

Clear cell carcinoma of the ovary arising in a mucinous cystadenoma

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Abstract

A 57 year old woman presented complaining of increasing abdominal swelling of six months duration. A mixed solid cystic left ovarian tumour measuring 24 cm in diameter was excised. Histology showed numerous cysts lined by benign mucinous epithelium blending imperceptibly into borderline clear cell and mucinous areas that in turn merged with an invasive clear cell carcinoma. To the best of our knowledge, this is the first reported case of clear cell carcinoma arising in a mucinous cystadenoma. The implications for the previously postulated pathogenesis of these tumours are discussed.

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Keywords: ovary; clear cell carcinoma; mucinous cystadenoma

The pathogenesis of clear cell carcinomas has been in dispute ever since their description in 1939.¹ Whereas some authors have suggested that they show a specific type of differentiation that mimics a population of normal cells, other authors have stressed their association with serous and endometrioid carcinomas.

We describe here, to the best of our knowledge, the first case of a clear cell carcinoma arising in a mucinous cystadenoma. Within this lesion clear cell carcinoma was seen contiguous with borderline forms and benign mucinous epithelium. This case, together with the previously reported finding of mucinous inclusions in clear cell carcinomas, indicates that clear cell carcinomas might arise more commonly from mucinous tumours than had been previously supposed, and we suggest that these findings add weight to the theory that clear cell carcinoma is an end stage appearance of many epithelial ovarian tumours.

Case report

A 57 year old woman presented with abdominal swelling, which had been increasing for the past six months. There was no evidence of ascites or tumour cachexia. Ultrasonography revealed an enlarged left ovary, which had a solid cystic echotexture. The contralateral ovary was of normal size. Hysterectomy with bilateral salpingo-oophorectomy was performed.

Pathological findings

A left ovarian tumour was removed that measured 24 × 15 × 8 cm and weighed 1750 g. No breaches of the ovarian capsule or omental deposits were seen at the time of surgery. The right ovary was of normal size. The cut surface revealed multiple cysts filled with mucinous brown coloured fluid and solid areas that comprised approximately 30% of the tumour volume. Microscopically the tumour was composed of numerous cysts lined by a single layer of tall columnar mucus containing cells with regular basal nuclei. There was a gradual transition to cystic areas that were lined by cells showing clear cell change, but which showed little pleomorphism or nuclear stratification. Other areas showed multilayered atypical cuboidal cells with hyperchromatic and pleomorphic nuclei. “Hobnailing” of the nucleus was seen (fig 1). Extensive areas of the tumour showed complex papillae lined by clear and hobnail cells (fig 2). These areas again merged with more complex and eventually solid areas composed of sheets of clear cells and hobnail cells with bulbous dark nuclei (fig 3). Several cyst lumina contained eosinophilic material and several of the atypical cells showed intracytoplasmic lumina. Special staining was carried out using periodic acid Schiff (PAS), with and without diastase and Alcian blue. This revealed diastase resistant PAS staining of the benign mucinous cells, and many of the clear

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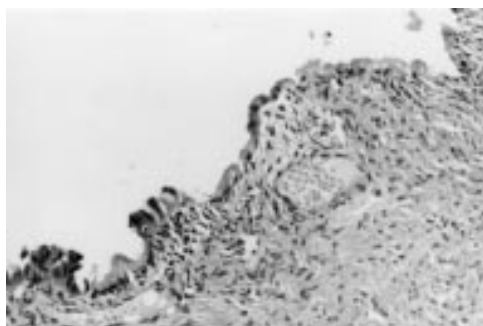


Figure 1 Cyst wall lined by a single layer of benign mucinous cells blending into multilayered cells with hobnailed nuclei.

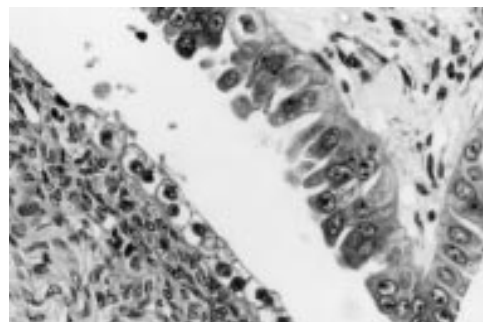


Figure 2 Borderline areas of clear cells showing stratification and mildly pleomorphic hobnailed and hyperchromatic nuclei.

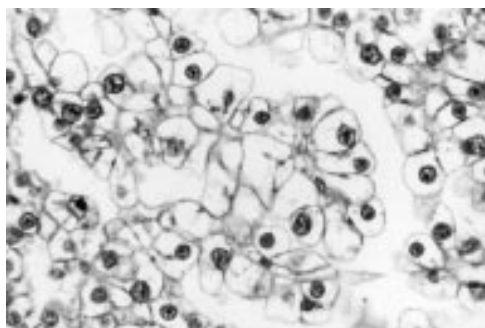


Figure 3 Pure clear cell carcinomatous areas featuring multilayered pleomorphic clear cells.

cells showed intracytoplasmic lumina with blue staining and purple red central mucoid inclusions.

Discussion

Clear cell tumours are epithelial tumours that can possess several characteristic cell types. Clear cells and hobnail cells are the most common, followed by cuboidal, flat, and oxyphil cell types.² Clear cell carcinoma was first described in 1939,³ when the typical features were described. The term mesonephroma was coined to describe its presumptive origin from mesonephric rests in the female reproductive system. Others have suggested a müllerian origin,⁴ citing a study group in which 50% of the cases had associated pelvic endometriosis against a 7.6% incidence of endometriosis given for cases of ovarian carcinoma in general.

More recently, a study of 17 cases of clear cell tumours⁵ categorised them as benign, low malignant potential, and invasive. The benign lesions were lined by a single layer of predominantly hobnail shaped cells with little or no atypia, separated from each other by a prominent ovarian type stroma. Tumours of low malignant potential showed moderate to pronounced nuclear atypia, including variation in size, chromatin clumping, irregular nuclear contours, and prominent nucleoli. Additional architectural irregularities consisted of layering, budding, and crowding of the tubular epithelium. These non-invasive variants have always been much more rare than their malignant counterparts, especially when compared with other common benign ovarian tumours.

The presence of intracytoplasmic lumina with mucinous inclusions and microcyst formation was described as part of the morphology of clear cell carcinomas.⁶ However, this finding did not lead the authors to hypothesise that this indicated a link with mucinous tumours, but rather that the presence of intracytoplasmic lumina and mucoid inclusions might indicate end stage morphology.

Clear cell elements have been reported admixed with every type of primary carcinoma of the ovary, although endometrioid and serous tumours were the most common.^{7,8} The association of clear cell carcinomas with mucinous lesions has been reported only infrequently. One case was a clear cell carcinoma admixed with mucinous components comprising less than 50% of the tumour. The case was part of a series and it is not known whether the mucinous component was benign, borderline, or malignant.⁷ The same authors also reported a case of clear cell change in "more than focal areas" in a mucinous cystadenocarcinoma. Thus, our present case appears to be the first that unequivocally shows clear cell carcinoma arising from a benign mucinous tumour. This assumes epidemiological relevance because mucinous cystadenocarcinomas have not been found in intimate association with endometriosis, which is frequently found with other ovarian neoplasms such as endometrioid and clear cell carcinomas.^{3,8,9}

No definite genetic association has been identified for clear cell carcinomas. Several genes, such as BRCA1, p53, and HER-2/neu, have been implicated in the origin of ovarian surface epithelial tumours in general, and K-ras and chromosome 17 alterations have been found to be associated specifically with mucinous and serous carcinomas.¹⁰ Our findings, the presence of mucinous inclusions, and a lack of a genetic association all add weight to the hypothesis that clear cell carcinomas should be regarded as an end stage transformation, which may arise from any of the other epithelial tumours.

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