

CASE REPORT

Postmenopausal virilization secondary to a large ovarian cystadenoma with stromal hyperthecosis

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Abstract

Ovarian cystadenomas may present in a functional manner. Biochemical workup of seemingly benign ovarian lesions should be considered in the appropriate clinical context.

KEYWORDS

cystadenoma, functional neoplasm, neoplasm, ovarian, postmenopausal virilization

1 | INTRODUCTION

Ovarian cystadenomas are typically considered nonfunctional tumors that may rarely present in a functional manner. We present the case, workup, and management of a postmenopausal lady with an incidentally found ovarian cystadenoma displaying functional features. Biochemical workup of benign appearing ovarian lesions should be considered in the appropriate clinical context.

Ovarian cystadenomas are benign ovarian tumors derived from surface epithelial cells.¹ Subcategorized on the basis of cyst contents, the majority of these tumors are either serous or mucinous cystadenomas.¹ Traditionally, these tumors are diagnosed in the third to fifth decade of life and are typically unilateral.² Increased utilization of cross-sectional imaging modalities has also translated into an increased detection of otherwise asymptomatic tumors that are usually small and considered “non-functional”.^{3,4} In rare circumstances, these tumors may present in a “functional” manner with the secretion of

excess androgens that subsequently produce virilizing features.^{5,6} We present a case of a postmenopausal woman with virilizing features present secondary to a symptomatic mucinous cystadenoma with stromal luteinization, an extremely rare presentation.

2 | CASE PRESENTATION

Our patient was a 63-Year-old African-American female who presented to our hospital seeking care after a fall at home with no reported syncope. Subsequent trauma workup revealed left-sided rib fractures without underlying cranial, thoracic, or abdominal pathology. A distended abdomen and a soft tissue hematoma overlying the right hip were conservatively managed. Consistent with her trauma evaluation, computed tomography of the abdomen was obtained. This demonstrated a large well-defined abdominal-pelvic cystic mass that measured 32 × 9.5 × 22.1 cm (Figure 1). The patient was admitted, and a more detailed history

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FIGURE 1 A and 1B: Cross-sectional imaging demonstrating Sagittal (Figure 1A) and Coronal (Figure 1B) views of the mass with maximum radiologic dimensions of 24 × 8 cm visible on sagittal view. Arrows point toward mass demonstrating outer surface, with noted displacement of abdominal organs

revealed a woman who had been having early satiety and eating very small meals. However, she did not complain of abdominal pain, nausea, vomiting, or change in her bowel habits. She had seen her primary care physician within the last 6 months and had lost some weight. Furthermore, upon closer scrutiny of her physical appearance temporal wasting was noted as well as masculine appearing facial features. The patient described these features as progressive. A multisystem review for additional complaints was unremarkable. Past medical history was notable for hypertension, dyslipidemia, recurrent falls and a prior stroke with residual left-sided blindness, and hemiplegia. She had undergone a prior laparotomy about 40 years prior but was unable to recall the indication. Additionally, there was no family history of malignancy. Obstetric history revealed one prior full-term vaginal delivery with an unremarkable perinatal and postnatal course. She had undergone menarche at age 10 and described an irregular menstrual frequency with early menopause at age 40. She had a prior 30 pack-year smoking history and occasional use of cocaine and marijuana.

On physical examination, vital signs were within normal limits. The abdomen was symmetrically distended with a midline incision and was soft to palpation with no palpable masses. Virilized facial features were noted including alopecia and facial hirsutism. Examination of the external genitalia was unremarkable without evidence of clitoromegaly.

2.1 | Differential diagnosis, investigations, and treatment

Routine laboratory studies were unremarkable. Tumor markers CA-19, CEA, and CA-125 were all within normal

TABLE 1 Review of currently reported cases of ovarian cystadenomas with virilizing features

Lab	Value	Reference
Serum Chemistry		
Sodium (mEq/L)	136	135–145
Potassium(mEq/L)	4.2	3.5–5.1
Chloride (mEq/L)	104	95–111
Bicarbonate (mEq/L)	25	22–32
BUN (mg/dl)	13	7–25
Creatinine (mg/dl)	0.98	0.6–1.1
Glucose (mg/dl)	115	70–100
Hematology		
Hemoglobin (g/dl)	10.4	12.1–15.9
Hematocrit (%)	31.1	34.3–46.6
Platelet (x10E9)	257	177–406
WBC (x10E9)	6.88	3.2–10.6
Neutrophil	46.2	38–80
Lymphocyte	34.6	11–49
Monocyte	14.4	4–12
Tumor markers and hormones		
Total Testosterone (ng/dl)	146	64–119
Free Testosterone (pg/ml)	12.5	0.1–6.4
Urine B-HCG	Negative	
CA 19–9 (U/ml)	12	<34
CA 125 (U/ml)	9	<35

limits but there was an elevation of testosterone (Table 1). A magnetic resonance imaging (MRI) study of the abdominal and pelvis demonstrated the large mass with low

signal intensity on T1 and high intensity on fluid sensitive sequences without restricted diffusion. Given these features, a differential diagnosis was formulated with high suspicion for a serous cystadenoma. Additional diagnoses under consideration included cystadenocarcinoma and mesenteric cysts. A multidisciplinary discussion was held with the patient, including contributions from the general surgery service, radiology department, and gynecology service. The patient was explained that the likely diagnosis was presumed to be a benign entity, but without histopathologic evidence, a definitive diagnosis, including the possibility of a malignant process, could not be made. Accordingly, the patient was inclined toward removal of the mass. Given the size of the mass, the possibility of malignancy, and her postmenopausal status, it was determined that a complete resection may entail a partial or supracervical hysterectomy and possible salpingo-oophorectomy. The patient was in agreement with this approach. Accordingly, informed consent was obtained preoperatively for resection of the abdominal mass and possible hysterectomy with possible salpingo-oophorectomy.

An exploratory laparotomy was performed. After complete and meticulous dissection, with care to avoid intraoperative spillage, the mass was partially delivered from the abdomen and noted to be attached to both the left colon and the right fallopian tube (Figure 2). These attachments were freed and eventually, the mass was isolated and a stalk-like attachment to the right pelvic wall was found. This was ligated and the mass was excised intact and in its entirety. The uterus and remaining reproductive organs appeared grossly abnormal. In accordance with patient consent, a supracervical hysterectomy with completion salpingo-oophorectomy was then performed and all specimens were sent for pathology; and a sample of cyst fluid was sent for cytology. Peritoneal washings were also sent for evaluation although the mass had no malignant features and only compressed abdominal and pelvic structures without invasion.

2.2 | Outcome and follow-up

Gross pathologic examination revealed a round to oval cystic mass with a smooth and shiny exterior surface. The cystic mass measured 25 x 24 x 8 cm and weighed 5.1kg. A total of 4500 cc of pink viscous fluid was obtained (Figure 3 and Figure 4). The cyst wall thickness ranged from 0.2 to 1.1cm. The right ovary was not identified. However, an area of firm thickening covered by fibrous tissue was noted adjacent to the fimbriated end of the right fallopian tube; microscopically this firm area contained a remnant of ovarian stroma consistent with residual right



FIGURE 2 Intraoperative appearance of cystic mass. Surgeon's hand is toward the patient's feet. Shiny appearance of mass with glistening surface can be appreciated

ovary. Microscopic examination revealed a cystadenoma without papillary excrescences lined by gastric type foveolar epithelium, having bland basally located nuclei. Noted within the cyst wall were clusters and linear arrays of lipid-poor, polygonal luteinized stromal cells, characterized by relatively abundant, agranular pink cytoplasm (Figure 5). The luteinized stromal cells strongly and diffusely with calretinin (Figure 6). Cytology of the cyst fluid was benign without evidence of malignancy. With the exception of characteristic submucosal leiomyomas, the uterus was unremarkable.

Postoperatively, the patient recovered well and tolerated a diet on postoperative day 2. She was discharged on postoperative day 5 after arrangements were made for home therapy, and fall prevention and safety guidance. Since discharge, she has been followed in clinic for 1 year and reports no residual complains and normal recovery.

3 | DISCUSSION

Ovarian cystadenomas are traditionally considered “non-functional”⁷ and therefore associated symptoms are

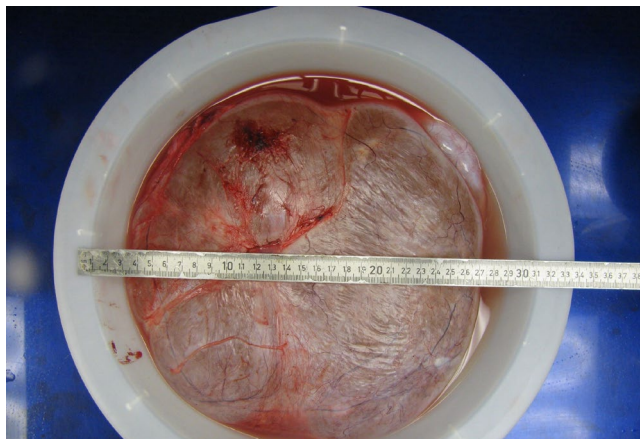


FIGURE 3 Large cystic mass with smooth external surface measuring 25 cm in diameter and weighing 5,110 grams



FIGURE 4 Unilocular cyst with thin wall and glistening smooth internal lining without papillary excrescences

generally secondary to compressive effects on adjacent organs such as the urinary bladder, colon, small bowel, ureters, and abdominal wall. In rare circumstances, such as seen here, these tumors may be a source of androgen secretion, a phenomenon more commonly occurring in adolescent and pregnant women.⁸ Accessory sources of androgen production should also be considered, most notably the adrenal glands⁹ which, in this case, were negative for abnormalities on CT and MRI. Our patient, as a postmenopausal individual, therefore represents a truly rare and unique presentation with only 4 previously existing reported cases to the best of our knowledge.^{5-7,10} We have highlighted the salient features of these cases in Table 2. These previously reported cases have ranged from 68–80 years of age and where clinical information is available, alopecia is a common feature. Two reported cases also displayed hirsutism, similar to our patient. Where available, all cases demonstrated an elevation of serum testosterone.

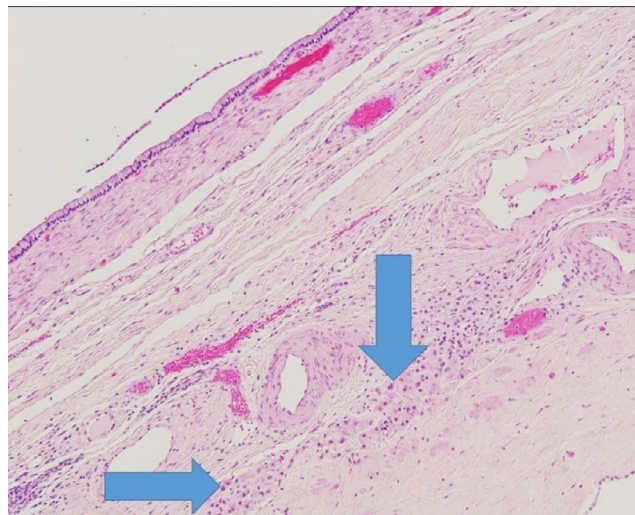


FIGURE 5 Microscopic image demonstrating histologic appearance with arrows point to linear arrays of luteinized stromal cells (40X magnification, H&E stain)

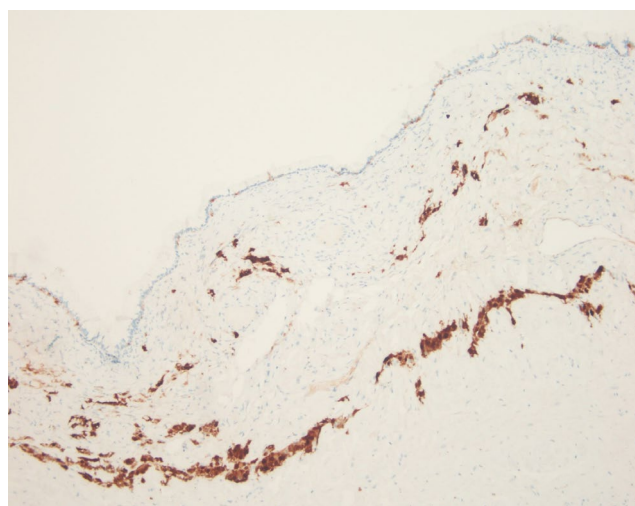


FIGURE 6 Microscopic image demonstrating calretinin immunostain highlighting clusters and linear arrays of luteinized stromal cells (40X magnification)

The underlying mechanisms that transform small sections of these nonfunctional tumors into androgen-secreting segments are poorly understood. Caron et al.⁵ previously put forth several suggestions to explain these exceptionally unique findings. One possible mechanism they mentioned was the excessive stimulation of ovarian stroma by high circulating LH levels in postmenopausal women. Similarly, stromal cell stimulation by the increased blood flow demand of these giant tumors or secretion of certain factors or antibodies from these tumors that may mimic the effects of LH could possibly explain these unique findings.⁵ However, in the absence of direct evidence and uniformity (one case had decreased LH levels⁷),

TABLE 2 Laboratory values and biochemical workup

Reference	Age	Virilizing features	Pathology	Tumor size and location	Biochemical profile
Current case	63	Alopecia Hirsutism	Mucinous Cystadenoma with a cluster of luteinized stromal theca cells	25 x 24 x 8 cm Right ovary	Testosterone: 146 ng/dl (ref: 64–119) Free Testosterone: 12.5 pg/ml (ref: 0.1–6.4)
7	77	Alopecia No hirsutism	Mucinous cystadenoma with stromal luteinization	24 × 9 × 11 cm Right ovary	Total testosterone: 659 ng/dl (ref: 10–70) Dehydroepiandrosterone sulfate of 1950 ng/ml (ref 170–900)
10	68	Not reported	Mucinous Cystadenoma with luteinized stromal cells	Not available	Not available
5	73	Alopecia Hirsutism Clitoral hypertrophy	Cystic cystadenoma with hyperplasia of stromal cells	10 × 10 cm Left ovary	Serum testosterone: 340 ng/dl (Ref 10–70)
6	80	Alopecia Hirsutism	Serous cystadenoma with a thin layer of luteinized cells in the cyst wall	10 cm Left ovary	Serum Testosterone: 58.5 pmol/L (ref: 1–12) Gonadotropins: postmenopausal range

these theories remain questionable. Another theory highlighted by Okolo et al.⁶ postulates that the pressure effect of these masses may induce luteinization and functional activity within certain areas. Further investigations and experiments are undoubtedly required to explain this unique pathophysiology.

4 | CONCLUSION

In conclusion, we report an extremely rare case of a postmenopausal patient with virilizing features and a biochemical profile secondary to an ovarian mucinous cystadenoma with histopathologic evidence of hyperplasia of luteinized ovarian stromal cells. We reviewed the previously reported cases and summarized their pathologic and clinical profiles and outlined the possible mechanisms underlying this stain unique presentation.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests and there are no relevant financial disclosures to report.

AUTHOR CONTRIBUTIONS

Wasay Nizam made substantial contributions to conception, design, data acquisition, and interpretation of the study and was involved in initial drafting of the manuscript and critically revised the final manuscript. Adil Aijaz Shah made substantial contributions to conception and design of the study and was involved in initial drafting of the manuscript and critically revised the final manuscript. Edward Cornwell made substantial contributions to conception and design of the study, acquisition, analysis, and interpretation of data and was involved in initial drafting of the manuscript and critically revised the final manuscript for important intellectual content. Tammey Naab made substantial contributions to conception and design of the study and was involved in initial drafting of the manuscript and critically revised the final manuscript for important intellectual content. Mallory Williams made substantial contributions to conception and design of the study, acquisition, analysis, and interpretation of data and was involved in initial drafting of the manuscript and critically revised the final manuscript for important intellectual content. All Authors reviewed the final manuscript and give approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately

investigated and resolved. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

PATIENT CONSENT

Written informed consent was obtained from the patient's family prior to submission.

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