**Case Analysis**

**Inpatient Diabetes Mellitus in the Oncology Setting**

**Nancy Schwab, RN, PhD, ANP, and Misty Porter, RN, PhD, FNP**

**Case Study:** A.B. is a 32-year-old Caucasian man with a significant, 12-year medical history of diabetes mellitus type I as well as a history of hypertension and hypercholesterolemia. He presented to his primary care doctor with blurred vision and was referred to a retinal specialist, who diagnosed hemorrhagic and leukemic retinopathy resulting in limited vision. A complete blood count was drawn during the visit with his retinal specialist. The results were abnormal, revealing a white blood cell count of 30,000/mm³, platelet count of 70,000/mm³, and a hemoglobin of 12.2 gm/dl. The peripheral smear showed peripheral blasts. A.B. was referred to a hematologist, who performed a bone marrow aspiration, confirming the diagnosis of pre-B-cell acute lymphocytic leukemia (ALL). Cytogenetic studies revealed positivity for the Philadelphia chromosome and a translocation of genes 4 and 11.

**Acute Lymphocytic Leukemia**

ALL accounts for 20% of all adult leukemias, which in themselves constitute about 3% of adult malignancies. The clinical signs and symptoms of ALL usually occur suddenly and derive from expansion of the leukemic cell in the marrow and from involvement of the peripheral blood and extramedullary sites such as the lymph nodes, liver, spleen, and central nervous system. Common symptoms include fatigue, fever, night sweats, weight loss, easy bruising or obvious bleeding, dyspnea, dizziness, and infections. Extremity and joint pain also may be present, sometimes leading to a misdiagnosis of arthritis (Faderl & Kantarjian, 2006).

Comorbid conditions such as diabetes mellitus with high-dose steroid administration leading to hyperglycemia often occur with treatment for ALL. Evidence suggests that hyperglycemia in patients with ALL contributes to increased infections, higher rates of recurrence, and mortality (Weiser et al., 2004).

**Evaluating A.B.’s Diabetes**

A.B. had been on insulin for 12 years. He had no history of diabetic ketoacidosis but did have mild peripheral neuropathy in his feet and hands. His blood glucose levels usually ran in the 200s, but he rarely checked his levels at home; he admitted that he did not follow a limited-carbohydrate diet. He typically received Humulin® 70/30 (isophane insulin [NPH]/regular, Eli Lilly and Company) twice a day: 45 units in the morning and 25 units in the evening. Upon evaluation of his diabetes mellitus, laboratory values revealed a hemoglobin A1C of 10%, C-peptide of 0.9 ng/ml, and negative urine ketones. When A.B. was given a dose of dexamethasone 40 mg IV as part of his chemotherapy regimen, his blood glucose rose to 400 mg/dl.

**Pathophysiology of Diabetes Mellitus**

A.B. originally was diagnosed as having diabetes mellitus type I. However, the C-peptide result, along with a lack of episodes of diabetic ketoacidosis, defined him as insulin deficient. C-peptide is a useful marker of insulin secretion and allows discrimination of endogenous and exogenous sources of insulin in evaluation of hyper and hypoglycemia (Powers, 2006). Diabetes type I is considered an autoimmune destructive process of beta cells that occurs over months to years (see Figure 1).
The autoimmune process is thought to be triggered by an infectious or environmental stimulus and to be sustained by a beta cell–specific molecule. In most individuals, an immunologic marker appears after the triggering event but before diabetes becomes clinically overt. Beta cell mass declines and insulin secretion becomes progressively impaired, although normal glucose tolerance is maintained. Features of diabetes mellitus do not appear until 80% of the beta cells are lost. The events that trigger the transition from glucose intolerance to frank diabetes mellitus often are associated with increased insulin requirements as might occur with infections or puberty (Powers).

**Signs and Symptoms of Diabetes Mellitus**

The symptoms of diabetes mellitus include polyuria, polyphagia, polydipsia, and weight loss. The signs include a random blood glucose concentration of > 200 mg/dl, fasting plasma glucose of ≥ 126 mg/dl, or a two-hour postprandial (after ingesting a meal) plasma glucose of ≥ 200 mg/dl. Hemoglobin A1C, which measures glycosylated hemoglobin, is used to determine a diabetic’s three-month glucose average and should be less than 7%. Fructosamine is a better indicator of glycemic control in patients with ALL because of rapid red blood cell turnover and multiple transfusions associated with the disease. Fructosamine, which measures glycated albumin, reflects average blood glucose over two weeks. It first was used to monitor the blood glucose averages of patients with cystic fibrosis–related diabetes mellitus because of their high red blood cell turnover (Hardin & Moran, 1999; Moran, 2002a, 2002b).

**Treating A.B.’s Diabetes**

A.B.’s severe hyperglycemia in response to the steroids used as part of his cancer treatment regimen dictated the need for basal and bolus insulin management. This treatment method includes a long-acting insulin, used to mimic the body’s basal needs, combined with a short-acting insulin titrated to respond to fluctuating glucose levels from meals and intermittent steroid provision.

The basal component is the amount of insulin needed when food is not being absorbed to regulate endogenous glucose output from the liver. The bolus insulin chosen was glargine. This decision was based on the fact that A.B.’s diabetes was not well controlled with his previous use of isophane (NPH) and regular human insulin (soluble).

The bolus or prandial component is the amount of insulin needed to cover the glucose requirements of a meal or steroids, which promotes the conversion of digestible nutrients into storage forms of energy (Hirsch, Braithwaite, & Verderese, 2004). The subcutaneous short-acting insulin chosen for A.B.’s glucose management was a rapid-acting insulin (e.g., lispro, aspart), which provides a quicker effect to bring down blood glucose related to meals and compounded by corticosteroid administration. Rapid-acting insulin can be given subcutaneously every two to four hours, essentially acting like an insulin drip.

An important component of the management of A.B.’s diabetes was the need to
obtain glucose control that would accommodate the on-and-off steroid regimen of his chemotherapy. The use of glargine and short-acting lispro accounted for variations for days when he may have had elevated blood glucose after steroid administration. The regimen included variations of insulin dosage to accommodate for the duration of biologic activity as well as the half-life of the steroids A.B. received and the subsequent blood glucose response.

A.B.’s Chemotherapy and Glucose Level Effects

The chemotherapy regimen initiated was modified hyper-CVAD (fractionated cyclophosphamide, mesna, doxorubicin, and vincristine, with or without rituximab). Rituximab is a monoclonal antibody that attaches to CD20 on the cells and destroying them. A.B. was initially CD20 positive. CD20 positivity is determined when greater than 20% of the leukemic blasts express CD20 by flow cytometry. With hyper-CVAD, dexamethasone was given on days 1–4 and repeated on days 11–14. Dexamethasone’s estimated potency is 30%–40% glucocorticoid and < 0.01% mineralocorticoid, with a half-life greater than 48 hours (Powers, 2006).

Because of dexamethasone’s strong potency, A.B. experienced severe hyperglycemia. His glucose levels frequently would be in the 500s on his days of steroid administration, and severe insulin resistance was noted. To account for the steroid-induced hyperglycemia and prandial meal coverage, as much as 60 units of rapid-acting insulin were given with each meal. A.B.’s blood glucose levels usually remained elevated one day after steroids were discontinued. Discussion regarding maintaining a stable glargine dose on all days versus varying the glargine dose when A.B. was on and off steroids was an important component of A.B.’s early glucose management. However, he experienced hypoglycemia when the glargine dose remained stable, which helped determine the final treatment plan.

A paucity of research exists on management of steroid-induced diabetes mellitus. Hence, clinical decisions on glucose management were made intuitively and based on A.B.’s previous response to insulin therapy. Some researchers believe that steroids are hypermetabolic, decrease glucose uptake, increase hepatic glucose production, and may directly inhibit insulin release (Ogawa et al., 1992). In an animal study, Delaunay et al. (1997) demonstrated that glucocorticoids directly inhibit insulin release in vivo and identified the pancreatic beta cell as an important target for the diabetogenic action of glucocorticoids. Glucocorticoids may cause postprandial hyperglycemia, but the present case study showed that with high-dose steroids, a fasting hyperglycemia also occurred. The two suspected responses (postprandial and fasting hyperglycemia) need to be documented further in animal and human research.

Considering the research, intuition, and A.B.’s clinical response to steroids and insulin, two treatment plans were developed: one for when he was on steroids and another for when he was off. His insulin regimen (all given subcutaneously) on steroids was glargine 50 units every evening and aspart/lispro 25–30 units with supplemental scale insulin of 10–26 units (range = 35–56 units) with each meal. Lantus is not mixed with any other insulin because of its acidic pH (Hirsch et al., 2004). The off-steroid regimen included glargine 35 units every evening with aspart/lispro 10 units plus a supplemental scale of 3–14 units (range = 13–24 units). The supplemental scale insulin also is called a correction dose and is administered with prandial insulin. The amount of supplemental insulin is determined by estimating how much the blood glucose level is lowered by one unit of rapid-acting insulin. For most patients, one unit of rapid-acting insulin lowers the blood glucose level, on average, by 30–50 mg/dl (Hirsch et al.).

To further combat insulin resistance from corticosteroids, metformin 1 g twice a day was added to A.B.’s regimen. Metformin decreases hepatic glucose output and increases insulin action. As a result of the improvement in glycemic control, serum insulin concentrations decline slightly. How metformin increases insulin action is not known. In addition to the suppression of hepatic glucose output, increased use of insulin-mediated glucose occurs in the peripheral tissues (such as muscle and liver), particularly after meals. Research has demonstrated that the substrate availability for gluconeogenesis is subsequently reduced (Hirsch et al., 2004). Use of metformin in steroid-induced diabetes has not been researched.

A.B.’s Glucose Control

A.B.’s average glucose level was 200 mg/dl, and his fructosamine levels were generally 250 IU, which is within the normal range of 200–300 IU. He was very difficult to manage because of the severe insulin resistance experienced with the high-dose corticosteroids given in the oncology setting.

Nurse Practitioner Role

The diabetes mellitus nurse practitioner (DMNP) saw A.B. from his initial admission until he went to the intensive care unit (i.e., a six-month time frame). The DMNP provided continuity in coordinating inpatient glucose management, provided outpatient follow-up, and coordinated the regimen with physicians. A.B.’s regimen was a collaborative effort.

The DMNP facilitated teaching A.B.’s family the basal and bolus regimen with the two schedules. A.B. had a very astute and adept family who was able to learn the regimen quickly and regulate his insulin coverage with his blood glucose levels. The family was very compliant with following the regimens that were developed. Blood glucose monitoring and documentation was initiated four times a day (i.e., before breakfast, lunch, and dinner and at bedtime). The bedtime and morning blood glucose levels were used to regulate the glargine doses, and the premeal blood glucose levels were used to determine the additional supplemental insulin A.B. needed along with his premeal scheduled insulin.

The DMNP also taught the nurses on the inpatient units about the regimen, the rationale for the regimen, and the need for large amounts of insulin. The issues were a large hurdle for the nurses to overcome because many were concerned about giving such high doses of insulin (60 units of aspart/lispro premeal) and causing hypoglycemia. The DMNP made progress through reinforced teaching, being available by pager to discuss concerns, and talking to the nurses daily about the rationale for the particular regimen. In-service programs were provided to the
nurses, which allowed them to discuss and understand the concepts of inpatient diabetes management and how they were adapted to a cancer center.

**Case Study Follow-Up**

A.B. went into complete remission after cycle 1 of modified hyper-CVAD. Because of his Philadelphia chromosome positivity and translocation of genes 4 and 11, his prognosis was poor. He received a stem cell transplantation from a relative. However, post-transplantation, he developed a fungal lung infection that progressed to septic shock, and he died.

**Summary**

In hospitalized patients, diabetes mellitus is the fourth most common comorbid condition, is responsible for 10%–12% of all hospital discharges, and adds one to three days to the hospital stay (Hogan, Dall, & Nikolov, 2003). Improving glucose control has been shown to reduce mortality, morbidity, and cost of care in the general hospital setting (Umpierrez et al., 2002). In the cancer setting (Weiser et al., 2004), remission rates were decreased with tighter glucose control. When blood glucose levels were greater than 200 mg/dl, the occurrence of sepsis and complicated infections increased in patients with cancer (Weiser et al.). Diabetes mellitus recently has come to the forefront of inpatient management, which has affected patient care and decreased hospital costs. Continued research in controlling glucose levels in patients with cancer should lead to longer survival.

**Author Contact:** Nancy Schwab, RN, PhD, ANP, can be reached at nschwab789@yahoo.com, with copy to editor at CJONEditor@ons.org.

**References**


