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Citation for this version and the definitive version are shown below.

Citation to Publisher Version: Heller, Debra, Ukazu, Adanna, Campbell, Damali & Cracchiolo, Bernadette. (2017). Carcinoma-in-Situ in a Benign Cystic Teratoma of the Ovary: A Possible Precursor of Invasive Squamous Cell Carcinoma of the Ovary. *Journal of Gynecologic Surgery* 33(1), 34-36. <http://dx.doi.org/10.1089/gyn.2016.0052>.

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**Carcinoma-in-Situ in a Benign Cystic Teratoma of the Ovary-a possible precursor
of invasive squamous cell carcinoma of the ovary.**

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Word count: Précis:17, Body of Text: 937

Running title: Carcinoma in situ of ovary

Tables 1, Figures 1

Institutional Review Board approval is not required at our institution for case reports.

Acknowledgements: None

Authors disclosure statement: The authors have no disclosures

Keywords: ovarian neoplasms, teratoma, squamous cell carcinoma, carcinoma in situ

Abstract:

Background: Squamous carcinoma-in-situ(CIS) within a benign cystic teratoma is exceptionally rare, particularly in the absence of an adjacent invasive squamous component. Most of the few reported cases of CIS without invasive carcinoma occur in postmenopausal women, and are usually incidental histopathologic findings.

Case: We present a case of CIS in a benign cystic teratoma, which preceded invasive squamous cell carcinoma in the contralateral ovary, and review the literature.

Conclusions:

In the absence of invasion, excision of the ovary with CIS appears to be adequate therapy. If CIS is detected histopathologically, a search for invasive elements should be undertaken.

Introduction:

Malignant degeneration within a benign cystic teratoma of the ovary is rare. The most common neoplasm identified in such cases is squamous cell carcinoma(1), not surprising, given the predominance of squamous epithelium in dermoids. Non-invasive squamous carcinoma-in-situ(CIS) in teratomas is exceptionally rare, and the expected behavior unclear. We present a case, and review the literature.

Case Report

A 35 year old G1P1001 woman underwent exploratory laparotomy and bilateral ovarian cystectomies for bilateral ovarian dermoid cysts. A 13x12 cm right and 15 x 13 cm left cyst were excised, and on histopathology confirmed to be benign cystic teratomas. Six months later, the patient presented with complaints of pelvic pain, and was found to have a 7 cm left adnexal cyst. She underwent laparoscopic oophorectomy for what was thought to be recurrent dermoid. The final diagnosis of the ovary was invasive squamous cell carcinoma(SCC). A re-review of the slides of the bilateral cystectomies showed a minute focus of carcinoma-in-situ in the right ovary(fig 1), opposite to the current invasive carcinoma. P16 immunostain was negative. There was no evidence of malignancy or dysplasia in the sections of cyst from the left ovary at the original excision.

Discussion:

Malignant degeneration in a benign cystic teratoma is estimated to occur in less than 2% of cases, and the majority of malignancies are squamous cell carcinoma(2). Squamous carcinoma-in-situ arising(CIS) in a dermoid is exceptionally rare, particularly in the absence of adjacent invasive carcinoma. A transition from CIS to invasion has been described in some cases(2,3,4), with two of fifteen invasive squamous cell carcinomas showing an in situ component in one series(4), but only a few cases of CIS without invasive squamous cell carcinoma have been reported(table 1)(5-12). CIS as the precursor lesion is further supported by the report of a case of “microinvasive” squamous cell carcinoma arising in the ovary(13). Because of the rarity of the finding, it is unclear what the expected behavior of CIS in a dermoid is, however in a literature review of SCC in dermoids, Chen et al(14) found 5 cases of CIS in dermoids, with 100% five year survival. While they did not specify which cases these were, there is sufficient overlap in their bibliography with the cases reviewed here to conclude that most if not all are the same.

The limitation in our case is the retrospective nature of the identification of the dysplastic focus in the original surgical specimen, and hence we can only claim no dysplasia in the ipsilateral ovary based on existing sections. However, it is reasonable to speculate that whatever molecular alteration caused the CIS in the contralateral ovary may have also exerted similar effect on the one that developed invasive carcinoma. It has been suggested that human papillomavirus may play a role in squamous neoplasia in dermoids(15), however p16 immunostain, a surrogate marker of high risk HPV was negative in our case as well as that of Gurrera et al(11).

The origin of CIS in the ovary is unclear. Of interest is a case of ovarian CIS arising 8 years after a radical hysterectomy for superficially invasive cervical squamous cell carcinoma, where there were no teratomatous elements in the ovary(16). It is unlikely that the superficially invasive cervical tumor metastasized 8 years later, but the association of squamous neoplasia of cervix and concomitantly in ovary has been reported, and it has been suggested as a field effect(16). Lending some credence to this is the finding of HPV in some squamous cell carcinomas of the ovary(15). In one case, CIS in the absence of teratoma or other neoplasia was described(17). While frankly invasive SCC can arise in the ovary de novo, the authors were unable to explain the origin of their case.

Although the majority of ovarian squamous cell carcinomas arise in conjunction with teratomas, association has also occurred with Brenner tumors, and endometriosis, and the associated elements should be sought(1,16). CIS within a dermoid has been suggested to arise in squamous metaplasia arising from columnar epithelium within the dermoid(1), much like the transformation zone of the cervix. Our case of invasive SCC at the second procedure did not at that time show teratomatous elements, however they were present in the previous cystectomy specimen, and hence it is likely the carcinoma overgrew any residual identifiable teratomatous elements.

It has been emphasized that findings suggestive of frank malignancy arising in a benign cystic teratoma include postmenopausal age, adhesions from the neoplasm, solid areas or areas of unusual thickness of the wall, and necrosis(5), however there are no specific preoperative findings indicative of CIS. It has been suggested that the infrequency of reported CIS in dermoids is due to the fact that these potentially small

microscopic foci, as in our case, are not detectable grossly(11), and may not be detected on routine representative sampling of a dermoid(6). Cytologic examination may miss a malignancy(12), and in our case, ovarian cyst fluid submitted during the first procedure only showed keratinaceous debris.

In summary, CIS arising in a dermoid may be the precursor lesion of invasive SCC arising from a dermoid. Most reported cases were seen in postmenopausal women(table 1). In isolated CIS, excision appears to be adequate therapy. If CIS is detected, extensive sampling is warranted. Given the rarity of CIS in dermoids, there is no reason, at this time, to alter existing recommendations for observation of smaller presumptive dermoids detected on ultrasound. There is not enough data to establish a definitive recommendation for whether or not to perform ipsilateral oophorectomy for CIS discovered at cystectomy. The approach to these cases should be individualized. Additional cases will add to our understanding of this rare lesion.

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