A 13-wk-old Polynesian infant presented for investigation of chronic abdominal distension from birth and failure to thrive despite insatiable feeding. Intrauterine growth restriction was detected late in the third trimester. Delivery was at term, and birth weight was 1960 g. Very mild initial hypoglycemia spontaneously resolved in the first day of life. At presentation, she weighed 2800 g (−2.5 SD score). Physical examination showed several dysmorphic features (Fig. 1), leading to a clinical diagnosis of Donohue syndrome. Biochemical analysis demonstrated hypoglycemia [32 mg/dl (1.8 mmol/liter)], postprandial hyperglycemia [206 mg/dl (11.4 mmol/liter)], severe hyperinsulinemia (3145 pmol/liter), raised androstenedione [17.4 (0.2–2.8) nmol/liter], and mild conjugated hyperbilirubinemia [37 (0–5) /H9262 mol/liter]. Abdominal ultrasound scan showed nephrocalcinosis and visceromegaly. Genetic analysis revealed two deletions in the gene encoding the insulin receptor gene: the first is an intronic splice site mutation (c.1610 /H11001 2delT), and the other is an in-frame deletion of seven highly conserved amino acids forming a critical /H9251 α-helix in the insulin-binding ectodomain (exon 4 deletion c.1054_1074del, p. Thr352_Arg358del). Fasting hypoglycemia was managed with continuous feeds delivering 195 kcal/kg /H18528 d and metformin (30 mg/kg /H18528 d). A 300-g weight gain followed glycemic stabilization, permitting discharge. However, she represented 1 wk later with an upper respiratory tract infection, resulting in upper airway obstruction and death at 5 months of age.

Donohue syndrome represents the most extreme insulin receptoropathy with autosomal recessive inheritance (1). Other syndromic forms of insulin resistance include Rabson-Mendenhall syndrome, type A and B insulin resistance, lipodystrophies, and HAIR-AN syndrome (2). Diagnosis is made on clinical (Fig. 1), biochemical (fasting hypoglycemia, postprandial hyperglycemia, and extreme hyperinsulinemia), and genetic grounds. Although postprandial hyperglycemia follows logically from the function of the mutated insulin receptor, many other features of the condition are not fully explained, such as fasting hypoglycemia, linear growth impairment, visceromegaly, soft tissue overgrowth, and resistance to ketoacidosis in infancy (3). Most patients die as a result of intercurrent respiratory tract infection before 2 yr of age (1).

There is a paucity of evidence for any effective treatment for Donohue syndrome. Management is not standardized but aims to normalize blood glucose. Continuous feeding may be useful. Some have shown beneficial metabolic effects using recombinant human IGF-I (4), whereas others have not (5). Regarding the use of IGF-I, optimal timing, dosing, and duration of therapy, as well as the relative risks and benefits, have not been properly established (4).

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Address all correspondence and requests for reprints to: Dr. Martin de Bock, The Liggins Institute, University of Auckland, Private Bag 92019, Auckland 1023, New Zealand. E-mail: m.debock@auckland.ac.nz.

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