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# Clinical Hirsutism Secondary to Ovarian Clear Cell Carcinoma: A Rare Case Report

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**ABSTRACT**

**Introduction**: Hirsutism affects 5–15% of premenopausal women, predominantly due to hyperandrogenemia (80–90% of cases), with the remainder classified as idiopathic or normoandrogenic. While virilizing ovarian tumors are known causes, the association between hirsutism and ovarian clear cell carcinoma (OCCC) has not been previously documented.

**Case Description**: A 51-year-old multiparous woman presented with progressive abdominal distension over one year and new-onset hirsutism (Ferriman–Gallwey score 13) involving the face, axillae, pubic area, and lower limbs. She reported abdominal pain, nausea, vomiting, anorexia, 5-kg weight loss, vaginal discharge, regular menses, and poorly controlled type 2 diabetes. Examination revealed an underweight habitus and a firm, irregular, mobile, tender pelvic-abdominal mass extending above the umbilicus. Laboratory evaluation showed hypoalbuminemia (3.22 g/dL), elevated creatinine (1.64 mg/dL), markedly raised CA-125 (1,480 U/mL), and normal serum testosterone (7.5 ng/dL). Imaging confirmed a 9.5 × 8.3 × 5.5 cm solid-cystic right ovarian mass with ascites and suspected peritoneal metastases. Total abdominal hysterectomy with surgical staging was performed; histopathology confirmed OCCC.

**Conclusion**: This is the first reported case of clinical hirsutism in OCCC with normal testosterone levels, supporting a diagnosis of idiopathic hirsutism. Potential mechanisms include increased peripheral 5α-reductase activity, androgen receptor hypersensitivity, or local androgen production, warranting further molecular investigation.

**Keywords**

Hirsutism, Ovarian Clear Cell Carcinoma, Normoandrogenic, Idiopathic Hirsutism

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## INTRODUCTION

Hirsutism is defined as excessive terminal hair growth in a male-pattern distribution among women, primarily affecting androgen-sensitive pilosebaceous units in areas such as the face, chest, abdomen, and thighs [1]. It affects 5–15% of premenopausal women worldwide, with significant psychosocial impact and variable etiology [2]. Approximately 80–90% of cases are attributable to hyperandrogenemia, driven by conditions such as polycystic ovary syndrome (PCOS), congenital adrenal hyperplasia, or androgen-secreting tumors, which promote the conversion of vellus to terminal hair through elevated circulating androgen levels [3,4]. The remaining 10–20% are classified as idiopathic hirsutism, characterized by normal serum androgen levels despite clinically evident hair growth, suggesting peripheral mechanisms of androgen action or sensitivity [5].

Ovarian androgen-secreting tumors, including Leydig cell tumors, Sertoli-Leydig cell tumors, and steroid cell tumors, are rare (<0.1% of all ovarian neoplasms) but well-recognized causes of virilization and hirsutism due to direct testosterone or androstenedione secretion [6,7]. In contrast, epithelial ovarian carcinomas, particularly ovarian clear cell carcinoma (OCCC), are not typically associated with endocrine

manifestations. OCCC accounts for 1–12% of epithelial ovarian cancers in Western populations and up to 25% in Asian cohorts, often linked to endometriosis and ARID1A/PIK3CA mutations [8,9]. It is characterized by chemoresistance, aggressive behavior, and presentation at an earlier stage than high-grade serous carcinoma, with a mean diagnostic age of 56 years (range: 50–55 years) [10,11].

Despite its non-steroidogenic histology, rare paraneoplastic syndromes have been reported in OCCC, including hypercalcemia and thrombotic events; however, hirsutism has not been documented previously [12]. The absence of reported androgen hypersecretion in OCCC raises questions about alternative pathomechanisms in cases of concurrent hirsutism, such as enhanced peripheral 5α-reductase activity, androgen receptor polymorphisms, or tumor-induced cytokine-mediated effects on hair follicle sensitivity [13,14]. This case report presents the first documented instance of clinical hirsutism in a patient with OCCC and normal serum testosterone levels, aiming to explore potential underlying mechanisms and contribute to the understanding of normoandrogenic hirsutism in the context of ovarian malignancy.

## CASE DESCRIPTION

A 51-year-old multiparous woman presented to the gynecology-oncology clinic with a one-year history of progressive abdominal distension, which markedly worsened over the preceding three months and significantly impaired her ambulation and daily activities. She described intermittent, activity-related lower abdominal pain, episodic dyspnea secondary to diaphragmatic compression, postprandial nausea with occasional bilious vomiting, profound anorexia, and unintentional 5-kg weight loss over three months. Additionally, she reported a non-malodorous, non-pruritic whitish vaginal discharge. Concurrently, she developed new-onset hirsutism involving the chin, mandibular rami, axillae, pubic escutcheon, and lower leg (Figure 1).

Figure 1. Clinical photograph demonstrating moderate hirsutism with terminal hair growth on the chin, upper lip, and mandibular regions (Ferriman–Gallwey score: 4/4 for chin).

Her medical history was notable for poorly controlled type 2 diabetes mellitus of 10 years' duration, managed with oral hypoglycemic agents, and regular menstrual cycles. Her obstetric history included four uncomplicated term vaginal deliveries. She underwent three therapeutic paracenteses in the previous month for symptomatic ascites. Physical examination revealed a chronically ill-appearing, underweight female (BMI 17.8 kg/m²) with marked abdominal distention. Hirsutism assessment using the modified Ferriman–Gallwey scoring system yielded a score of 13, indicating moderate-to-severe androgen-dependent hair growth. A firm, irregular, mobile pelvic-abdominal mass was palpable, extending two fingerbreadths above the umbilicus, with an elastic consistency and tenderness on deep palpation. Bimanual vaginal examination confirmed an irregular, fixed, and tender mass occupying the right adnexa and cul-de-sac.

The laboratory investigations are summarized in Table 1. Notable findings included hypoalbuminemia (3.22 g/dL), mild renal impairment (creatinine 1.64 mg/dL), and markedly elevated CA-125 (1,480 U/mL). Serum total testosterone levels were within normal limits (7.5 ng/dL; reference range: 6–82 ng/dL for adult females). The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and comprehensive surgical staging. Intraoperative findings included a 10 × 10 cm encapsulated right ovarian tumor with surface excrescences, dense adhesions to the posterior uterus and rectosigmoid, hemorrhagic ascites (2,800 mL), and multiple nodular implants on the liver capsule, omentum, and parietal peritoneum. Frozen section analysis indicated the presence of carcinoma. Final

histopathology confirmed stage IIIC ovarian clear cell carcinoma with endometrioid differentiation and extensive lymphovascular invasion.

Table 1. Key Laboratory Parameters

| Parameter | Value | Reference Range |
|---|---|---|
| Hemoglobin | 11.2 g/dL | 12.0–15.0 g/dL |
| Albumin | 3.22 g/dL | 3.5–5.0 g/dL |
| Creatinine | 1.64 mg/dL | 0.6–1.1 mg/dL |
| CA-125 | 1,480 U/mL | <35 U/mL |
| Total Testosterone | 7.5 ng/dL | 6–82 ng/dL |
| FSH | 8.2 mIU/mL | Follicular: 3.5–12.5 |
| LH | 6.1 mIU/mL | Follicular: 2.4–12.6 |

Note: Values reflect preoperative assessment; CA-125 was markedly elevated, consistent with malignancy; testosterone was normal, excluding hyperandrogenemia; mild anemia, hypoalbuminemia, and renal impairment were secondary to advanced disease.

Transabdominal ultrasonography revealed a complex 10.96 × 10.77 cm right ovarian mass with mixed solid-cystic components, thick septations, and internal vascularity, accompanied by massive ascites and echogenic peritoneal deposits, suggestive of carcinomatosis. Non-contrast computed tomography (CT) of the abdomen and pelvis revealed a 9.5 × 8.3 × 5.5 cm heterogeneous solid-cystic mass arising from the right ovary, with adhesions to the uterine fundus and sigmoid colon, gross ascites, omental caking, and suspicious osteolytic lesions in the T12 vertebra, right ilium, and bilateral femoral heads (Figure 2).

Figure 2. Axial non-contrast CT image showing a large heterogeneous solid-cystic right ovarian mass (white arrow) with adjacent ascites and omental nodularity (black arrowhead).

## DISCUSSION

Hirsutism, characterized by excessive terminal hair growth in androgen-dependent areas such as the face, chest, and lower abdomen, is a clinical hallmark of hyperandrogenism in most affected women [10]. Approximately 80–90% of cases are driven by elevated circulating androgens, predominantly testosterone and its potent metabolite dihydrotestosterone (DHT), which prolongs the anagen phase of the hair cycle, enlarges the dermal papilla, and promotes vellus-to-terminal hair transformation [3,11]. In contrast, idiopathic hirsutism, diagnosed in 10–20% of patients, occurs despite normal serum androgen levels and ovulatory function, implicating peripheral mechanisms of androgen action rather than systemic overproduction [14]. A comprehensive literature review revealed no prior association between hirsutism and ovarian clear cell carcinoma (OCCC), a subtype comprising 1–12% of epithelial ovarian cancers, known for its aggressive biology, platinum resistance, and frequent linkage to endometriosis and ARID1A/PIK3CA mutations [6,7]. With a median diagnostic age of 50.2–55.7 years, OCCC rarely exhibits endocrine activity, making concurrent hirsutism in this case unprecedented [9].

Instead, the clinical presentation aligns with idiopathic or normoandrogenic hirsutism, in which heightened end-organ sensitivity amplifies androgenic effects without elevating circulating levels [15]. Central to this phenotype is enhanced cutaneous 5α-reductase type 1 activity within pilosebaceous units, catalyzing the irreversible conversion of testosterone to DHT, a fivefold more potent androgen receptor agonist [16]. Additional contributors include androgen receptor (AR) gene polymorphisms on the X chromosome, where

shorter CAG trinucleotide repeats correlate with heightened transcriptional activity and exaggerated phenotypic responses to normal androgen concentrations [17]. Impaired peripheral aromatization, reflected by reduced estradiol-to-testosterone ratios, may further shift the hormonal milieu toward relative hyperandrogenism [18]. Emerging evidence positions the skin as an autonomous steroidogenic organ, expressing the full enzymatic cascade, from StAR protein and P450scc to P450c17, enabling de novo synthesis of DHT from cholesterol or DHEAS independently of gonadal or adrenal input [19,20]. Supporting this, increased mRNA expression of steroid sulfatase and 17β-hydroxysteroid dehydrogenase type 5 has been documented in hirsute skin, facilitating local androgen activation from circulating precursors, such as dehydroepiandrosterone sulfate (DHEAS) [21]. The normal serum testosterone level (7.5 ng/dL) observed herein excludes tumor-derived hyperandrogenemia, a mechanism well-established in ovarian steroid cell neoplasms, such as Leydig or Sertoli-Leydig cell tumors, which secrete testosterone or androstenedione directly [22].

Although OCCC lacks steroidogenic histology, tumor-derived cytokines or paracrine factors could theoretically upregulate these pathways in distant pilosebaceous units; however, this remains speculative pending molecular validation. This case represents the first documentation of clinically significant hirsutism in OCCC with a normoandrogenic profile, challenging conventional etiological frameworks and underscoring the need for integrated genomic, metabolomic, and dermatopathological studies to elucidate non-classical mechanisms of androgen-independent hair growth in malignancy [23].

## CONCLUSION

This is the first reported case of hirsutism associated with ovarian clear cell carcinoma with normal testosterone levels, indicating idiopathic normoandrogenic hirsutism. Peripheral mechanisms, such as enhanced 5α-reductase activity and androgen receptor hypersensitivity, likely drive virilization, necessitating molecular studies to elucidate malignancy-related non-hyperandrogenic pathways.

## DECLARATIONS

None

## CONSENT FOR PUBLICATION

The Authors agree to be published in the Journal of Society Medicine.

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## COMPETING INTERESTS

The authors declare no conflicts of interest in this case report.

## AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to the case report. DFN was responsible for patient management, data collection, and initial drafting of the manuscript. All authors reviewed and approved the final version of the manuscript, ensuring its accuracy and integrity, and are accountable for all aspects of the work.

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