Squamous cell carcinomas of the ovary: report of four cases and literature review

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Summary

Two cases of squamous cell carcinoma developing in mature cystic teratoma and two cases with a malignant change involving an ovarian epidermal cyst diagnosed in our institution over a 15-year-period are reported. This is a reminder that such changes may occur and issues regarding the problem of the differential diagnosis and management of these rare complications are discussed.

Key words: Squamous cell carcinoma; Teratoma; Epidermal cyst; Ovary.

Introduction

Teratoma is one of the most common ovarian tumors (15-20% of all ovarian tumors). They are germ cell tumors arising from a single germ cell after the first meiotic division, according to recent studies [1]. The rare epidermal cyst is considered as an epithelial ovarian tumor that arises from epithelial cell nests and ovarian Brenner tumors [2, 3].

Malignant transformation of teratomas is rare, occurring in approximately 1% of all ovarian teratomas [4]. Though malignant transformation may occur from any of the embryonic germ layers, the most common malignancy arising in these predominantly benign tumors is squamous cell carcinoma. We present two cases of squamous cell carcinoma developing in mature cystic teratoma and two cases with a malignant change involving ovarian epidermal cysts that were diagnosed in our institution over a 15-year-period. Issues regarding the problems of the differential diagnosis and management of these rare complications are discussed.

Materials and Methods

We analyzed retrospectively the clinical and pathological characteristics of 87 teratomas of the ovary examined in the Pathology Laboratory during the last 15 years. Teratomas constituted 5% (87/1,680) of all ovarian tumors. We found only four cases of squamous cell carcinoma arising in teratomas and epidermal cysts of the ovary (4.59%). In addition to routine studies immunohistochemistry for the study of p53 (D07, Novocastra, Newcastle, UK) and CEA (CD66, Neomarkers, CA, USA) was performed.

Clinical features

Case 1

A 66-year-old woman was admitted to our hospital due to acute abdominal pain. Pelvic examination revealed a large palpable mass filling the pelvis located mainly on the left side. Ultrasonographic examination revealed a large, semicystic mass measuring 14 cm x 12 cm approximately, replacing the left ovary. The cyst was filled with hair and sebaceous material and presented a nodule measuring 3 cm in the greatest diameter. Frozen section biopsy showed an ovarian teratoma and a left salpingo-oophorectomy was perfomed. The cyst was removed intact.

Case 2

A 50-year-old woman was admitted to our hospital suffering from acute abdominal pain. Ultarasonographic examination revealed a large cystic mass filling the pelvis measuring 10 cm x 8 cm approximately, replacing the right ovary. A right salpingo-oophorectomy perfomed. The cyst was removed intact and was filled by hair and sebaceous material. The wall 0.5-1 cm in thickness, presented a firm nodular area measuring 4 cm.

Case 3

A 26-year-old patient was admitted to our hospital for acute abdominal swelling and pain. The physical examination and pelvic CT revealed an ovarian mass measuring 11 x 5 cm approximately. A right salpingo-oophorectomy was perfomed and the cyst was removed intact.

Case 4

A 65-year-old patient was admitted to our hospital due to abdominal pain and constipation. Pelvic examination revealed a large mass filling the pelvis on the right side, probably of ovarian origin. Total hysterectomy and bilateral salpingo-oophorectomy were perfomed.

Pathology reports

Cases 1 and 2

A routine histological examination was carried out and sections were stained with hematoxylin and eosin.

Multiple microscopic sections from the cystic parts of the specimens revealed a mature cystic teratoma, lined partially by skin, containing hair follicles and sebaceous glands. Deeper in the fibrous wall of the cyst cartilage surrounding cystic spaces lined by respiratory-type pseudostratified columnar epithelium was observed. Microscopic sections from the nodular areas revealed in both cases an situ squamous cell carcinoma that showed limited and focal invasion of the underlying stroma which presented a considerable inflammatory reaction (Figure 1).

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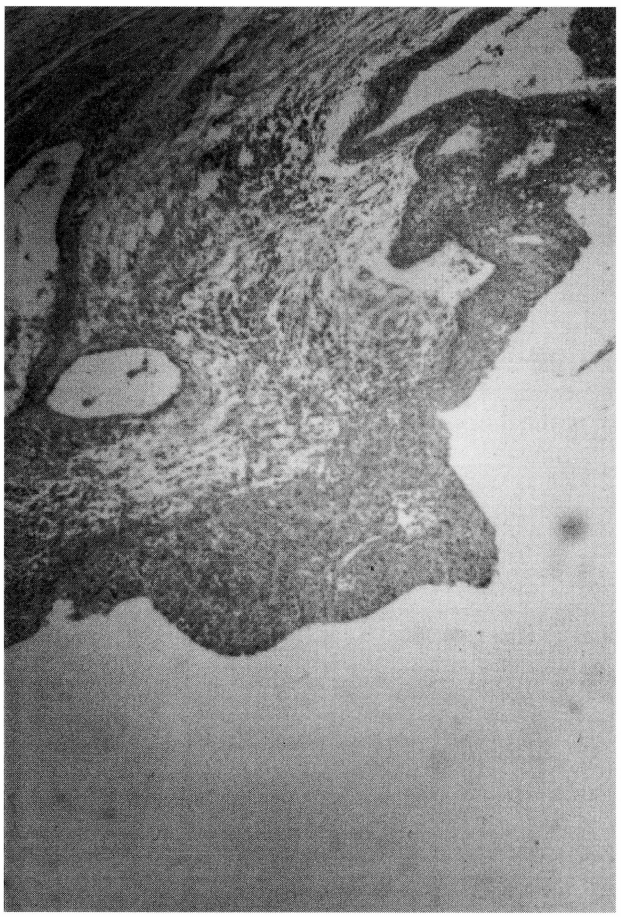

Figure 1. — Histological appearance of in situ squamous cell carcinoma arising in mature cystic teratoma (hematoxylin and eosin x 250).

Cases 3 and 4

Both tumors were cystic, containing whitish sebaceous material and were lined by a multilayered squamous cell epithelium while the absence of skin adnexae and other tissues was noted in multiple sections. According to these findings these two ovarian tumors fulfill the criteria to be classified as epidermal cysts and not as teratomas. In both cases malignant tumor with the morphological features of squamous cell carcinoma was diagnosed. The cysts were obviously malignant, being large and thick-walled with a nodular inner surface. In no case was infiltration through the wall and into the adjacent structures noted.

All malignant ovarian tumors were unilateral tumors (3/4 in the right and 1/4 in the left ovary) measuring 10-14 cm. No extension outside the ovary or evidence of distant metastasis was found during the investigation. These patients were referred to the Oncology Department and are well two to four years after diagnosis. Additional sections of all malignant tumors were investigated by a streptavidin-biotin immunohistochemical method and showed a positive reaction for CEA and a p53 overexpression in all cases.

Discussion

Cystic teratoma is a very common ovarian lesion that makes up almost 20% of all ovarian neoplasms of adults, being in the majority of cases benign [1]. They are unilateral in 88% of all cases and provoke symptoms relating to mass size (pain, urinary and gastrointestinal complaints and menstrual irregularities) [5]. Microscopically they present ectodermal derivatives in 100% of the tumors, mesodermal structures in 93% and endodermal derivatives in 71% [1].

The rare epidermal cysts of the ovary are distinguished from mature cystic teratomas on thorough sampling by the absence of skin adnexae and other tissues [2].

Gonadal germ cell tumors continue to be the cause of diverse diagnostically challenging issues for the pathologists. Within the teratoma group there is strong evidence that ovarian teratomas are derived from benign germ cells. When an uncommon somatic-type malignancy occurs in mature cystic teratomas of the ovary it is a de novo form of malignant transformation [6].

The most common malignant change in cystic teratoma is squamous cell carcinoma, which accounts for approximately 80% of the total [4, 7], followed by carcinoid tumor and adenocarcinoma [8]. Most squamous cell carcinoma (SCC) arises from dermoid cysts and is classified in the germ cell category. Less commonly they occur in association with endometriosis, as a component of Brenner tumors or in pure form and are considered to be surface epithelial-stromal tumors. Histologically, SCC are usually high grade and show a variety of patterns. They must be distinguished from endometroid adenocarcinomas with extensive squamous differentiation and from metastatic squamous cell carcinoma from the cervix and other sites.

Moreover there are no significient data presented in the literature about the recently recognized and rare epithelial epidermal cysts and their propensity for malignant change. Epidermal cysts are benign ovarian epithelial cysts lined by squamous epithelium devoid of skin appendages and unaccompanied by teratomatous elements. All up-to-date presented cases have been small (2-46 mm) unilateral cysts. The presence of commonly observed small epithelial cell nests resembling Walthard cell nests in the wall of epidermoid cysts is in accordance with an epithelial rather than a teratomatous origin.

Benign cystic teratomas have been seen in all age groups, the peak incidence being in the third and fourth decades [7]. On the other hand malignant changes have been seen in greatest incidence in the fifth and sixth decades, as in three of our cases the mean age being 55.2 years [8]. The possibility of a malignant change must be remembered particularly in patients who present with an ovarian cystic mass at an older than the average age.

Furthermore all our patients presented with abdominal pain, a symptom which is unusual in benign dermoid cysts unless rare complications such as torsion have occurred [8].

Tumor size is an important diagnostic factor. In general, malignant ovarian tumors are larger than benign tumors [9]. Kikkawa *et al.* [7] analyzed 37 cases of squamous cell carcinoma arising in cystic teratomas and reported that the mean tumor size was 152.3 mm, the same as in our cases.

From the pathology findings, gross changes that suggest malignant transformation are adherence to surrounding structures, nodules or thickenings in the cyst wall, areas of hemorrhage or necrosis [10]. Microscopically the tumor shows malignant transformation in one of the constituent tissues, most frequently the squamous epithelium which presents the typical squamous cell carcinoma morphology. Transitional cell ovarian tumors often display focal squamous differentiation and on very rare occasions are the site of origin of invasive SCC.

Preoperative diagnosis of squamous cell carcinoma arising in cystic teratoma or an epidermal cyst of the ovary is a difficult task. The malignant component of squamous cell carcinoma sometimes is observed focally only in the lesion, as in our cases, causing difficulty in the preoperative diagnosis of malignant transformation of these lesions. Squamous cell carcinoma (SCC) antigen and carcinoembryonic antigen (CEA) until recently were considered rather poor diagnostic markers. Combined use of serum tumor markers, macrophage colony-stimulating factor (M-CSF) and SCC antigen seem to be useful in the selective diagnosis of ovarian cystic teratomas harboring malignant squamous cell carcinoma, discriminating it from that without malignant tumor [11].

Evaluating the presence or absence of intratumoral blood flow, together with blood flow resistance, in tumor vessels with transvaginal color Doppler ultrasound (TV-CDU) may be more useful in differentiating malignant from benign teratomas of the ovary, than by measuring serum SCC antigen levels [12].

The generally accepted treatment for older women with squamous cell carcinoma arising in cystic teratomas or dermoid cysts with limited spread of disease has been total hysterectomy and bilateral salpingo-oophorectomy [9]. For patients in the reproductive age group the therapy is less radical in some instances. The prognosis of ovarian squamous cell carcinoma is much worse than that of other epithelial ovarian cancers (5-year survival, 63%) and it depends to a large extent on the presence of tumor outside the ovary, adhesions to surrounding tissues or rupture of the tumor at the time of operation [9].

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