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Case Report

Testosterone-Secreting Ovarian Tumor: A Rare Cause of Erythrocytosis and Pulmonary Embolus

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ABSTRACT

Objective: To raise awareness of the clinical presentation of a testosterone-secreting steroid cell tumor, not otherwise specified, causing pulmonary embolus (PE) and erythrocytosis.
Methods: Report of the first known case of ovarian steroid cell tumor not otherwise specified leading to PE.
Results: A 67-year-old Caucasian postmenopausal woman was referred for endocrine evaluation of a 1-year history of hirsutism, weight gain, and elevated total testosterone level of 672 ng/dL (normal, <75 ng/dL). She reported increased hair growth on her chin for the past year, unintentional weight gain, and low energy levels. Laboratory data from the initial visit included a total testosterone level of 672 ng/dL (normal, <75 ng/dL), hemoglobin level of 18.0 g/dL (normal, 11.7-15 g/dL), and hematocrit level of 50.4% (normal, 35%-45%). Four months after initial presentation, the patient developed acute-onset chest pain and shortness of breath and was diagnosed with a right PE on computed tomography chest angiogram. Evaluation with imaging for an ovarian mass revealed a negative workup including computed tomography abdomen pelvis, transvaginal ultrasound, and pelvic magnetic resonance imaging. Despite negative findings during imaging, because of the markedly elevated testosterone levels, this presentation was thought to correspond to a testosterone-secreting ovarian tumor. The patient was referred for bilateral oophorectomy. Pathology of the right ovary revealed a 2-cm steroid cell tumor, not otherwise specified.
Conclusions: PE and erythrocytosis can be presentations of a testosterone-secreting ovarian tumor, not otherwise specified. This case is the first known presentation of an ovarian steroid cell tumor, not otherwise specified, leading to PE and erythrocytosis.

Introduction

We present a case of an ovarian steroid tumor, not otherwise specified presenting with a pulmonary embolus and erythrocytosis.

Case Report

A 67-year-old Caucasian postmenopausal woman was referred for endocrine evaluation of a 1-year history of hirsutism, weight gain, and elevated total testosterone level of 672 ng/dL (normal, <75 ng/dL). She reported an increased hair growth on her chin for the past year. She denied any male pattern hair loss or increased hair growth on her legs or chest. She also reported unintentional weight gain of 13 pounds and low energy levels and her past medical history was remarkable for gastroesophageal reflux disease. Her last menstrual period was at the age of 40 years and periods occurred at regular intervals without heavy bleeding. She never became pregnant by choice. Her physical examination was notable for shaved terminal hair on her chin and vellus hair on her abdomen, but no hirsutism or voice change were noted. There were no abdominal striae, moon facies, or buffalo hump.

Laboratory data from the initial visit included a total testosterone level of 672 ng/dL (normal, <75 ng/dL), 2 PM cortisol level of 5.6 μg/dL (normal, 2.7-10.5 μg/dL in PM), thyroid-stimulating hormone level of 2.28 μiU/mL (normal, 0.27-4.20 μiU/mL),

Abbreviation: PE, pulmonary embolus.

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androstenedione level of 133 ng/dL (normal, <10-93 ng/dL), 11-deoxycortisol level of 29.3 ng/dL (normal, <32 ng/dL), adrenocorticotropic hormone level of 12 pg/mL (normal, <46 pg/mL), dehydroepiandrosterone sulfate level of 87 μg/dL (normal, 13-130 μg/dL), free testosterone index of 24.2 (normal, <2.1), 17-hydroxyprogesterone level of 207 ng/dL (normal, <272 ng/dL), follicle stimulating hormone level of 26.1 miU/mL (normal, 25.8-134.8 miU/mL), luteinizing hormone level of 17.9 IU/L (normal, 7.7-58.5 IU/L), hemoglobin level of 18.0 g/dL (normal, 11.7-15 g/dL), hematocrit level of 50.4% (normal, 35%-45%), and HbA1c level of 5.4% (36 mmol/mol).

Four months after this initial presentation, the patient developed acute-onset chest pain and shortness of breath, and she was diagnosed with a right pulmonary embolus (PE) on computed tomography chest angiogram. Evaluation with imaging for an ovarian mass revealed negative findings. Computed tomography abdomen pelvis did not reveal any adrenal masses. Transvaginal ultrasound did not demonstrate any ovarian masses. Magnetic resonance imaging of the pelvis did not show any adnexal masses. Despite the negative imaging findings, because of markedly elevated testosterone levels, this presentation was thought to correspond to a testosterone-secreting ovarian tumor. The patient was referred for laparoscopic bilateral salpingo-oophorectomy, which showed an ovarian steroid cell tumor in the right adnexa with an unremarkable fallopian tube. The pathology of the right ovary revealed a 2-cm steroid cell tumor, not otherwise specified. Repeat testosterone level after the surgery demonstrated normalization to 10 ng/dL (normal, <75 ng/dL).

Discussion

Steroid cell tumors constitute about 0.1% percent of ovarian tumors. There are 3 subtypes of steroid cell tumors, which include stromal luteoma, Leydig cell tumor, and steroid cell tumor not otherwise specified.[1] In a clinicopathologic analysis of 63 steroid cell tumors not otherwise specified, the most common symptom was virilization, which occurred in 41% of patients.[2] Another case report describes a patient with a similar presentation of recurrent PE, erythrocytosis, and virilization who was found to have a Leydig cell tumor that produced testosterone.[3] Our patient is the first known case of steroid cell tumor causing PE and erythrocytosis. In our patient, the normal adrenal hormone levels and significantly elevated testosterone level was consistent with the neoplasm range. The high levels of testosterone are known to not only cause a hypercoagulable state leading to PE but also increase the mass of red blood cells, leading to marked elevations in hemoglobin levels.

The mechanism by which testosterone causes thrombosis is not clear. In 2014, the U.S. Food and Drug Administration issued a warning about the potential risk of venous blood clots and PEs in patients using testosterone products.[4] There is some evidence of an association between thromboxane A2 receptor density and testosterone therapy in male patients; this was demonstrated in a randomized placebo-controlled trial in which the authors elucidated that testosterone could regulate the expression of thromboxane A2 receptors on platelets, leading to an increased aggregation of platelets, thereby predisposing the patients to venous thromboembolisms.[5]

In hypogonadal men on testosterone replacement therapy, secondary erythrocytosis is a known complication. A systematic review and meta-analysis have demonstrated that testosterone-treated men were at a higher risk of developing erythrocytosis than placebo-treated men.[6] Furthermore, it can be predicted by high trough serum testosterone concentrations.[7] The mechanisms underlying secondary erythrocytosis are poorly understood. One proposed explanation is that testosterone can lead to an increased production of erythropoietin in the kidneys.[8] Additionally, in vitro, testosterone and erythropoietin have been shown to exert synergistic effects on erythroid colony formation.[9] Another proposed mechanism is that testosterone suppresses hepcidin, an iron regulatory peptide produced in the liver, which binds to and destroys ferroportin, an iron channel. It is thought that the decreased hepcidin level leads to increased iron transport and erythropoiesis, which results in higher hematocrit levels.[10] After our patient's tumor was removed, her hematocrit levels normalized and erythrocytosis was resolved. She tested negative for *JAK2* mutation, which signified a low likelihood of polycythemia vera as a cause of her erythrocytosis.

Conclusion

This is the first known case of a testosterone-secreting steroid cell ovarian tumor, not otherwise specified, that led to pulmonary embolism and erythrocytosis. Testosterone-secreting tumors should be considered in the diagnosis of PE as a rare cause of hypercoagulable state.

Disclosure

The authors have no multiplicity of interest to disclose.

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