Introduction

Acinic cell carcinoma is a rare salivary gland tumour generally thought to have a good prognosis. The tumour is composed of malignant cells with acinar features [1]. The architecture may be a mixture of solid, microcystic and follicular [1]. Individual cells are polygonal with granular, basophilic cytoplasm and round eccentric nuclei [1]. The granules are PAS positive and resistant to digestion by diastase [1]. The tumour cells show low grade features, with few (if any) mitoses, necrosis, or pleomorphism (1). Neural invasion is associated with more aggressive tumours [1]. A subset of tumours may show areas of poor differentiation or dedifferentiation with glandular patterns and areas of necrosis [1]. Immunohistochemical staining with DOG1 and SOX10 can be seen in acinar and intercalated duct cells, but this is non-specific [1]. Of note, acinic cell carcinoma is negative for mammoglobin, which is useful in differentiating it from secretory carcinoma [1]. The usual clinical presentation is an un-fixed, slow growing, unilateral tumour of the salivary gland with good prognosis. Visceral metastasis is rare.

Case

A 32-year-old parous woman was diagnosed with a left parotid gland tumor (March 2013) and underwent a total parotidectomy. Pathology reported acinar cell carcinoma. Post-operatively she received adjuvant radiation therapy (60 Gy in 30 fractions) to the surgical bed. She smoked a half pack per day for 15 years. Her family history includes testicular cancer, and her father diagnosed with colon cancer in his 60s.

In August 2016, she developed a left neck mass which was excised, and pathology confirmed the recurrence of acinar cell carcinoma. A CT scan of the neck and chest post-operatively showed no definite signs of metastatic disease.

In March 2017, she underwent a repeat wide local excision for a second recurrence. The final histopathology reported the deep margin of the surgical resection was positive for recurrent disease, and four lymph nodes removed were negative. Follow up CT scan...
performed two months later demonstrated interval deterioration with new mediastinal lymphadenopathy and new pleural masses in the right hemithorax. She was then offered palliative radiation therapy (64 Gy in 30 fractions), as part of the disease recurrence was below the level of the previous radiation field. In August 2017 she commenced four cycles of Durvalumab and Tremelimumab as part of the IND 228 clinical trial.

CT scan after 3 cycles of immunotherapy showed the development of a large right sided pleural effusion, requiring thoracentesis; cytology was negative for malignant cells. In December 2017, while the patient was still on immunotherapy, a CT scan of the chest showed progression of the right medial pleural mass. Despite the radiologic evidence of disease progression, symptomatically the patient felt improved. In February 2018 immunotherapy was discontinued due to further radiologic disease progression in the chest.

CT abdomen & pelvis, a new 3.2 x 3.4 cm hyperdense lesion of the left ovary was seen; Repeat imaging in March 2018 demonstrated a new right pararenal nodule, and an increase in size of the left ovarian lesion to 4.9 x 4.5 cm (Figures 1 & 2).

In July 2018 she presented with worsening left pelvic pain and pressure, abdominal bloating and a sensation of incomplete voiding. A pelvic ultrasound done described a large, predominantly solid pelvic mass, measuring 12.7 x 11.6 x 8.8 cm as well as newly developed ascites. Her CA 125 was 122 U/ml. She was referred to Gynecologic Oncology, and after discussion was consented for surgery to rule out a second primary. In September 2018 she underwent a laparotomy, hysterectomy, bilateral salpingo-opherectomy and omental biopsy. Intraoperatively, the uterus and both fallopian tubes appeared normal and there was no peritoneal carcinomatosis noted. The right ovary contained an 8 cm solid mass (Figure 3), and the left ovary contained a 12 cm solid mass (Figure 4). Pathologic review showed both ovaries contained acinic cell carcinoma (Figures 5-7) consistent with her
The United States National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) and the National Cancer Database have been carried out to investigate the demographics, incidence and prognostic factors of acinic cell carcinoma [2-4]. One such study, using SEER data from 1973 to 2009, found the incidence of acinic cell carcinoma was 0.13/100,000 persons years [2]. Over this time period, there were 9,980 cases of salivary gland tumours. Acinic cell carcinoma in major salivary glands comprised 11.42% of all salivary gland tumours [2]. The highest incidence of acinic cell carcinoma is seen in Caucasians (82-85%), and there is a slight female predominance (59-61%) [2-4]. Female sex appears to be a positive prognostic factor [2-4]. Negative prognostic factors include tumours larger than 3 cm, high-grade histology, high T-stage, regional or distant metastases, and age over 70 [2, 3]. Cases with distant metastasis showed survival rates of 59.24% at 5 years, 31.52% at 10 year, 21.99% at 15 and 20 years; as compared to 82.14%, 78.94%, 76.85%, and 72.43% in patients with regional spread; and 100%, 99.15%, 94.91%, and 94.37% in patients with localized disease [2]. The rate of metastatic disease at diagnosis remains low [4].

Distant metastases in cases of acinic cell carcinoma have been reported at various sites and often include bony metastases [5-9]. In the context of widely disseminated disease, metastasis in the pancreas [5], liver [5], and lung [10] have been seen in association with bony metastases. Other patients have presented with isolated metastases to sites including the orbit [11], the occipital lobe [12], and the lung and superior vena cava (resulting in SVC Syndrome) [13]. Cases of bone, CNS, and lung metastases tend to occur in the first 5 years after initial diagnosis [5-9, 13]. On the other hand, abdominal visceral metastases seem to occur later, with reported cases of liver and pancreatic metastases at 12 and 18 years respectively [5, 6]. To date no comprehensive study of cases of acinic cell carcinoma with distant metastases has been performed. Data from the SEER or National Cancer Database could be used to assess the distribution of distant metastases in acinic cell carcinoma.

Our case represents the first reported case of acinic cell carcinoma metastatic to the ovary. In fact, the ovary is a rare site of metastasis for salivary gland tumours in general. A case of adenoid cystic carcinoma metastatic to the bilateral ovaries, 10 years after the initial presentation in the submandibular gland, was reported.
in 1996 in a patient that had also had a liver metastasis seven years earlier [14]. Another case of adenoid cystic carcinoma with widespread metastases including the ovary was reported in 1970 [15]. These are the only case reports of any salivary gland tumour metastasizing to the ovary.

**Conclusion**

Metastasis to rare locations highlight the importance of a good clinical history. The excised specimen in our case was initially evaluated by frozen section without knowledge of the patient’s previous salivary gland tumour five years earlier, with subsequent local recurrence one year ago. This poses a diagnostic challenge for the pathologist given the rarity of salivary gland metastases to the ovary. Once the clinical history was known, the morphologic features fit well with the diagnosis of metastatic acinic cell carcinoma once compared with original tumor. The histology in this case showed low-grade histology, despite the aggressive behavior of the primary tumor.

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**References**