INTRODUCTION

Malignant ovarian lesions encompass many clinicopathologic entities, some with bizarre histomorphologic features. Although many ovarian malignancies have comparable presenting clinical features, much of the intrigue they arouse stems from the subsequent pathologic work-up. Not only do the histopathologic features of an ovarian lesion better define its ontogeny and biology, they may also predict prognosis. Furthermore, their identification may assist in planning adjuvant therapy. What follows is a case report of an exceedingly rare primary ovarian lesion, squamous cell carcinoma (SCC). A relevant review of the literature, encompassing both the clinical and pathologic features of this lesion, is also presented.

CASE PRESENTATION

A 58-year-old female presented to her general practitioner complaining of buttock and abdominal pain. Approximately three months prior she had been admitted to hospital with chest pain, whereupon a thoracic angiogram revealed a pulmonary embolus. She was started on heparin, bridged to warfarin and was sent home for follow-up in the community upon resolution of her acute symptoms. Concerned about a potential second clotting event, her general practitioner ordered immediate lower limb and abdominal ultrasounds as well as basic bloodwork. Although there was no evidence of a clot in her lower limbs, the abdominal ultrasound incidentally revealed a right adnexal mass. An abdominal CT was subsequently performed, confirming a cystic and solid lesion, adherent to the right fallopian tube as well as the appendix. There was no past history of malignancy and no history of abnormal Pap tests; her family history was also non-contributory. She was referred to the gynecology service for surgical work-up and planning.

Pre-op bloodwork revealed a slightly elevated CA-125 of 41 \(\mu g/mL\) (normal = 0-35 \(\mu g/mL\)). She was bridged to heparin, and taken to the operating room for excision of the mass. The right adnexal mass, along with the adherent right fallopian tube and appendix, was sent to the pathology department for intra-operative consultation.

The specimen consisted of a solid and cystic mass, approximately 10 cm in maximal dimension, with a roughened and granular external surface and no grossly evident normal ovarian tissue. The cut surface demonstrated several yellow-white cystic structures containing pasty sebaceous material and necrotic debris, with a white and slightly fibrous intervening stroma (Figure 1). The fallopian tube and appendix were identified as adherent to the larger lesion. Frozen section revealed invasive squamous cells with zones of pseudo-gland formation. On analysis, there were no teratomatous or true gland formations, and no evidence of transitional cell or endometrioid components was observed. A frozen section diagnosis of SCC was rendered.

Figure 1. Gross photograph with cut surface demonstrating solid and cystic components, the latter showing sebaceous contents (arrow)
Further histological examination showed several areas with pronounced keratinization (Figure 2). The invasive component also showed prominent keratin pearl formation. Detailed sampling confirmed the absence of true glands, as well as teratomatous and transitional cell components. A small remnant of normal ovarian cortex was also identified in the original specimen (Figure 3). Finally, a small focus of endometriosis, involved by tumour, was identified (Figure 4). There was no evidence of endometrioid adenocarcinoma in the primary specimen nor in the completed hysterectomy specimen. Detailed histological examination of the cervix was also undertaken, revealing no abnormality. The immunohistochemical profiles of both the pseudogland formations and the typical squamous components were identical (Figure 5). The tumour was strongly positive for MA903, p63 and CK5/6. Since the tumour was also found to involve the pelvic peritoneum, omentum, one pelvic lymph node group and the uterine serosa, it was assigned a FIGO stage IIIc.

Figure 2. Photomicrograph of tumour demonstrating pronounced keratinization (arrow) (H&E, 200X)

Figure 3. Photomicrograph demonstrating pseudogland formations (arrow) as well as a small amount of residual ovarian cortex (arrowheads) (H&E, 100X)

Figure 4. Photomicrograph demonstrating tumour (open arrow) involving a focus of endometriosis (solid arrow) (H&E, 100X)

Figure 5. Immunohistochemistry photomicrographs demonstrating positive staining for MA903 (above, cytoplasmic staining, 200X) and p63 (below, nuclear staining, 200X) stains
The patient recovered from her primary surgery and was discharged within a week. Her case was reviewed at the gynecological oncology clinicopathological rounds and a course of carboplatin/paclitaxel chemotherapy was recommended. Unfortunately, she experienced a negative reaction to paclitaxel and was therefore switched to single agent carboplatin. She returned to hospital five weeks post-surgery with confusion and obitipation. She was diagnosed with a bowel obstruction secondary to massive recurrent peritoneal disease, confirmed by abdominal CT. A CT scan of the head ruled out brain metastases and investigations for a potential paraneoplastic syndrome were undertaken. Unfortunately, before the latter investigations were completed, she developed severe respiratory distress and died.

SQUAMOUS CELL CARCINOMA OF THE OVARY

SCC of the ovary presents an intriguing diagnostic challenge to clinical and pathology teams. SCC more commonly arises from non-ovarian sources, making the above diagnosis exceedingly rare. When this entity occurs, however, it presents an interesting insight into the histopathological variation that may be seen in epithelial malignancies of the ovary.

Primary ovarian lesions are classified into the epithelial, germ-cell or sex-cord-stromal categories. Mature teratomas (dermoids), included in the germ-cell category, are the single most common ovarian tumour and can occur at any age. Squamous elements are most commonly identified in ovaries as part of a mature teratoma. Although the squamous component in a teratoma is often benign, SCC can arise from mature teratomas; this entity, in fact, is the most common malignant component arising from a mature teratoma. Only one to two percent of mature teratomas harbour a malignant component, but up to 80% will be squamous. Squamous elements arising in the absence of a teratomatous component (i.e. arising as a purely epithelial lesion) are distinctly rare. Generally, these occur as metastases from extra-ovarian squamous lesions or as part of a metastatic process in an endometrioid adenocarcinoma or Brenner tumour. Endometrioid adenocarcinoma of the ovary typically presents post-menopausally and is typified by areas of squamous differentiation arising within neoplastic endometrioid glands. Brenner tumours are primary ovarian tumours that occur chiefly at age 40-50 and show predominantly transitional (urothelial) differentiation; these more infrequent tumours may also show areas of squamous differentiation. Rarer still are SCCs showing none of the above features. Some primary pure SCCs will arise in concert with foci of endometriosis, and rarely, others are noted entirely de novo.

SCC of the ovary generally behaves aggressively. The lesion is typically identified as an enlarging pelvic mass, coinciding with symptoms of abdominal pain in the absence of significant ascites. Other symptoms are related to tumour invasion of neighboring structures, such as the urinary system and other gynecologic organs, and to distant metastases. The routine use of CA-125 may be helpful in differentiating cases of SCC from other types of ovarian malignancies. It appears to be normal or moderately elevated in SCC, but is present in high levels in other aggressive ovarian malignancies.

While there are no pathognomonic radiological features in SCC, pelvic imaging remains important in the workup of ovarian malignancies. The radiologic and gross pathologic findings generally show a heterogeneous solid and cystic mass, approximately 10-15 cm in maximal dimension. This latter fact may be helpful in sorting out the preliminary differential diagnosis given that many aggressive ovarian neoplasms are often much larger. Areas of necrosis are often visible and there are often adhesions to surrounding pelvic structures.

SCC of the ovary can only be confidently diagnosed histologically. It is identified by the presence of architectural and/or cytological features that resemble those found normally in squamous elements but that also show evidence of invasion. As in other SCCs throughout the body, the clinically aggressive character of SCC of the ovary is recapitulated histologically by its tendency to form invasive ribbons and tongues of tumour cells that may extend well beyond the original tumour focus. In its well-differentiated form, SCC will show squamous maturation, keratin formation and intracellular bridging. In its poorly differentiated form, few normal squamous features may be identifiable; such cases may require ancillary immunohistochemical or electron microscopic studies to confirm the diagnosis. Infrequently, SCC may show “pseudogland” formations; these structures may confuse the diagnosis, especially in tissue more likely to harbour an adenocarcinoma than an SCC. In the latter scenario, the use of immunohistochemical markers specific for squamous elements can be very helpful.

Intraoperative pathology consultation, comprising of tissue sampling and frozen section interpretation, is often requested at the time of surgery for intra-operative and post-operative planning. A diagnosis of SCC can be made, provided that the histological features are present. The underlying etiology should not be guessed at, however, given that extensive sampling of the surgical specimen is required to rule out the more common squamous lesions. Detailed examination of the cervix is required to rule out a cervical SCC, since ovarian metastases in such cases have been documented. With a diagnosis of ovarian SCC, full gynecological staging should be undertaken including completion of total abdominal hysterectomy and bilateral salpingo-oophorectomy as well as peritoneal, omental and lymph node biopsies as indicated. Invasion of nearby tissues may require resection and reconstruction.

In addition to surgery, adjuvant treatment may also be attempted. Some case reports have noted a response to early paclitaxel in combination with a platinum agent. However, outcomes remain poor in most cases. In particular, most cases (80% in one study) of SCC arising with or without endometriosis result in death within a few months of diagnosis.
Based on the few published reports available, radiotherapy is also of limited value.3,4

CONCLUSION

Our case of SCC of the ovary occurring in association with endometriosis is an exceedingly rare example of an ovarian tumour demonstrating squamous elements and an even rarer example of SCC without an associated teratoma. As in our case, debate persists over the pathogenesis of SCC associated with endometriosis. Most authors suggest the SCC in this context arises from neoplastic transformation of pre-existing endometrial epithelium.3 This is in keeping with the varied neoplasia that may arise in concert with endometriosis.13 Cases of SCC of the ovary showing no other associated lesions are an even greater etiological conundrum; some authors suggest that these lesions may arise due to seeding from occult pre- or fully-malignant squamous lesions in other locations.1

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REFERENCES


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