detected in 16 of 21 patients with isolated MMA. Most mutations were clustered in exons 2 and 3 (50%).

Disclosure Statement

The author has nothing to declare and confirms independence from the sponsors.

References

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