

Case Report

Life-threatening autoimmunity with diabetes: management with an insulin pump

Franklin VL, Torrance T, Peebles M, Wilkie R, Greene S. Life-threatening autoimmunity with diabetes: management with an insulin pump. *Pediatric Diabetes* 2003; 4: 151–154. © Blackwell Munksgaard, 2003.

Abstract: A 2-yr-old boy presented initially with type 1 diabetes (T1D). Over the next 9 yrs, he developed multiple autoimmune conditions including Evans' syndrome, alopecia, and autoimmune bowel disease. Autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED) syndrome was considered, but no mutations were found in the autoimmune regulator-1 (*AIRE-1*) gene, making this diagnosis unlikely, and he did not fulfil the clinical criteria for immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome. We describe the challenges created by the combination of these diseases and how introduction of insulin pump therapy revolutionized his care.

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A 2-yr-old boy presented with classic symptoms of type 1 diabetes (T1D) and was managed with conventional insulin therapy (twice daily premixed insulin). There was no family history of diabetes, but his mother has celiac disease and alopecia.

A year later, he presented with widespread purpura and a platelet count of $3 \times 10^9/L$, and idiopathic thrombocytopenic purpura (ITP) was diagnosed. Multiple relapses followed, requiring steroid treatment. He later developed autoimmune hemolytic anemia, leading to the review of the initial diagnosis of ITP and the diagnosis of Evans' syndrome. Recurrent hemolytic crises followed despite splenectomy, and he became steroid dependent until cyclosporine was introduced.

At age 11, he developed abdominal pain, bloody diarrhea, and weight loss and had pneumatosis intestinalis on X-ray. Findings in the investigation for celiac disease (because of family history and association with diabetes) were negative. He had colonic mucosal inflammation and

positive antiparietal antibodies, and autoimmune bowel disease was diagnosed. This has been treated with monoclonal antibody therapy (Rituximab and Infliximab). Weight loss was treated initially with elemental feeding and then total parenteral nutrition (TPN). Enterocolitic episodes continue and nutrition depends on bowel symptoms, varying between TPN, elemental feeds, and cautious introduction of a very limited diet.

Central access for TPN has been complicated by thrombotic episodes and infections secondary to the combination of immune suppressants, absent spleen, and diabetes. Inevitably, prolonged corticosteroid use has had multisystem effects, including cushingoid facies, osteoporotic vertebral crush fractures, and hypertension.

Diabetes management

Our patient has presented considerable challenges to diabetes management (Fig. 1). These have changed

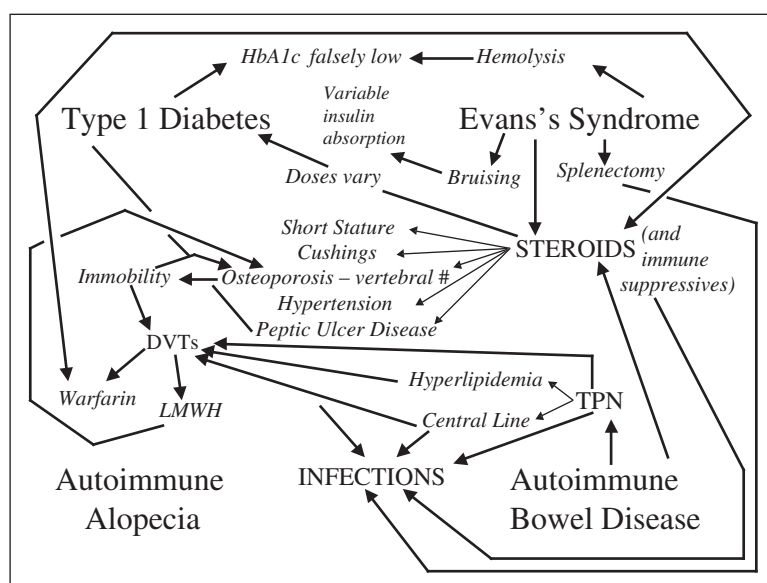


Fig. 1. Challenges in diabetes management. DVT, deep vein thrombosis.

with the evolution of coexisting autoimmune diseases and their various therapies. Episodes of profound thrombocytopenia and anemia led to periods of increased steroid requirement, impacting on his glycemic control and requiring compensatory changes in insulin therapy. Additional problems included significant needle phobia and bruising around injection sites. Recurrent hemolytic episodes affected the glycosylated hemoglobin measurement, and therefore hemoglobin A1c (HbA1c) has not been a useful marker of his glycemic control.

Development of autoimmune bowel disease, with associated vomiting, malabsorption, and steroid requirement, led to further destabilization of his metabolic control, and he frequently required TPN and intravenous insulin therapy to regulate his glucose levels. TPN was given overnight to minimize disruption and allow school attendance whenever possible. He was initially commenced on twice daily insulin injections, but on this regimen he had frequent problems with morning hypoglycemia after the TPN had been discontinued.

At this stage, an insulin infusion pump (Disetronic H-TronTM) was introduced using rapid-acting analog insulin (Novorapid), and this revolutionized his diabetes management. Insertion of a subcutaneous cannula alleviated the need for frequent injections and minimized bruising at injection sites. The ability to alter hourly basal rates on the pump allowed reduction of his insulin rate prior to discontinuation of the TPN, eliminating the problem of early morning hypoglycemia. Since the introduction of the pump, he has had no further need for regular intravenous insulin to stabilize his blood glucose. Regular adjustments of his basal insulin rates can be made according to changes in steroid dose and activity levels. The pump can also be programmed to accommodate changes in feeding regimen, to cover continuous TPN or elemental feeds,

overnight TPN, bolus elemental feeds, real food when bowel symptoms permit, and any combination of these (Figs. 2–4). The pump also provides the facility to administer small boluses of insulin in response to periods of hyperglycemia. Although he has never been entirely comfortable with wearing the pump, he has developed considerable self-management skills and appreciates the flexibility the pump provides. This allows longer periods at home than would be possible if he was on conventional therapy. He follows standard advice to change the cannula every 3 d but has had several soft-tissue infections at the cannula site, prompting immediate cannula removal and oral antibiotic therapy.

Differential diagnosis

Autoimmune diseases associated with T1D are common. Of young people with diabetes, 20.1% have positive thyroid autoantibodies (1) and the average prevalence of celiac disease is 4.5% (range 0.97–16.4%) (2). It is now recommended that these be screened for annually (3) and considered in any child with diabetes and poor growth or glycemic control.

Evans' syndrome is an autoimmune hemolytic anemia and thrombocytopenia. A fatal case of Evans' syndrome associated with diabetes has previously been reported (4). Evans' syndrome associated with a protein-losing enteropathy (5) and enteropathy associated with T1D (6, 7) have also been described. In the literature, there are no reported cases of the combination of Evans' syndrome, T1D and autoimmune enteropathy. Syndromes with similar clinical features, however, have been described. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is a rare X-linked disorder of immune dysregulation, polyendocrinopathy, and enteropathy (8).

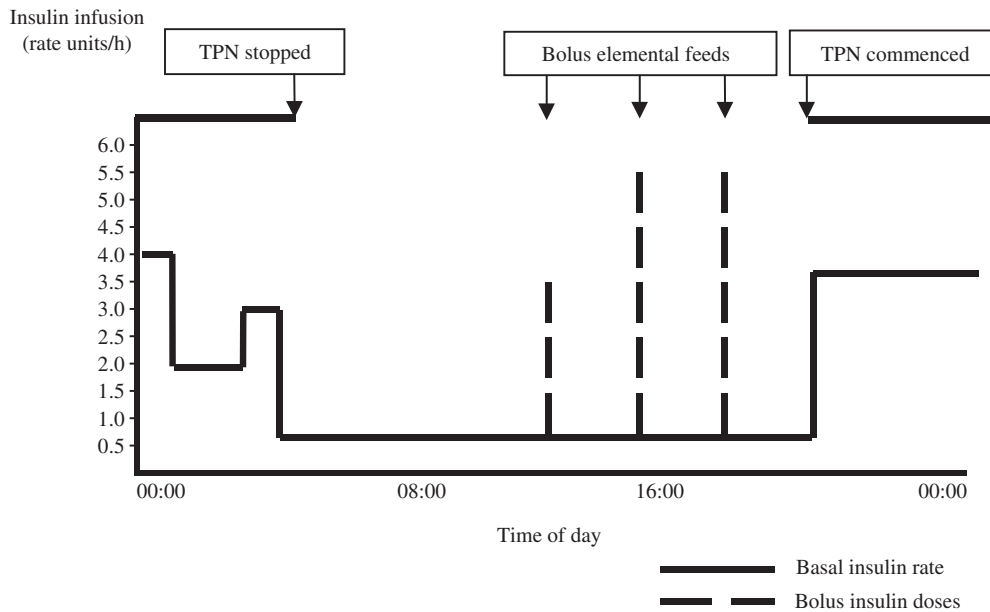


Fig. 2. Overnight total parenteral nutrition (TPN) and daily elemental feeding regimen: insulin pump basal and bolus doses. Insulin basal rates are increased during period of overnight feeding and lowered just prior to discontinuation of TPN. Insulin bolus doses are administered to cover carbohydrate content of the daily elemental feeds.

Mutations in the *FOXP3* gene have recently been identified in patients with IPEX syndrome, resulting in the lack of functional regulatory T cells leading to immune dysregulation. Diagnosis of IPEX syndrome is dependent on the clinical presentation and family history. Children with IPEX syndrome classically present in the neonatal period or early infancy, whereas our case presented first at

2 yr of age, and the strong family history of autoimmune disease is consistent with autosomal dominant inheritance. Autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED) syndrome was considered, but no mutations were found in the autoimmune regulator-1 (*AIRE-1*) gene, making this diagnosis unlikely.

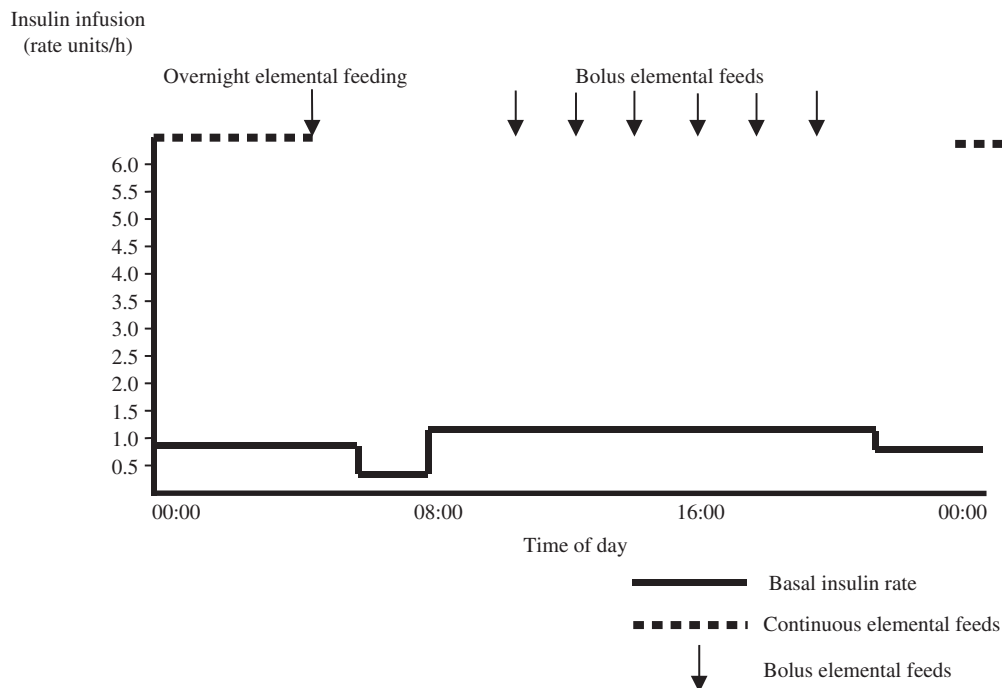


Fig. 3. Elemental feeding regimen continuously overnight and bolus daytime feeds: insulin pump basal and bolus doses. Insulin basal rates are adjusted for overnight feeding and lowered after discontinuation of feeds. An increased daytime basal rate is set to compensate for small, frequent bolus elemental feeds.

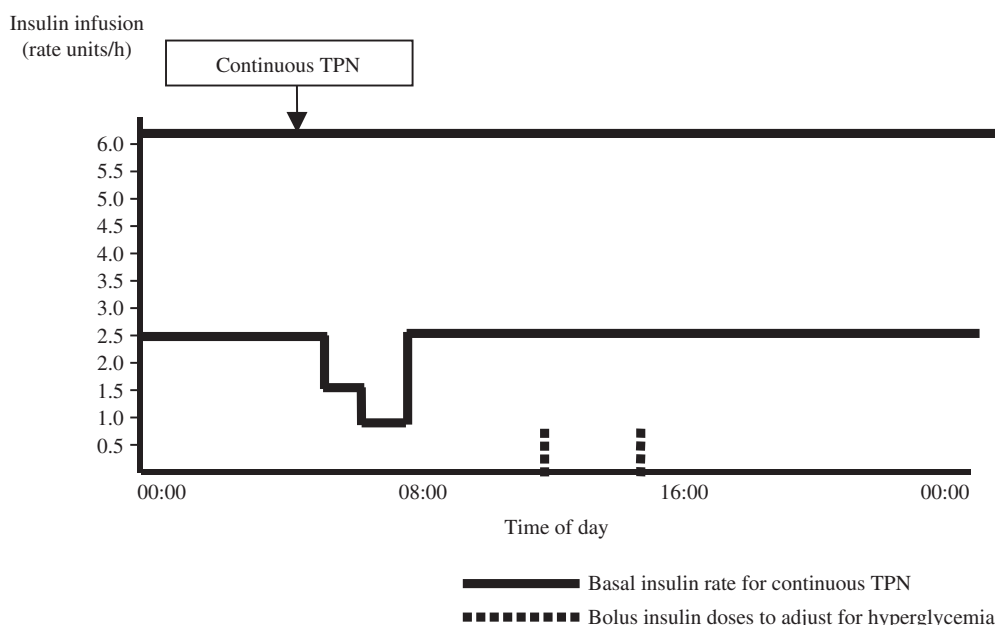


Fig. 4. Acute colitis treated with continuous total parenteral nutrition (TPN) and steroids: insulin pump basal and bolus doses. Background basal rate of insulin is increased during steroid treatment and continuous TPN therapy. Variable background rates are programmed to prevent early morning hypoglycemia and bolus doses are administered to adjust for high blood glucose levels.

Discussion

This case represents the severe end of the spectrum of autoimmune disease. The interaction of autoimmune enteropathy with nutritional regimens changing according to bowel symptoms, and hemolytic and thrombocytopenic crises requiring variable steroid doses has posed unique problems to diabetes management.

Continuous subcutaneous insulin infusion (CSII) use has been advocated for frequent unpredictable hypoglycemia or a marked dawn phenomenon (9). Insulin pump use in adult patients with coexisting gastrointestinal disease requiring TPN was described in the 1980s (10). Since the introduction of pump therapy, our patient has not experienced ketoacidosis or severe hypoglycemia. His average HbA1c is 8.6% (currently an accurate marker, as he has not had hemolytic episodes in the last few years).

This case illustrates the use of insulin pump therapy to enable complete individualization of diabetes care. Changing basal and bolus regimens has allowed tailoring of his insulin therapy to compensate for the changing steroid and feeding regimens needed to manage his complex autoimmune disease and has provided a degree of flexibility not possible with conventional insulin therapy.

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