

Eighty Six Years Duration of Type 1 Diabetes Mellitus

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Abstract

The case study focuses on a woman who lived for 91 years, she was insulin-dependent for 86 years and has been treated by a single physician the author for over 55 years. She was diagnosed with diabetes in 1932 at the age of five. Her diabetes was first treated with rapid-acting insulin three times daily, then from 1940 with rapid-acting and protamine zinc insulin once daily, while later on pork, then human crystalline zinc insulin was used, followed by a mixture of rapid-acting and NPH insulin for the last 16 years. The reason behind the above treatment regimen was that the patient obsessively insisted on a once daily insulin dose and the duration was shown to be 24 hours for each insulin. The continuous overdose of a single insulin for decades have resulted in hypoglycemic episodes almost daily, with consequent high fluctuations in blood glucose levels. She performed urine glucose tests using a polarimeter from the mid-thirties to the sixties, then used test strips until the early eighties, and later switched to blood glucose self-testing. Her HbA1c levels have been around 7% (53 mmol/mol) for the last 25 years. She did not develop retinopathy or nephropathy, only severe neuropathy caused complaints during the last years of her life. In addition, her vision continued to deteriorate due to age-related dry macular degeneration. She is a Joslin 75-year medalist. For the last two months of her life, she gave permission for degludec+glulisine insulin intensive treatment. Her death was caused by myocardial infarction.

Keywords: Type 1 Diabetes; Once daily insulin; Extreme long diabetes duration

Case Report

The patient was born in 1927 to a wealthy middle class family from Buda. Before she was born, her maternal uncle died of type 1 diabetes, probably of diabetic ketoacidosis at the age of 22. Her family members were not long-lived. She was diagnosed with diabetes in 1932 at the age of five. Her condition was immediately treated with rapid-acting ("regular") insulin, which was administered three times a day. In the mid-thirties, her father purchased a Zeiss polarimeter and the urine collected in three fractions was polarized three times daily and the dose of insulin was adjusted to the urine glucose levels obtained. In the early forties, they switched to a once daily mixture of protamine zinc and regular insulin. Her subsequent insulin therapy will be discussed below. In the thirties until the late forties, she maintained the usual ketogenic diet at the time with up to 60-70 grams of carbohydrates.

As for self-testing, she switched from polarimetric glucose self-monitoring until the mid-sixties to the then available urinary glucose assay using Diastix strips. She started using a home blood glucose self-monitoring in 1982 until her death.

She lived like other healthy children except for her diabetes, did several sports, such as cycling, horse riding, tennis, volleyball, swimming, and skating. She maintained regular daily exercise for the rest of her life. She had a lean body. Subcutaneous fat was almost completely absent; except for the one palm-sized area on the anterior surface of the thighs where insulin was always administered.

She married in 1952. Her husband adored her and basically devoted his life to her. Before his death in the early 2000's, he said he had been sleeping half-awake for decades holding his wife's hand watching out

for the signs of hypoglycemia, which had occurred almost every night due to a then daily overdose of insulin. The patient was so used to being pampered since childhood that she has always insisted on her often unrealistic ideas, even in the face of her caring doctor.

The author was in his third postgraduate year as a doctor at St. John's Hospital, Budapest, II. Department of Internal Medicine, when he first met the patient at the end of 1962. She immediately selected him as her treating and caring physician and this relationship was retained for more than 55 years until the patient's death. She was admitted to St. John's Hospital once in 1967 during 15 years. She then injected a total of 60 units of insulin daily, half as rapid-acting and half as protamine zinc insulin. She later switched to crystalline pork, then to human zinc insulin. At that time no diabetic complications were detected in the patient. From 1978 until 2001 her treatment continued in the "B" Department of Internal Medicine at the Budapest Péterfy Sándor Hospital. Following the retirement of the author, she was treated at the Diabetes Outpatient Department. She was hospitalized once at Péterfy Hospital in 1988. Two C-peptide tests were performed at that time with negative results.

She was the first in Hungary to receive the Joslin 75-Year Medal and award for her achievement in living with diabetes without serious diabetic complications for more than 75 years, which she was very proud of. In 2012, she underwent bilateral cataract surgery, but her vision continued to deteriorate due to the progression of age-related dry macular degeneration (No signs of diabetic retinopathy were observed during the eye examinations). The deterioration of her vision later made the self-management of her diabetes more and more difficult.

It is very important to discuss her insulin therapy in more detail. Except for the last two and a half months of her life, she has not given permission to the use of any form of advanced insulin treatment. The

reason for the consent of her doctor was that the 24-hour duration of action was clear for the once-daily administration of premixed rapid-acting plus NPH insulin which replaced crystalline zinc insulin. However, she checked her blood glucose 5-10 times a day, and corrected each jump with 1-2 units of insulin lispro injection. Her daily dose of insulin has been around 22 units for two decades.

This brings us to her dietary issues. When her fasting blood glucose was around 8-10 mmol/l, she would delay her breakfast up to 11 o'clock checking her glucose every hour. She rarely ate cooked food, she consumed most of her daily 150 g of carbohydrates in the form of buns, eating very little meat, vegetables and fruits. So, besides her absolute non-physiological and out-of-date insulin therapy, her diet was extremely deficient, and certainly not healthy.

Nonetheless, all her HbA1c values since 1993 have been around 7% (53 mmol/mol), sometimes dropping below 6% (42 mmol/mol). Meanwhile, her impaired vision and worsening neuropathy, which has not improved with alpha lipoic acid and pregabalin administration, as her only diabetic complication caused severe lower extremity complaints and made the self-management of her diabetes more difficult.

Serious problems with her treatment/care developed in the fall of 2017. The reason for this was that although she measured her blood glucose values 8-10 times a day (she did not feel the finger prick pain due to neuropathy), her earlier stable blood glucose fluctuations of 4-10 mmol/l started to fluctuate strongly. This was due to the fact that her eyesight was impaired, so she had repeatedly made errors in her blood glucose measurement, and also often had her pen needles bent at 90 degrees, which she had not noticed either and did not actually inject insulin. This has worsened until 2018 to such an extent that due to severe hypoglycemia she had to be hospitalized 7 times in 3 months in the II. Department of Internal Medicine of our hospital. So she spent a total of 57 days in hospital in the spring before she died.

Her ECG was normal. Her laboratory parameters measured at this time were: RBC: 3,4 million, Hb: 102 g/l, WBC: 7,400, Creatinine: 64 µmol/l, eGFR: 79 ml/min, Total cholesterol: 4.2 mmol/l, HDL cholesterol: 1.5 mmol/l, Triglycerides: 0.8 mmol/l. CRP: 57, HbA1c: 6.8% (49 mmol/mol), Urinary glucose excretion: 42 mg/24 hours. Thus, apart from anemia and inflammation, no other differences suggestive of diabetic complications could be detected.

In May, the patient returned home and agreed to 24-hour care at her apartment following very strong persuasion. With the presence of a nurse trained in blood glucose control, insulin administration and proper diet, the patient's condition began to improve rapidly, her appetite increased and she exercised regularly on a daily basis. Her blood sugar levels stabilized at 5-7 mmol/l and the hypoglycemic episodes were abolished with degludec and glulisine insulin given for two months. Her final insulin doses proved to be extremely low, with 8 units of degludec and 3 × 2 units of glulisine insulin.

She sent away the 24-hour nurse a month later, saying that if she was able to look after herself for 86 years, she would continue to be able to do so. Her high-level intellect has proved to be completely wrong this time. After the nurse left, she spent more and more time in bed with hypostatic pneumonia and bronchitis, refused hospital admission, collapsed at home and died 23 days later, two months after she was 91 years old.

Myocardial infarction localized to the interventricular septum was reported as the main cause of death, dilated cardiomyopathy,

hypostatic pneumonia, bronchitis, and acute pulmonary edema were reported as additional findings during autopsy. The calcareous plaques at some places reduced the coronary arteries to a pinpoint lumen. Extreme levels of arteriosclerosis have been found throughout her arterial system.

Discussion

The DCCT-EDIC study [1] clearly confirmed that good metabolic control reduces the risk of mortality and prolongs life span. In particular, glycemic control following the onset of diabetes plays a role in the mortality of type 1 diabetics, particularly in children and adolescents [2]. The life expectancy of persons with Type 1 diabetes is lower than that of their non-diabetic counterparts, but this has dramatically improved over the past century, primarily due to the introduction of insulin [3,4]. Nevertheless some individuals who had diabetes since childhood may have a longer duration of diabetes and thus may live for longer, although the number of these individuals is not high [5-8]. On the basis of available data, we cannot find an explanation for the very long diabetes duration.

Conclusions

Although there is no example of longevity in the patient's family, a special constellation of the genes may be responsible. Another important fact is the patient's resilience, namely her extremely positive outlook on life, her life-affirming attitude, and above all, her tremendous pride in herself and her performance. If we add that in the last 55 years of patient's life she has been cared for by a single, attentive and helpful doctor it weighs heavily, but only in addition to what was mentioned above.

Summary of the "clinical pearls" exemplified by this case:

- Extreme long duration of Type 1 diabetes
- No advanced insulin treatment during 86 years
- Great blood glucose fluctuations during the first 60 years of the disease
- No severe late complications except neuropathy
- No exact explanation for the patient's longevity
- Patient was treated/cared by a single doctor during the last 55 years.

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