

## Metastatic colorectal adenocarcinoma involving the ovary with elevated serum CA125: A potential diagnostic pitfall<sup>☆</sup>

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Received 19 July 2006

Available online 1 March 2007

### Abstract

**Objectives.** Elevated serum levels of CA125 are observed not only in association with primary ovarian epithelial neoplasms but also in a variety of other clinical settings, including ovarian involvement by metastatic disease. There is considerable overlap in gross and histologic features between primary ovarian tumors and metastatic colorectal adenocarcinoma, which can make diagnosis particularly challenging in the setting of an increased CA125 level. The aims of this study were to determine how frequently serum CA125 is elevated in women with ovarian involvement by metastatic colorectal adenocarcinoma and to compare the features of cases with and without associated elevations of serum CA125.

**Methods.** Eighty-nine cases of histologically confirmed ovarian involvement by metastatic colorectal adenocarcinoma were identified by retrospective review. Clinicopathologic data were analyzed, including preoperative serum CA125 level (available in 42 cases). Features of cases with an associated increase in serum CA125 were compared with those of cases with no such elevation.

**Results.** Twenty-nine patients had an elevated serum CA125 level (>35 U/mL) preoperatively (range 39.0–556.3, median 143.0, mean 199.1). Thirteen patients had a serum CA125 level within the reference range, while forty-seven patients had no preoperative testing for serum CA125. Clinical, gross, and histologic features of cases with an associated increase in serum CA125 were generally similar to those of cases with a non-elevated serum CA125 concentration. In three cases, the tumor was initially diagnosed as an ovarian primary.

**Conclusions.** At least 32.6% of women with ovarian involvement by metastatic colorectal adenocarcinoma have an elevated serum CA125 level prior to oophorectomy. Such cases do not differ significantly from cases lacking such an association with respect to a variety of clinicopathologic features. The possibility of metastasis from a colorectal carcinoma merits consideration in the formation of the differential diagnosis for a woman with an adnexal mass and elevated serum CA125, even in the absence of an established history of gastrointestinal malignancy.

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**Keywords:** Ovary; Tumor; Carcinoma; Metastasis; Colonic adenocarcinoma; Rectal adenocarcinoma; Secondary tumors; CA125; Tumor markers

### Introduction

CA125 is a glycoprotein first identified in 1981 following the development of a monoclonal antibody against a serous carcinoma cell line [1]. Serum CA125 levels have been found

to be elevated in most women with ovarian epithelial neoplasms and to be useful in monitoring for recurrence of disease [2]. Studies assessing serum CA125 levels as a possible screening test for ovarian neoplasia in apparently healthy women have demonstrated the lack of specificity of CA125 elevations; investigators have shown that CA125 is produced not only by neoplastic cells, but also by non-neoplastic ovarian surface epithelial cells and mesothelial cells [3,4]. Elevation of the serum concentration of CA125 has been reported in association with non-ovarian tumors

<sup>☆</sup> Presented in part at the 95th Annual Meeting of the United States and Canadian Academy of Pathology, Atlanta, Georgia, February 11–17, 2006.

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(e.g., hepatocellular carcinoma and pancreatic adenocarcinomas), as well as in association with benign conditions (e.g., endometriosis, pericarditis, cirrhosis) [5].

When a woman presents with a pelvic mass and is subsequently found to have an elevated serum CA125, clinical suspicion of a primary ovarian epithelial neoplasm rises [6]. The well-documented overlap in gross and histologic features between primary ovarian tumors and metastatic colorectal adenocarcinoma makes distinguishing a primary ovarian neoplasm from a metastatic tumor particularly challenging in such a scenario [7]. Given the aforementioned lack of specificity of elevated serum CA125 levels, gynecologic oncologists and pathologists could benefit from knowing (a) whether such elevations are observed frequently in association with metastases from common sites such as the intestinal tract, and (b) if so, whether there are any distinguishing features of such cases. The aims of this study, therefore, are to determine the frequency of serum CA125 elevation in a series of women with ovarian involvement by metastatic colorectal adenocarcinoma and to compare the features of cases with and without associated elevations of serum CA125.

## Materials and methods

Eighty-nine cases of ovarian involvement by metastatic colorectal adenocarcinoma, all initially examined during a period of 11 years and 2 months (January 1, 1995 to February 28, 2006), were retrieved from the files of the Department of Pathology of The University of Texas M. D. Anderson Cancer Center after identification through searches of the Department of Pathology's database and of the Department of Medical Informatics' Tumor Registry database. To be included in this series, histologic confirmation of ovarian involvement and confirmation of the colorectal primary tumor histologically or by clinical means (e.g., imaging studies) were required. Features of eighty-six of these cases have been previously reported [7]. The institutional review board of The University of Texas M. D. Anderson Cancer Center approved this project.

Clinical data were retrieved from medical records of The University of Texas M. D. Anderson Cancer Center, from the clinical history provided on pathology reports, and in some cases through the kind assistance of pathologists from referring institutions. Clinical features recorded included age, presenting symptoms, preoperative serum CA125 levels (when noted in the medical record), anatomic site in which malignancy was first clinically suspected, initial and subsequent treatment, additional sites of tumor involvement, and survival data. Details pertaining to the colorectal primary tumors were recorded when available. Not every feature of the clinical history was available in every case;

determinations of percentages were based on the number of cases for which the pertinent data were available.

Gross features of the ovaries that were recorded included laterality, size, surface involvement, and characteristics on sectioning. Hematoxylin-and-eosin stained sections of one or both ovaries involved by metastatic tumor were reviewed in all cases. In 13 of the 50 cases with bilateral involvement noted in the pathology report, sections of only one ovary were available for review, and as a result sections of a total of 126 ovaries were reviewed. The number of sections reviewed averaged six per case, with a range of 1 to 31.

Histologic features, including architectural patterns, the presence of features that typify colorectal metastases as delineated by Lash and Hart [8] (dirty necrosis, garland pattern, and segmental necrosis of malignant epithelium), the presence of epithelium with features compatible with mucinous cystadenoma or mucinous neoplasm of low malignant potential (i.e., non-carcinomatous epithelium), and evidence of surface involvement, were recorded.

In order to perform statistical analyses, cases were divided into three groups on the basis of whether a preoperative measurement of serum CA125 concentration was documented in the clinical record and, if so, whether the concentration was elevated (>35 U/mL) or non-elevated (i.e., within the reference range: 35 U/mL or less). Statistical comparisons between the two groups of patients for whom a preoperative CA125 value was available (elevated CA125 vs. non-elevated CA125) were carried out using Student's *t* test (two-tailed) for continuous variables and Fisher's exact test (two-tailed) for categorical variables.

## Results

Twenty-nine women (33%) had a preoperative serum CA125 concentration above 35 U/mL (range 39.0–556.3, median 143.0, mean 199.1). These women ranged in age from 34 to 85 (median 51); 8 of 29 (28%) were ≤40 years of age. Thirteen women had a preoperative serum CA125 concentration of less than 35 U/mL (range <7.0–31.0, median 18.9, mean 18.4). The women comprising this group ranged in age from 24 to 73 (median 50). The age distributions in these two groups were similar ( $p=0.86$ ; Table 1). As was true both for women with a non-elevated serum CA125 and for those in whom CA125 had not been assessed, abdominopelvic pain was the most common presenting symptom (15/29) among women with an elevated serum CA125; 3 patients were asymptomatic.

In 13 of 26 cases (50%) with an associated elevation of serum CA125, an ovarian mass was the first manifestation of disease; ten patients had a history of colorectal adenocarcinoma. An ovarian mass was detected prior to the primary tumor in 27% of cases (3/11) with a non-elevated serum CA125 ( $p=0.28$ ). Data regarding order of presentation were not available for three women with elevated CA125 and two

Table 1  
Clinical and pathologic features: comparison of cases with elevated serum CA125 versus those with non-elevated serum CA125 and those in which serum CA125 was not measured

	Elevated CA125	Non-elevated CA125	<i>p</i> *	No CA125 level
<i>n</i>	29	13		47
Age range (median)	34–85 (51)	24–73 (50)	0.86	19–77 (48)
Most common presenting symptom	Abdominopelvic pain	Abdominopelvic pain		Abdominopelvic pain
Ovarian mass detected prior to colorectal primary tumor	50% (13/26)	27% (3/11)	0.28	24% (9/38)
Bilaterality	52% (15/29)	62% (8/13)	0.74	63% (27/43)
Mean size of ovarian mass	12.1 cm	10.1 cm	0.24	9.3 cm
Median size of ovarian mass	12.2 cm	10.0 cm		8.1 cm
Most common histologic patterns	Glandular and papillary	Glandular and papillary		Glandular and papillary
Ovarian surface involved by tumor	33% (5/15)	60% (3/5)	0.60	52% (13/25)
Metastases to sites other than ovary present at diagnosis	69% (20/29)	77% (10/13)	0.72	60% (28/47)

\* *p* values pertain to comparisons between the elevated CA125 group and the non-elevated CA125 group.

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