A Case Report on Synchronous Adult Granulosa Cell Tumour and Endometrial Cancer

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Summary

Granulosa cell tumours (GCTs) are a rare type of ovarian cancer, representing only 2-5% of all ovarian malignancies. They are mainly estrogen secreting tumour. These tumours can be diagnosed either by ovarian cancer symptoms or endometrial pathologies. The estrogenic effect of the tumour gives rise to an abnormal uterine bleeding pattern. We report a case of GCT associated with endometrial carcinoma. The aim is to review the clinical features of GCT, along with its prognosis, treatment and follow-up recommendations, given in the available literature.

Keywords: Granulosa cell tumour; Endometrial cancer; Postmenopausal bleeding.

Introduction

Granulosa cell tumour (GCT) comprises 5 % of all ovarian malignancies but accounts for 70% of malignant sex- cord- stromal tumours. GCT is of two variety, juvenile (5%) and adult (95%) type. The adult type occurs more commonly in post-menopausal woman with a mean age of 50-54 years.[1] Symptoms of GCT are abdominal pain, abdominal distention due to large tumour size (average diameter of 12 cm), abnormal vaginal bleeding and secondary amenorrhea. GCT produces estrogen resulting in an abnormal uterine bleeding pattern- menorrhagia, metrorrhagia and post-menopausal bleeding. Prolonged exposure of estrogen to endometrium results in endometrial hyperplasia and endometrial adenocarcinoma.[2] Endometrial adenocarcinoma associated with GCT are often well- differentiated, present in early stage and have good prognosis.[3]

Case Report

A fifty-year-old nulliparous, post-menopausal woman was referred to our hospital with endometrial biopsy report suggestive of moderately differentiated, endometroid adenocarcinoma. She had complaint of multiple episodes of bleeding per vaginum for 15 to 20 days. She had attained her menopause two years back. On abdominal examination, a 10x10 cm firm mobile mass was felt extending from right iliac fossa up to the umbilical region. On sterile speculum examination, cervix and vagina were normal. On bimanual examination, a 10x10 cm mass was felt on the right side of the pelvis, uterus was bulky in size. Both parametrium and pouch of Douglas were uninvolved. C.T. scan of abdomen and pelvis revealed heterogeneously enhancing mass of 114x113x112 mm with a solid and hypodense area in the pelvic cavity, and thickened endometrium measuring 26 mm. CA-125 level was 533 U/ml, carcino-embryonic antigen and CA 19-9 were within normal limits. Papanicolaou test was negative for malignancy. Upon slide review of the endometrial biopsy revealed well differentiated, endometroid adenocarcinoma. The provisional diagnosis was endometrial carcinoma with ovarian tumour (possibility of GCT). The patient underwent staging laparotomy. Intraoperatively, a solid cystic right adnexal mass of about 10x11x9 cm was found, uterus was bulky, left adnexa, rest of the pelvis and abdominal viscera appeared to be normal. Frozen section of mass was suggestive of granulosa cell tumour of the right ovary. Total abdominal hysterectomy, left salpingo-oophorectomy, bilateral pelvic lymph node dissection (BPLND), infracolic omentectomy and multiple peritoneal biopsies were performed. Ascitic fluid cytology was negative for malignant cells. The final histopathology revealed well – differentiated, micro follicular, insular, solid pattern GCT of right ovary (10 x 9 cm) with mitosis of 1-2 /10 HPF and capsular infiltration without capsular breach. It also showed well-differentiated endometroid adenocarcinoma of the uterus, lesion measuring 5x4.5x1.8 cm and myometrial invasion of < 50 % without lymph vascular permeation. Lower uterine segment, cervix, left adnexa, bilateral pelvic lymph nodes, peritoneal biopsies and omentum were free of tumour. FIGO stage of GCT was stage IC2 and carcinoma endometrium stage IAG1. After tumour board discussion, she received 6 cycles of adjuvant chemotherapy (carboplatin and paclitaxel) for GCT stage IC2. After consultation with radiotherapist patient was kept on observation for endometrial cancer stage IAG1. She is on regular follow up and disease free till date (34 months).

Discussion

GCT is the most common estrogen producing ovarian tumour. The adult type GCT is responsible for

abnormal vaginal bleeding, breast tenderness and pelvic pain .[4] GCT can be solid (28%) or cystic tumour (30%). They are usually unilateral but bilateral occurrence can occur in 10% cases. They usually have a favourable outcome because of low grade with indolent growth. Radiologically, adult GCT presents as a solid large mass measuring up to 12 cm in diameter, with the multicystic appearance or solid tumour with heterogeneous echogenicity.[5] So, whenever the patient presents with large, unilateral, solid, cystic, adnexal mass associated with abnormal bleeding per vaginum, differential diagnosis can be GCT, primary endometrial cancer metastasising to the ovary, primary ovarian cancer with metastasis to the uterus and synchronous epithelial ovarian and endometrial cancer. On microscopy, call-exner bodies, nuclear grooves and coffee bean nuclei are pathognomic diagnostic features of GCT.[6] Microfollicular, trabecular, solid, tubular, diffuse and water- silk patterns are histological pattern seen in GCT. Endometrial hyperplasia is reported in 25-50% of cases.[7] Low-grade endometrial adenocarcinoma develops in approximately 10% of patients of GCT. [3] They are usually well-differentiated, and detected in an early stage with favourable prognosis as seen in our case.[3] Diagnostic work up includes imaging, tumour marker - inhibin B and, endometrial biopsy. Serum inhibin has 89% sensitivity with 100% specificity to diagnose recurrent disease and should be used when available. In our case, inhibin B testing was not done due to non-availability of this testing in our institute and patient could not afford to get it done outside.We followed the patient with clinical examination, USG, and CA-125(which was increased pre-operatively). The most important prognostic factor in ovarian GCT is stage. Other prognostic factors are mitotic activity, DNA ploidy and S-phase fraction.[8] Surgery remains the cornerstone of the treatment. Comprehensive staging surgery should be done to establish the real extent of disease. Staging laparotomy with total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, multiple peritoneal biopsies and peritoneal cytology should be performed in whom child bearing is completed. As there is no evidence that nodal dissection has improved the survival rate, so, BPLND is not recommended in surgical staging of GCT.[9] Suspicious nodes should be excised or sampled. In our case bilateral lymph node dissection was carried out as it is recommended in the management of the endometrial cancer. Approximately 75% of GCT are diagnosed in stage I A-C, 20% stage II, 8% stage III and 6% stage IV of tumour disease.[10] In GCT five-year survival with early disease (I A or I B) is 96% and no adjuvant treatment is required. However, patients with, stage1C with poor prognostic factors (large tumour size, high mitotic index or tumour rupture), stage III and IV are candidates for adjuvant platinum-based chemotherapy because of increased risk of relapse. Lifelong follow-up with clinical examination, ultrasound, and inhibin B measurement is recommended as GCT is known for late recurrences.

Ethical issues: None

Abbreviation

GCT: Granulosa Cell Tumour, BPLND: Bilateral pelvic lymph node dissection

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