International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Kumar D et al. Int J Reprod Contracept Obstet Gynecol. 2026 Sep;15(9):3656-3659
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20263055

Case Report

Squamous cell carcinoma of ovary in young premenopausal female: a case report and literature review

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Received: 13 May 2026
Revised: 15 August 2026
Accepted: 17 August 2026

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ABSTRACT

Mature cystic teratoma (MCT), also known as dermoid cyst, is a germ cell neoplasm commonly seen arising in the ovary of young females. It is usually benign but carries a malignant transformation risk of 0.5–2% of cases. Squamous cell carcinoma is the most common subtype of malignant transformation, followed by adenocarcinoma. We report a case of squamous cell carcinoma arising in a dermoid cyst of the ovary, presenting at an early stage, in a 44-year-old pre-menopausal female with a one-month history of lower abdominal pain and a large abdominopelvic mass on examination. Final histopathology confirmed squamous cell carcinoma of the left ovary arising from a mature cystic teratoma.

Keywords: Dermoid cyst, Mature cystic teratoma, Squamous cell carcinoma, Ovary, Malignant transformation

INTRODUCTION

Ovarian teratoma is an ovarian neoplasm of the germ cell family. Teratomas arise from a single germ cell and may contain any of the three germ layers-ectoderm, mesoderm, and endoderm-typically in a disorganized arrangement. Mature cystic teratoma (MCT), also known as benign cystic teratoma or dermoid cyst, is the most common type of ovarian teratoma and is usually benign in nature. It constitutes 10-25% of all ovarian neoplasms and 60% of all benign ovarian neoplasms.[1] Dermoid cysts are usually slow growing, mostly measuring between 5-10 cm in size, and are bilateral in 10% of cases.[2] The cut section mostly appears unilocular and one area of localized growth-known as the Rokitansky protuberance-is thought to be the site of malignant transformation, appearing as a mural nodule on ultrasound. The risk of malignant transformation is 0.5-2%, with squamous cell carcinoma being the most common subtype, followed by adenocarcinoma. Mature cystic teratoma (MCT) arises through asexual parthenogenesis, and almost all MCTs have a 46, XX karyotype.[3] Squamous cell carcinoma arising in MCT is commonly seen in postmenopausal females and is rare in young premenopausal females.[4] Common risk factors for malignant transformation include tumor size >10 cm, age >50 years and a raised CA-125 value; CA 19-9 levels are elevated in 30% of cases. Microscopically, the ectodermal component predominates, with endodermal and mesodermal elements also present. The cyst is lined by keratinized squamous epithelium and contains sebaceous and sweat glands; hair, fat, bone and teeth may also be seen. Mature cystic teratoma (MCT) can often undergo torsion. Magnetic resonance imaging (MRI) is the most sensitive investigation for a dermoid cyst presenting as a complex adnexal mass; however, in the absence of consensus on definitive clinical features, tumor markers and imaging criteria, malignancy is mostly diagnosed postoperatively.

Tumors limited to the ovary have a better prognosis and survival. Treatment is usually conservative, consisting of cystectomy in most cases, though intraperitoneal rupture must be avoided to prevent chemical peritonitis. We present a case of squamous cell carcinoma of the ovary that was diagnosed at an early stage and managed appropriately, keeping in mind the poor prognosis of this condition.

CASE REPORT

A 44-year-old multiparous woman presented to the outpatient department with a one-month history of pain in the lower abdomen, which had increased in intensity over the preceding 7 days. Her general condition was good. Per-abdominal examination revealed a large, well-defined, firm-to-hard, non-tender, mobile mass in the hypogastric region arising out of the pelvis, corresponding to a 16-18-week gravid uterus. Pelvic examination revealed the same mass, occupying predominantly the left side, moving without cervical movement. Routine and specific investigations were carried out. Ultrasound of the whole abdomen and pelvis suggested a dermoid cyst of the left ovary, a normal right ovary and features of adenomyosis in the uterus. MRI of the pelvis showed a large complex solid-cystic pelvic mass with hair-like structures, calcification and a mural nodule, suggestive of a mature cystic teratoma of the left ovary. Tumor marker values were as follows: CA-125, 27 U/ml, CEA (carcinoembryonic antigen), <0.2 ng/ml and CA 19-9, 61.52 U/ml.

As the preoperative work-up suggested a dermoid cyst, the patient was planned for laparoscopic cystectomy. On laparoscopy, a 12 × 12 cm irregular mass arising from the left ovary was seen, adherent to the sigmoid colon, with the left fallopian tube stretched over it and loss of the fat plane between the sigmoid colon and the mass. The uterus, right fallopian tube and right ovary appeared normal. As the mass appeared suspicious for malignancy, laparotomy with frozen section was performed after obtaining consent from relatives. Left salpingo-oophorectomy was done and the specimen sent for frozen section was suggestive of mature cystic teratoma with a solid area containing atypical dyskeratotic cells. Complete surgical staging was then carried out, including removal of enlarged pelvic lymph nodes.

Final histopathology confirmed squamous cell carcinoma of the left ovary arising from the dermoid cyst (Figure 1, 2, 3 and 4). Both fallopian tubes, parametrial tissues, peritoneal biopsies, uterus, cervix, omentum and pelvic lymph nodes were free of tumor and peritoneal fluid was negative for malignant cells. The patient was staged as squamous cell carcinoma of the left ovary arising in an MCT, surgical stage Ia. Her postoperative course was uneventful. Following discussion at our multidisciplinary tumor board, adjuvant chemotherapy (six cycles of paclitaxel and carboplatin) was initiated in view of the poor prognosis associated with this disease.

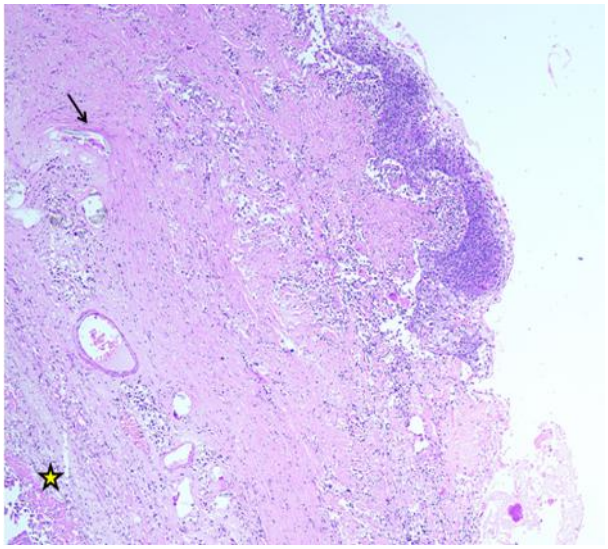

Figure 1: Photomicrograph showing the ectodermal component in the form of stratified squamous lining with dysplasia, with a hair shaft (arrow) in the stroma and keratinous material (star) (H&E, 40X).

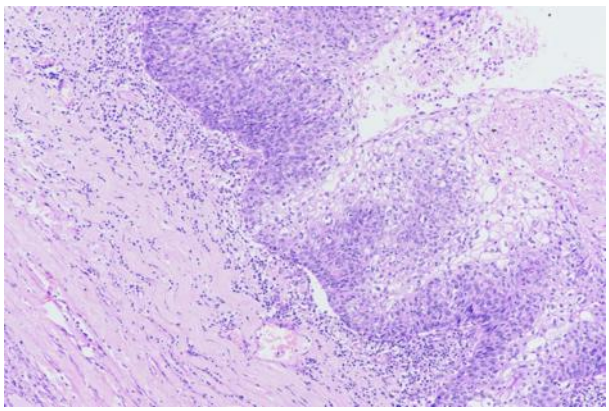

Figure 2: Photomicrograph showing the ectodermal component (stratified squamous epithelium) with full-thickness dysplasia-cytological and architectural-and mitoses at all levels (H&E, 100X).

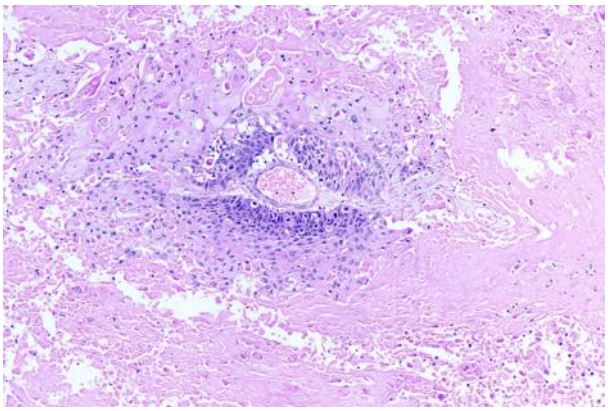

Figure 3: Photomicrograph showing tumor cells with squamoid morphology, with single-cell keratinization and adjacent sheets of keratin (H&E, 200X).

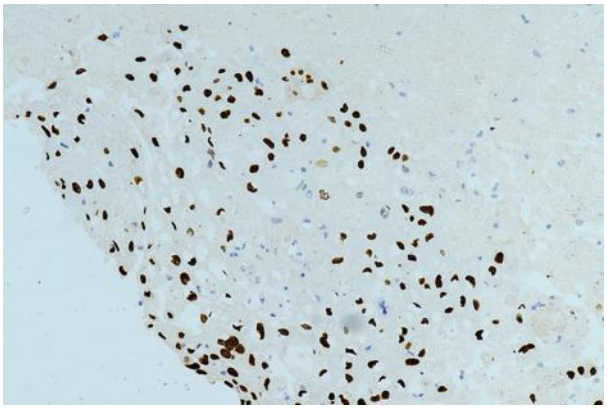

Figure 4: Photomicrograph showing p63 immunohistochemistry with nuclear positivity in tumor cells (IHC, 200X).

DISCUSSION

Squamous cell carcinoma (SCC) of the ovary is a rare malignancy that most commonly arises in a pre-existing mature cystic teratoma (MCT) of the ovary, in up to 2% of cases and is usually diagnosed postoperatively.[4] Preoperative diagnosis is difficult, although MRI may be helpful; Takagi et al found CEA to be more useful than CA -125 and CA 19-9 for diagnosing malignant transformation of an MCT.[5]

In our patient, however, CA -125 and CEA were within normal limits and only CA 19-9 was mildly elevated, which illustrates the limited reliability of tumor markers for preoperative diagnosis in individual cases; malignancy was suspected only intraoperatively, on the basis of adhesion to adjacent viscera and loss of the fat plane, and was confirmed on frozen section, which allowed the surgical plan to be escalated appropriately in a single sitting.The key findings of the present case are threefold. First, the patient was diagnosed at an early surgical stage (International Federation of Gynecology and Obstetrics-FIGO Ia), which is uncommon, as most reported cases of SCC in MCT present at an advanced stage.[4]

Second, she was relatively young (44 years) and premenopausal, whereas SCC arising in MCT typically occurs in postmenopausal women older than 50 years.[4,6] Third, she remained disease-free at 6 months of follow-up after surgery and adjuvant chemotherapy, an outcome consistent with the favourable prognosis reported for stage Ia disease.[4]

Hackethal et al published a systematic review and analysis of 64 studies comprising 277 patients and found that SCC in MCT mainly occurred in women older than 50 years, with raised CA -125 levels and ovarian tumors larger than 10 cm; they also found that FIGO stage Ia disease had better survival than advanced disease, that complete resection followed by adjuvant chemotherapy was associated with better survival and that adjuvant radiotherapy did not improve survival.[4] Similarly, Kikkawa et al in a clinicopathological analysis of SCC arising from MCT, reported that tumor size, patient age, and stage at diagnosis were important prognostic determinants, with early-stage disease carrying a markedly better outcome than advanced disease.[6] Tangjitgamol et al reported four cases of SCC among 425 dermoid cysts over a 10-year period (incidence 0.94%); three of their patients had early-stage disease and remained disease-free on long-term follow-up, while the one patient with stage III disease died within a year despite chemotherapy, again highlighting the prognostic importance of stage at diagnosis.[7] In a report of 37 cases of primary ovarian SCC, Pins et al similarly found that survival correlated closely with stage, with the poorest outcomes seen in patients with extraovarian spread at diagnosis.[8]

In contrast to these predominantly early- or mixed-stage series, a retrospective case series and review of the literature published in European Oncology and Hematology in 2013, conducted over 24 years (1986-2010), described six women treated for SCC in MCT, all of whom presented at FIGO stage III/IV.[9] Durable responses were difficult to achieve in this cohort; the best response was seen in a patient who had a partial response to chemo-radiotherapy, with survival of 19 months and the authors suggested that concurrent chemoradiation could be considered for disease confined to the pelvis, although median survival in their series was only 12.5 months.[9] This markedly poorer outcome, compared with our patient's disease-free status at 6 months, reinforces the premise that early diagnosis and complete surgical staging are the most important determinants of survival in this disease.

Sporadic case reports have also been published by Indian authors on this subject. Khajuria et al and Santwani et al reported SCC in dermoid cysts at younger ages-37 and 40 years, respectively-both diagnosed postoperatively on histopathology, similar to our case.[10,11] Our patient was likewise young at presentation, was diagnosed following intraoperative suspicion of malignancy and was started on adjuvant chemotherapy after complete surgical staging; she tolerated treatment well and has remained disease-free 6 months after completing treatment. Taken together, these comparisons suggest that although SCC arising in MCT typically carries a poor prognosis-particularly in older women with advanced-stage disease-early intraoperative suspicion, frozen-section-guided complete surgical staging, and prompt initiation of platinum-taxane-based adjuvant chemotherapy, as in our patient, can achieve favourable short-term outcomes even when the diagnosis is unexpected.

CONCLUSION

Keeping in view the rarity and poor prognosis of squamous cell carcinoma of the ovary arising in a mature cystic teratoma, a gynecologist needs to be aware of this condition and be equipped and prepared to deal with it. Given the rarity of the disease, adjuvant treatment options, along with treatment response and follow-up, must

continue to be reported to help inform future treatment guidelines.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Kumar D, Yadav G, Sharma R, Singh P. Squamous cell carcinoma of ovary in young premenopausal female: a case report and literature review. Int J Reprod Contracept Obstet Gynecol 2026;15:3656-9.