Martinez-Frias, however, reported two cases of postaxial polydactyly as result of valproic acid mono therapy (one) and valproic acid in combination with carbomazepine (one) [1]. It is not clear whether these children had associated anomalies. Polydactyly must be added to the spectrum of limb defects caused by valproic acid. In our patient as in most patients also the preaxial side of the upper limb is involved. The mechanism of this predilection is unclear.

References

1. Martinez-Frias ML (1990) Clinical manifestation of prenatal exposure to valproic acid using case reports and epidemiologic information. Am J Med Genet 37:277–282
2. Verloes A, Frikiche A, Gremillet C, Paquay T, Decortis T, Rigo J, Senterre J (1990) Proximal phocomelia and radial ray aplasia in fetal valproic syndrome. Eur J Pediatr 149:266–267

Asymptomatic lesions of the basal ganglia in a patient with methylmalonic aciduria

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Sir: Methylmalonic aciduria (MMA) is an inborn error of metabolism affecting the degradation of the aminoacids valine, isoleucine, methionine and threonine, of cholesterol and of odd-numbered long-chain fatty acids (OLCFA). Acute episodes of metabolic decompensation manifest with vomiting, drowsiness, ketoacidosis and hyperammonaemia. Persistent neurological signs, mainly extrapyramidal, have been reported in some patients with MMA [3, 4–6].

We observed a patient with MMA diagnosed at the age of 3 weeks by highly elevated urinary concentrations of methylmalonic acid (11 mol/mol creat). Enzyme studies in cultured fibroblasts indicated a mut 0 genotype. His dietary intake of natural protein was 0.8–1.2 g/kg per day and carnitine was supplemented in doses of 50–100 mg/kg per day. During metabolic equilibrium urinary methylmalonic acid excretion ranged between 0.5 and 22 mol/mol creatinine (mean value = 10.5 mol/mol creatinine, $n = 14$). Until 7 years of age he had nine episodes of metabolic decompensation characterised by vomiting, refusal to take oral fluids and metabolic acidosis. Laboratory findings during these episodes included mildly decompensated metabolic acidosis, plasma concentrations of ammonia and lactic acid were mildly elevated on one occasion. Urinary methylmalonic acid excretion ranged between 12 and 23 mol/mol creatinine (mean value = 17.6 mol/mol creat, $n = 7$). An episode at the age of 36 months was the only one to be accompanied by reduced consciousness without neurological signs. Methylmalonic acid excretion was 20 mol/mol creatinine. Brain MRI at the age of 4.5 and 6.5 years revealed symmetrical lesions within the central parts of the basal ganglia (globus pallidus) (Fig. 1). These lesions were never complicated by corresponding neurological signs. There is evidence of intellectual

Abbreviations: MMA = methylmalonic aciduria; OLCFA = odd numbered long-chain fatty acids

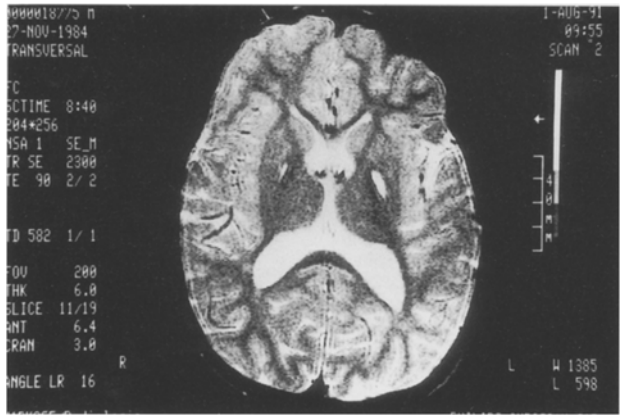

Fig. 1. MR image (1.5 Teslar superconductive magnet system) of a 4.5-year-old boy with MMA: left demonstrating symmetrical areas of low signal intensity within the central portions of the basal ganglia (globuls pallidus) on T1-weighted partial saturation spin echo and inversion recovery pulse sequences; right demonstrating high signal intensity areas, isointense to cerebrospinal fluid on proton density and T2-weighted images

develomental delay: At the age of 6.5 years his IQ (Snijders-Oomen [P]) was 68.

Lesions of the basal ganglia with corresponding neurological, mainly extrapyramidal signs have been demonstrated in other patients with MMA [1, 3–6]. So far they were thought to result from acute, stroke-like events during episodes of metabolic decompensation. However, our patient never demonstrated extrapyramidal signs and there has been no clinical evidence of a stroke-like event during the episodes of metabolic decompensation. This suggests that the damage to the basal ganglia results from a chronic process rather than from an acute one. Accumulation of OLCFA within the basal ganglia was demonstrated in a patient with a vitamin B_{12}-dependent type of MMA [5]. In our patient high urinary excretion of MMA occurring even during states of metabolic equilibrium reflects poor metabolic control. This should lead to accumulation of OLCFA [7] which might be a reason for the chronic damage to the basal ganglia. We conclude that MRI should be performed in all patients with MMA even if there are no signs of neurological involvement. In patients with lesions, metabolic control should be carefully re-evaluated. Aggressive treatment monitored by additonal parameters such as quantitative determination of urinary MMA and of OLCFA in blood lipids should be initiated in order to avoid neurological deterioration caused by further progression of these lesions.

References

1. Dayan AD, Ramsey RB (1974) An inborn error of vitamin B12 metabolism associated with cellular deficiency of coenzyme forms of the vitamin. J Neurol Sci 23:117–128
2. Gompertz D (1971) The distribution of 17 carbon fatty acids in the liver of a child with propionicacidemia. Lipids 6:576–580
3. Heidenreich R, Natowicz M, Hailine E, Berman P, Kelley RI, Hillman R, Berry GT (1988) Acute extrapyramidal syndrome in methylmalonic acidemia: "metabolic stroke" involving the globus pallidus. J Pediatr 113:1022–1027
4. Korf B, Wallman JK, Levy HL (1986) Bilateral lucency of the globus pallidus complicating methylmalonic acidemia. Ann Neurol 20:364–366
5. Roodhooft AM, Baumgartner ER, Martin JJ, Blom W, Van Acker KJ (1990) Symmetrical necrosis of the basal ganglia in methlymalonic acidemia. Eur J Pediatr 149:582–584
6. Thompson GN, Christodoulou J, Danks DM (letter) (1989) Metabolic stroke in methylmalonic acidemia. J Pediatr 115(3):499–500
7. Wendel U (1989) Abnormality of odd-numbered long-chain fatty acids in erythrocyte membrane lipids from patients with disorders of propionate metabolism. Pediatr Res 25:147–150