New-Onset Type 2 Diabetes and Virilization in a Benign Sex Cord Tumor

Firouzeh Feiz1, Afsaneh Tehranian2, Somaye Sadat Heidary3 and Akram Seifollahi4

ABSTRACT

The stromal leydig cell tumor (SLCT) is a very rare benign tumor of ovary which occurs more often in young women in reproductive age. In this report, we describe a SLCT in a postmenopausal woman with high level of testosterone and triggering of type 2 diabetes, occurring 3 months after removal of the tumor.


INTRODUCTION

Sertoli-Leydig cell tumors (SLCT) are of rare neoplasms accounting for less than 0.5% of the all primary ovarian neoplasms.1 However, elevated plasma androgens have been observed in approximately 80% of patients,2 and can be diagnosed by clinical signs and symptoms related to excess androgens like testosterone.3 Although high level of testosterone is one of the major causes of type 2 diabetes, this metabolic disorder has not been reported in women with SLCT, which may be due to the short duration of hyperandrogenism. High level of bioavailable testosterone in postmenopausal women increases the risk of type 2 diabetes for a long period of time; and factors such as family history and BMI (body mass index) are involved in this situation.4 Hence, the occurrence of type 2 diabetes in a treated SLCT patient after 3 months is not expected.

Here below, for the first time, the authors reported an SLCT of ovary in a postmenopausal woman which led to type 2 diabetes.

CASE REPORT

A 57-year postmenopausal woman presented to the outpatient specialist clinic of Arash Hospital, Tehran, Iran, with a 4-month history of progressive hirsutism, severe odoriferous sweating, acne, hair loss, hoarseness, rapid nail growth, increased libido, and bone pain. She had no significant past medical history. On systemic review, she had a mild weight loss and aggressive behaviour. Progressive hirsutism, started 3 months ago, was prominently observed around her submental area with score of around 16. She had never used tobacco, alcohol or an intravenous drug and did not have any history of metabolic disorders in her family or herself. Her body mass index was 23.4 kg/m². There was no mass or pain in the abdominopelvic region.

Investigations for hirsutism and virilization in laboratory tests showed increased total serum levels of testosterone and free testosterone. Tumor markers CA125, CA19-9, and inhibin A were in normal ranges. Dehydroepiandrosterone sulfate (DHEA SO₄) and 17 Hydroxyprogesterone (17 OHP) were within the normal range. Impaired fasting glucose (IFG) was detected before surgery (Table I).

Transabdominal sonography showed a small amount of fluid in the cul-de-sac. Transvaginal sonography showed a heterogeneous mass of 43 x 27 cm, located within the left ovary with no extension or lymphadenopathy, but with some fluid collection in pelvic area. Endometrial thickness was normal (4.4 mm). An abdominal and pelvic computed tomography scan (CT) with contrast revealed a 2.5 x 2.3 cm cystic lesion in the left ovary.

Staging laparotomy found features of a benign sex cord stromal tumor with size of 3.5 x 2.5 x 2 cm on histology of frozen sections. Therefore, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. No abnormality was found in abdomen and...
pelvic areas. At macroscopic examination, the tumor was yellow with focal hemorrhage, measuring 3.5 cm in diameter. On microscopy, Figure 1 showed the tumor was composed of packed sheets and nests of uniform polyhedral eosinophilic cells with central round nuclei.

Four lymph nodes with 2 cm diameter and without histological evidence of malignancy were recorded from the pelvic specimen. On follow-up, 3 months after surgery, she had normal nail growth and her hoarseness and hirsutism signs were improving. There was no excess of androgens, but high amount of fasting blood sugar was in the range of diabetes, and type 2 diabetes was confirmed by measuring 2 hours blood sugar. Metformin was administered for that.

**DISCUSSION**

Sertoli-Leydig cell tumors (SLCT) are subgroups of sex cord-stromal tumors (SCST) of the ovary and accounts for < 0.2% of all ovarian neoplasms. Masculinization and virilization are major symptoms, which can help the clinician to have a precise diagnosis. However, amenorrhea requires more investigations. Excess serum level of testosterone, DHEA, and estrogen are the basic biochemical parameters that increase remarkably. This patient was a postmenopausal female who was not in the usual age range of SLCT (which is between 20-30 years). Determining the cause of her main complaints of hirsutism and increased libido, indicated high level of testosterone and normal DHEA. Therefore, the patient was suspected to have an androgen producing tumor. Transvaginal sonography and computed tomography tests confirmed the diagnosis.

According to the results of the diagnostic tests, surgical treatment was selected. In contrast to the patients in reproductive age with no fertility consideration and advanced SLCTs, total hysterectomy and bilateral salpingo-oophorectomy or cytoreductive surgery is applied. Chemotherapy is suggested for both types of patients with grade 2-3 disease and advanced tumors with heterologous elements.

Clinical expression of rapid growing nails was a remarkable finding in this patient. Androgens receptors (AR) increase in 64% of patients with prostate and ovarian malignancies; and play an important role in clinical manifestations and increasing of growth factors due to high levels of androgens. There was a case report of unusual nail growth in SLCT in a postmenopausal woman with severe hyperandrogenemia and mild hyperestrogenemia. They assumed that this change of nails growth pattern can be attributed to high expression of AR in nail bed tissues due to hormonal changes. Although the laboratory tests did not show high amount of estrogen in this postmenopausal patient, possibility of androgen effects on their receptors in this case can be proposed for both nail growth speed and male pattern hair loss.

A positive association has been demonstrated between high level of testosterone and insulin resistance in postmenopausal women; and this can effect insulin function in both skeletal muscle and adipose tissue, resulting in hyperglycemia. In addition to high level of testosterone, studies showed that low concentration of sex hormone binding globulin (SHBG) is associated with impaired glucose content and conversely elevated level of SHBG is strongly associated with a reduced risk of type 2 diabetes. Until now, there is only one study about the occurrence of type 2 diabetes in SLCT in which 12 months follow-up of 5 women with Leydig cell tumour or SLCT did not show any difference in insulin sensitivity in baseline and after the surgery. So, the development of new-onset type 2 diabetes in a postmenopausal woman within less than one year with a negative background of diabetes in her family and medical history was not expected. The laboratory data shows abnormal amount of blood glucose in favour of impaired glucose tolerance before the surgery, and diabetes mellitus was observed after 3 months. Considering the role of SHBG in diabetes, this metabolic disorder in the patient can be explained by the adverse effects of prolonged androgen excess and probably low concentration of SHBG in circulation, as a trigger factor for persistent hyperglycemia and insulin resistance.

**REFERENCES**


