Squamous cell carcinoma arising in a mature cystic teratoma of the ovary with synchronous invasive lobular breast cancer: case report

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Summary

Malignant transformation of a mature ovarian cystic teratoma is the most serious complication of this relatively common neoplastic lesion. While any constituent tissue of the teratoma can undergo malignant transformation, squamous cell carcinoma represents approximately 80% of those malignancies. Furthermore, the synchronous occurrence of a second malignancy in that setting is extremely rare.

Preoperative diagnosis of malignant transformation within a mature cystic teratoma is extremely difficult and poses a great challenge to current clinical surgical practice. The particularly aggressive behavior of this rare tumor, also poses significant surgical managing dilemmas.

We present a case report of a premenopausal woman with an invasive squamous cell carcinoma arising in a mature cystic teratoma and a synchronous invasive lobular carcinoma of the breast.

Key words: Mature cystic teratoma; Squamous cancer; Synchronous neoplasia; Multiple gynecological cancers.

Introduction

Mature cystic teratoma (MCT) is the most common ovarian tumor, accounting for nearly 20% of all ovarian neoplasms. Although MCT is found in all age groups, it is prevalent in 20 to 40-year-old women. However, malignant transformation is mainly observed in postmenopausal women [1]. Although mature cystic teratoma is composed of well-differentiated cells of benign behavior, malignant transformation is possible, with reported incidence rates from 0.3% to 4.8% [2].

Squamous cell carcinoma, deriving from the ectoderm, constitutes the most common form of malignant transformation of a mature cystic teratoma, comprising 80% of cases [2], followed by carcinoid and adenocarcinoma [3]. Less common types include melanoma, sarcoma and thyroid carcinoma [4].

Unfortunately, prognosis of squamous cell carcinoma is quite unfavourable compared to other types of epithelial ovarian cancers [1, 2, 5, 6]. Because of its rarity, there is no consensus regarding optimal therapy [1].

Moreover, detecting malignant transformation within a mature cystic teratoma preoperatively is extremely difficult, if not unlikely, due to the complexity of the contents of the teratoma and the fact that a possible malignant component may exist in only part of the tumor. A definitive diagnosis is often achieved postoperatively by the pathology report.

Synchronous or metachronous malignancies are not infrequently observed, especially for gynecological primaries. Ovarian and endometrial cancers are the most frequently encountered synchronous malignancies [7]. Though the development of a second malignancy in the same region may be explained by the common influence of the same carcinogenic factors, this simplified explanation is difficult to apply in our case. Such cases, however, present a difficult managing problem necessitating carefully planned surgical strategy and use of multimodality treatment.

We are presenting what we consider to be the first report in the literature of a simultaneous occurring squamous cell carcinoma arising in a mature cystic teratoma and invasive lobular carcinoma of the breast. The clinical and pathology data as well as the management and outcome of the presented case are reported.

Case report

A 41-year-old Greek woman presented in January 2004 at our clinic complaining of lower left quadrant abdominal pain, tenderness, flatulence, constipation and painful urination. Symptoms had begun four weeks earlier and progressed to frequent colic tenderness of the hypogastrium and dysmenorrhea during her last menstrual cycle. She had had one child with a normal birth and her family medical history was comprised of coronary disease for both parents. Her vital signs were normal. Physical examination revealed a large palpable mass in the pelvis. Plain radiographic examination of the abdomen revealed a large mass with smooth borders (Figure 1). Abdominal ultrasound was subsequently performed and showed a complex left adnexal mass measuring approximately 13.65 cm x 11.92 cm without ascites (Figure 1).

Moreover, an abdominal computed tomography (CT) scan confirmed the size, the origin and the semi-cystic nature of the

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Fig. 1

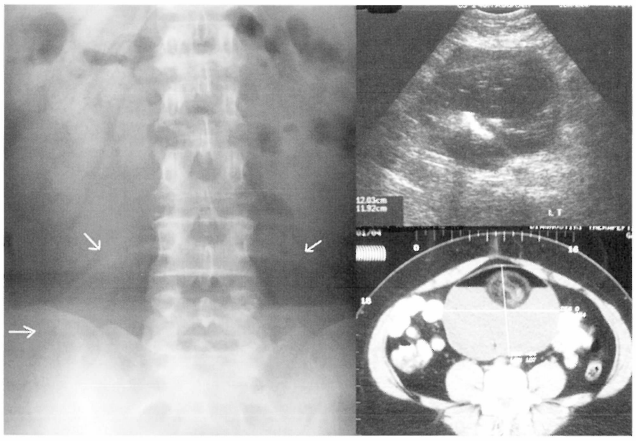

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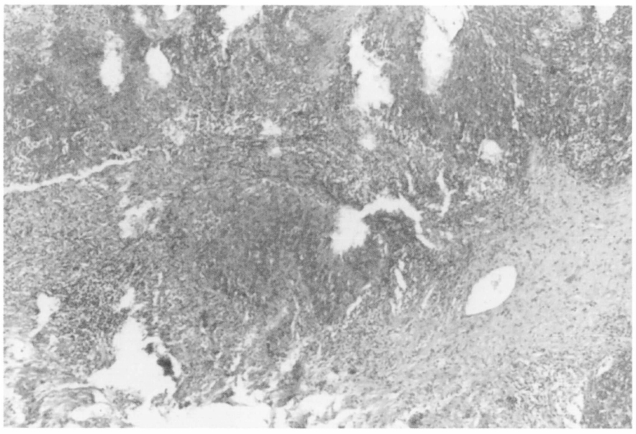
Fig. 3



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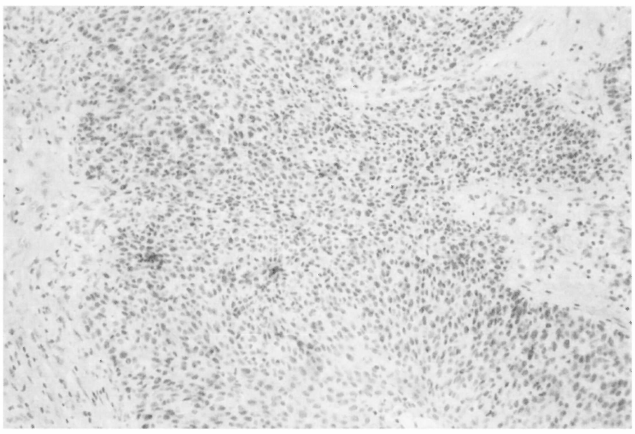

Figure 1. — Plain abdominal X-ray revealing the presence of a large well-circumscribed pelvic mass (white arrows). Abdominal ultrasound showing a large hypoechogenic left complex pelvic mass measuring approximately 12 x 11.92 x 13.65 cm. An intracystic hyperechoic mass was noted and was well demarcated from contiguous structures. Abdominal CT scan was suggestive of mature cystic teratoma based on the complexity of the mass, the presence of fatty tissue and the evident Rokitansky protuberance.
Figure 2. — Permanent section of the specimen showing hyperplasia of the squamous epithelium with papillary architecture. Upper corner: Magnification of the hyperplastic epithelium (H&E x 100).
Figure 3. — Malignant transformation of the mature cystic teratoma is evident as malignant squamous cells focally infiltrate the stroma (H&E x 100).
Figure 4. — Squamous cells of the carcinoma within the mature cystic teratoma of the ovary positively stained in more than 30% with p53 (x 100).

mass. The lesion demonstrated fat attenuation, while a raised protuberance projecting into the cyst cavity, known as the Rokitansky nodule, was also seen. Such imaging findings could not prove a certain diagnosis, but were suggestive of a mature cystic teratoma in high specificity (Figure 1) [8].

Serum cancer markers AFP, CEA, CA125 and SCC were within normal range, while CA19-9 was elevated: 661U/ml (normal range: 0-37). Preoperative exams including chest X-ray, blood count, chemistry and thyroid function tests (T_3, T_4, TSH, fT_3, fT4) were within normal range. During the preoperative work up a palpable lesion was found in the left breast for which mammographic examination was scheduled.

Laparotomy revealed a large (12 cm x 13 cm) heterogeneous mass originating from the left adnexa. The patient underwent left salpingo-oophorectomy. There were no adhesions involving adjacent organs or the large omentum. There was no ascites or gross peritoneal-retroperitoneal adenopathy and the mass was removed without rupture. Frozen section biopsy confirmed the preoperative diagnosis of mature cystic teratoma and peritoneal cytology plus tissue sampling biopsies yielded negative results.

The subsequent mammographic examination of the breasts was consistent with multifocal invasive tumor in the left breast. Intraoperative frozen biopsy diagnosed invasive lobular tumour of the breast and afterwards modified radical mastectomy was performed. Pathology staged the tumor as Stage IIb (T3,N0,M0). Excisional biopsy of the breast lesion followed and intraoperative frozen biopsy revealed invasive lobular carcinoma. Modified radical mastectomy was performed, including level II axillary lymph node dissection. The patient returned to the ward, had an uneventful postoperative course and was discharged on the fifth postoperative day.

Permanent section biopsy of the adnexal mass revealed the presence of squamous cell carcinoma with focal invasion and no penetration of the cystic wall; Stage IA (Figure 2, Figure 3). The treating surgeon recommended that the patient undergo complete total hysterectomy with removal of the contralateral ovary. The operation was performed two weeks later.

Pathology staged the breast tumor as IIb (T3,N0,M0) with positive estrogen/progesterone receptors and the patient was referred for adjuvant chemotherapy plus endocrine treatment. Four cycles of cyclophosphamide and doxorubicin were successfully completed and the patient is intended to receive

tamoxifen for a total of five years. Fifteen months afterwards, follow-up consisting of tumor marker measuring, abdominal and chest CT scan and mammography revealed no signs of recurrence in either region.

Discussion

Squamous cell carcinoma (SCC) arising in a mature cystic teratoma is a rare tumor, with an incidence rate of 1-2% and a very poor prognosis [1]. In fact, patients with squamous cell carcinoma who are classified beyond Stage I do not survive for long [5, 6].

Preoperative diagnosis of malignant transformation of a mature cystic teratoma is of extreme importance since it alters the prognosis and determines surgical planning. However, there is no reliable preoperative marker that would reveal or even suggest malignant transformation, and the complex nature of the teratoma makes radiological diagnosis virtually impossible.

Mori *et al.* [9] reported that the SCC level was significantly related to tumor stage and volume. However, there was no significant relation between the preoperative SCC levels and any clinicopathologic parameter in another report [10]. SCC and CEA have been found superior to CA125 and CA19-9 as screening markers, whereas age and tumor size were quite important in distinguishing malignant transformation in a mature cystic teratoma [10]. Recently, several cancer markers, the patient's age, and the size of the tumour were evaluated for diagnostic efficiency. Cutoff values for age < 45, size < 99 mm and SCC antigen < 2 ng/ml have been advocated but still clinical correlation is poor [6]. In our case Ca19-9 was persistently elevated but Ca19-9 does not correlate well with malignant degeneration since it has been shown to be positive in a large number of benign MCTs with only the higher values being an indication of malignant transformation [6]. Intraoperative findings that suggest malignant degeneration are adherence to the surrounding structures, thickening of the cystic wall and presence of hemorrhagic and necrotic regions in the lesion [3].

Surgery is the treatment of choice for mature cystic teratoma as well as, its malignant transformation. For simple cases of MCT, laparoscopic excision of the mass is the treatment of choice. Treatment options for malignant transformation vary from salpingo-oophorectomy for Stage I, to total hysterectomy with bilateral salpingo-oophorectomy and omentectomy in case of advanced disease. Conservative unilateral oophorectomy without adjuvant therapy is the treatment modality for patients with Stage Ia in childbearing age that are interested in future fertility [1]. It should be mentioned that in case of cystic teratoma rupture during surgery, FIGO Stage Ia rises up to Ic.

The prognosis for squamous cell carcinoma arising in a mature cystic teratoma that is confined to the cyst and removed without spillage is 63% for 5-year survival [2]. For more advanced disease, wider and more radical surgical excision are practiced in combination with multimodality therapy, yielding however, grave results. The generally accepted therapy for older women with limited spread of the disease is total hysterectomy with bilateral salpingo-oophorectomy. We choose to perform total hysterectomy and salpingo-oophorectomy based on the patient's preference and the focally invasive pattern of the disease. Recently there have been reports of increased survival rates for patients with advanced disease that undergo aggressive cytoreduction followed by cisplatin-based chemotherapy and radiotherapy [1]. In this case, no adjuvant treatment was deemed necessary for the squamous carcinoma, but our patient received four cycles of treatment with cyclophosphamide and doxorubicin for the invasive lobular breast cancer.

Simultaneous occurrence of two primary gynecological malignancies has been observed in several reports [7]. Malignant degenerative teratoma has been associated with primaries arising mainly from the cervix and the ovary [11, 12] and rarely the teratoma may be the site of metastatic spread mainly from breast cancer [13]. There have been no reports in the literature on simultaneous occurrence of invasive breast cancer with squamous cell carcinoma arising within a mature cystic teratoma. Common genetic abnormalities could be implicated in the development of synchronous malignancies. In the report of Yoshioca and Tanaka p53 overexpression has been implicated in the malignant transformation of mature cystic teratoma [14] and it has been shown that p53 overexpression is also implicated in the pathways for the development of invasive breast cancer [15]. In our case immunochemistry showed p53 overexpression in > 50% of the breast cancer cells (Figure 4).

We conclude that mutated p53 over-expression in both carcinomas of the reported case may indicate a probable common evolution and the association of p53 abnormality with prognosis should be investigated.

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