## **Diabetes in a Bearded Woman**

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#### Case Report

A 61-year-old woman with no past medical history was admitted with nonketotic hyperosmolar state that was complicated by seizures. At presentation, her serum glucose was 800 mg/dL with negative ketones. Glycosylated hemoglobin (HbA1c) was 14.1%. The patient was started on intravenous insulin and fluids. Serum insulin levels were not measured since the patient was already started on an insulin drip. She was also noted to have virilization. She had normal menarche, regular menses until menopause, and had delivered 4 children without any difficulty. Virilization developed gradually over 2 years, and the patient had been shaving daily for the past 1 year. There was no prior history of diabetes mellitus. Her weight was 176 pounds, with a height of 66 inches (body mass index of 28 kg/m<sup>2</sup>). Physical examination showed temporal recessions, balding vertex, and a full beard (Figure 1A through C). There was terminal hair on the chest, abdomen, and extremities (Figure 1D and E). Clitoromegaly was present; however, her voice was normal. Acanthosis nigricans was absent, and there were no stigmata of Cushing syndrome. Serum total testosterone was 525 ng/dL (49-102), free testosterone measured 101 pg/mL (1.0-8.5), and bioavailable testosterone was 190 ng/dL (3-29). The rest of the work-up showed dehydroepiandrosterone measuring 314 µg/dL (130-980), luteinizing hormone measuring 32.6 mIU/mL (14.4-62.2), follicle-stimulating hormone measuring 53.1 mIU/mL (25-160), and 24-hour urine free Cortisol of 20 µg/d (<50). Pelvic examination was normal.

# **Case Report**

After hospital discharge, the patient's glycemic control remained poor despite nutrition counseling (American Diabetes Association diet). Her glucose values (at all times) ranged between 250 and 350 mg/dL on daily dose of 80-100 U of Neutral Protamine Hagedorn (NPH) insulin. To determine the etiology of virilization, a transvaginal ultrasound and abdominal/pelvic magnetic resonance imaging were performed. The ovaries and the adrenal glands were completely normal. An occult, highly functional ovarian tumor was suspected. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Surgical pathology showed a 1.3-cm stromal luteoma in the left ovary (Figure 2A). The right ovary showed stromal hyperthecosis (Figure 2B). Either (or both) of these lesions could have been the source of hyperandrogenism in this woman.

Postoperatively, total testosterone levels became undetectable (and remain so at 1-year follow-up). Although her temporal baldness persists, baldness of the vertex has completely resolved. The patient currently shaves only once a week. Interestingly, surgery resulted in a dramatic improvement in her diabetes control, with a significant decrease in insulin requirements (Figure 3). Currently, she is only on 25 U of NPH and Metformin 500 mg twice daily. She is gradually being switched completely to oral agents.

Although unclear, the relationship between hyperandrogenism and insulin resistance in women is fascinating. On one hand, hyperinsulinemia in insulin-resistant women leads to increased androgen production by the ovaries (Poretsky, 1991). On the other hand, hyperandrogenism, regardless of its etiology, has also been associated with insulin resistance. Hence, in many cases it is difficult to identify the primary abnormality. Hyperandrogenism resulting from luteomas and hyperthecosis also induces insulin resistance, which improves after resection of these lesions (Givens et al, 1974; Leedman et al, 1989; Mantzoros et al, 1995). Our case is one such example. These observations indicate that in women who harbor such functional tumors, hyperandrogenism is the primary abnormality that leads to the development of insulin resistance and, in some cases, frank diabetes (Leedman et al, 1989). These findings in women bear significant contrast to those observed in men, in whom low androgen levels are associated with insulin resistance and increased risk of diabetes (Haffner et al, 1994). The exact relationship between hyperandrogenism and insulin resistance in women is not completely understood.

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Figure 1. Clinical features showing virilization. (A) Full beard and temporal recessions, (B) balding vertex, (C) terminal hair on the back, (D) coarse abdominal hair, and (E) terminal hair on lower extremities.



Figure 2. (A) Left ovary harboring a 1.3-cm luteoma. There was no mitotic activity. Reinke crystals were not seen. The lower inset shows pink polygonal luteal cells with abundant cytoplasm. The upper inset shows positive staining for inhibin, a feature of luteomas. (B) Right ovary showing steroid-producing cells mixed with fibrous stroma (inset).



Figure 3. Patient's diabetes control before and after surgery.

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