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TEACHING CASES

Mixed ovarian large cell neuroendocrine carcinoma, mucinous adenocarcinoma, and teratoma: A report of two cases and review of the literature

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Abstract

Large cell neuroendocrine carcinoma of the ovary is a rare recently established entity. Few cases have been reported in the literature, and they are usually associated with another type of surface epithelial tumor. The association of a large cell neuroendocrine carcinoma with a surface epithelial tumor and a teratoma is even rarer, with only two cases previously described. We report the cases of two patients in their fifties who presented with a growing abdominal mass and died of metastatic disease within less than a year. Histological assessment revealed large cell neuroendocrine carcinoma admixed with mucinous adenocarcinoma and teratoma. Different hypotheses regarding the origin of large cell neuroendocrine carcinoma of the ovary are discussed. The immunohistochemical pattern of staining for cytokeratin 7 and cytokeratin 20 suggests that the composite epithelial tumors originated from the pre-existing teratoma.

Keywords: Large cell neuroendocrine carcinoma; Mucinous carcinoma; Teratoma; Ovary

Introduction

Ovarian tumors with neuroendocrine differentiation include a spectrum of tumors, such as carcinoids, stromal carcinoids, surface epithelial tumors with neuroendocrine cells, Sertoli-Leydig cell tumors with heterologous elements containing neuroendocrine cells, teratomas with neuroendocrine cells, small cell carcinoma of pulmonary type, and large cell neuroendocrine carcinoma (undifferentiated non-small cell neuroendocrine carcinoma) [1]. Large cell neuroendocrine carcinoma (LCNC) of the ovary is a rare and newly described entity characterized by the presence of large cells with ample cytoplasm, highly malignant nuclei, abundant mitotic activity, and necrosis. Trabecular architecture, insular architecture with or without central necrosis, and cytoplasmic granularity usually suggest the neuroendocrine differentiation, which can be confirmed with histochemical and immunohistochemical analysis [1–3]. In the current paper, two cases of LCNC and mucinous

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adenocarcinomas that arose simultaneously within a teratoma are presented. It appears that only two similar cases have been described in the literature [4,5].

Case report

Patient A

Patient A is a 53-year-old woman, gravida 2 para 2 aborta 0, who presented with an enlarging abdominal mass. She had no significant personal or familial illnesses. Her pre-operative radiological investigation revealed a 20 cm heterogeneous mass filling her lower abdomen. Four hepatic lesions ranging from a few millimeters to 3.1 cm in diameter were also identified. Furthermore, both ureters were dilated secondary to compression by the mass. Her pre-operative serum tests and cancer markers were as follows: lactate dehydrogenase (LDH) 1900 U/L, carcinoembryonic antigen (CEA) 6.7 μg/L, and cancer antigen 125 (CA-125) 80 kU/L. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and a left iliac lymphadenectomy. The lady, in addition, had a nodule removed from the Douglas pouch.

Gross examination of the left ovary revealed a 20 cm and 1970 g multicystic mass filled with sero-mucoid fluid and displaying partly necrotic solid areas. Eighteen samples were taken for histological examination.

The sections showed two distinct components, a glandular mucinous tumor and a solid neuroendocrine tumor. The former consisted of a proliferation reminiscent of a borderline mucinous tumor of intestinal type with focal malignant transformation into an invasive mucinous adenocarcinoma (Fig. 1). The adenocarcinoma invaded the para-ovarian tissues where extensive capillary-space involvement was identified. The solid neuroendocrine component was composed of irregularly shaped and closely packed islands of highly atypical cells with central necrosis (Fig. 2). Cells had ample eosinophilic and focally granular cytoplasm with large vesicular nuclei and prominent nucleoli. Mitotic activity was plentiful (Fig. 3). Finally, the presence of pseudostratified ciliated epithelium consistent with respiratory-type epithelium confirmed the presence of an underlying teratoma (Fig. 4). Some foci of benign ciliated serous epithelium were also identified. This serous epithelium might represent foci of mullerian metaplasia within the mucinous tumor or simply remnants of endosalpingiosis. However, it appears more likely that the serous epithelium was part of the teratoma, because it was located next to the respiratory epithelium and appeared intermingled with it. No other germ cell tumor or immature neural tissue was found. Histological analysis

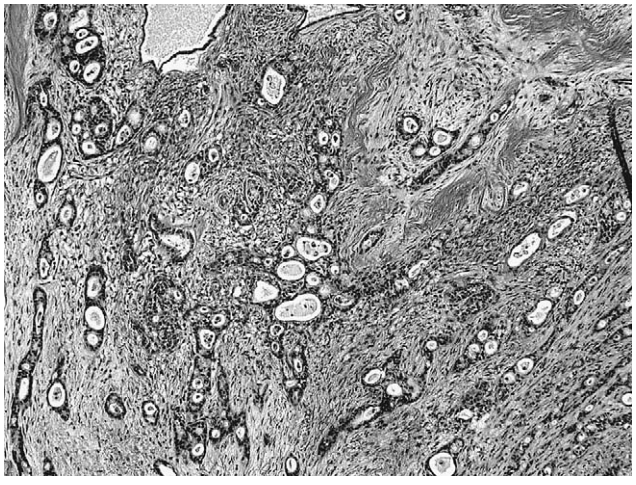

Fig. 1. Mucinous adenocarcinoma (H&E, 100 ×).

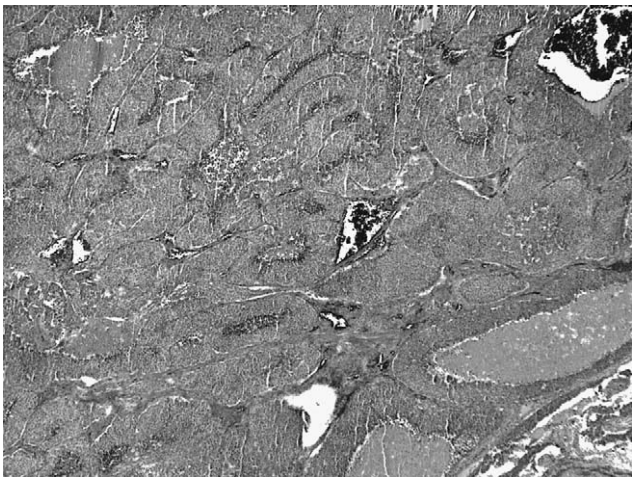

Fig. 2. Neuroendocrine carcinoma showing cellular islands with central necrosis (H&E, 25 ×).

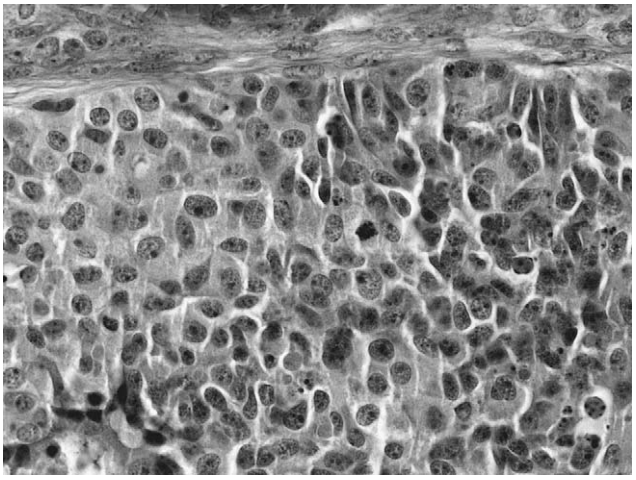

Fig. 3. Neuroendocrine carcinoma: cells with large vesicular nuclei, prominent nucleoli, and mitotic activity (H&E, 400 ×).