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Case Report

Imaging features of mucinous carcinoma arising from mature teratoma showing cytokeratin 7+ and cytokeratin 20+ expression profile: A case report[‡]

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ABSTRACT

Ovarian mature teratomas are benign, but malignant transformation can occur infrequently, especially in women of advanced age. The tissue that undergoes malignant change is mostly squamous cell carcinoma, although adenocarcinoma has been reported in a small number of cases. The immunostaining results of adenocarcinoma usually show a cytokeratin (CK)7-/CK20+ expression profile, corresponding to lower gastrointestinal tract origin. In this report, we describe a case of mucinous carcinoma arising from an ovarian mature teratoma showing a CK7+/CK20+ profile and discuss its imaging features. A 40-year-old woman presented to her primary care physician with abdominal distension and poor oral intake, and she was referred to our hospital. She had been diagnosed with an ovarian mature teratoma at our institution 3 years earlier. At the current presentation, pelvic magnetic resonance imaging showed a large multilocular cystic mass with adipose tissue extending into the upper abdomen. Densely packed cysts were observed inside the mass, which showed weak contrast enhancement on contrast-enhanced imaging and a mildly high signal on diffusion-weighted imaging. A portion of the cysts also showed abnormal 18Ffluorodeoxyglucose uptake (maximum standardized uptake value, 13.2) on positron emission tomography/computed tomography. The patient was subsequently diagnosed with mucinous carcinoma showing a CK7+/CK20+ profile arising from a mature teratoma by pathologic examination. This mucinous carcinoma arising from a mature teratoma showed a

Abbreviations: CK, cytokeratin; MRI, magnetic resonance imaging; FDG, fluorodeoxyglucose; PET-CT, positron emission tomographycomputed tomography; SUV max, maximum standardized uptake value.

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CK7+/CK20+ profile and took the form of densely packed multilocular cysts. In this respect, it was similar to primary ovarian epithelial mucinous carcinoma on both magnetic resonance imaging and pathologic examination despite showing a much higher maximum standardized uptake value than that of primary ovarian mucinous carcinoma. When a large ovarian teratoma contains a large multilocular cyst, the presence of densely packed multilocular cysts should not be missed even in a mass without solid components. Clinicians should consider the possibility of mucinous carcinoma showing a CK7+/CK20+ profile arising from a mature teratoma in such cases.

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Background

Malignant transformation occurs only in 0.17%-2% of mature teratomas, especially in the sixth or seventh decade of life. The malignant component usually consists of squamous cell carcinoma (75%-85%) [1], whereas adenocarcinoma accounts for only 6.8% [2]. Among adenocarcinomas, mucinous carcinomas account for the largest proportion (33%) [3]. Most reports of mucinous carcinoma arising from a mature teratoma show a cytokeratin (CK)7-/CK20+ immunohistochemical expression profile, corresponding to a tumor most likely derived from lower gastrointestinal tract origin. In this report, we describe a case of ovarian mucinous carcinoma arising from a mature teratoma showing a CK7+/CK20+ expression profile, similar to primary ovarian mucinous carcinoma. To the best of our knowledge, this is the first report to describe the magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT) features of mucinous carcinoma arising from a mature teratoma showing a CK7+/CK20+ profile.

Case presentation

A 40-year-old woman (gravidity 1, parity 1) visited a local doctor because of a 1-month history of abdominal distension and poor oral intake. An abdominal ultrasound revealed a multicystic tumor containing mucus-like fluid occupying the whole abdominal cavity, and she was referred to our hospital.

The patient had been diagnosed with a mature teratoma of the left ovary 3 years earlier, which had not been treated in our hospital. Compared with 3 years before, her serum tumor markers showed an increase in cancer antigen (CA) 19-9 from 25.6 to 41.2 U/mL (reference range, 0-39 U/mL) and CA125 from 30.0 to 51.4 U/mL (reference range, 0-35 U/mL). Squamous cell carcinoma (SCC) antigen and carcinoembryonic antigen (CEA) at the present visit were 0.9 ng/mL (reference range, < 1.5 ng/mL) and < 1.8 ng/mL (reference range, < 5.0 ng/mL), respectively, and neither had increased.

Pelvic MRI 3 years before showed a multilocular cystic lesion of approximately 49 \times 37 \times 30 mm³ in the left ovary with adipose tissue (Fig. 1). The lesion showed no solid com-



Fig. 1 – Pelvic MRI performed 3 years before the current presentation. (A) Axial T1-weighted imaging (TR/TE, 100/4 ms) showed a 5-cm multicystic lesion with high signal intensity in the left ovary (arrow). (B) Axial subtraction image showed that the lesion contained no substantial components except for a 7-mm nodule that appeared to be Rokitansky protuberance (arrow).



Fig. 2 – Pelvic MRI. (A) A multicystic lesion occupying the abdominal cavity was shown on axial T1-weighted imaging (gradient echo; TR/TE, 7/4.6 ms). A portion of the cyst showing a high signal (arrow) was suppressed on (B) fat-suppressed T1-weighted imaging (gradient echo; TR/TE, 5/0 ms), corresponding to a fat component (arrow). (C) Axial T2-weighted imaging (TR/TE, 4897/100 ms) showed a dense cystic mass in a portion of the lesion (arrow). (D) The dense cystic portion showed slight contrast enhancement on axial subtraction images (arrow).



Fig. 3 – Pelvic MRI and FDG-PET/CT. (A) The dense cystic portion showed a slightly high signal on a diffusion-enhanced image (b = 1000 s/mm²; TR/TE, 6255/78 ms) (arrow). (B) On whole-body FDG PET/CT, high FDG uptake (SUVmax, 13.2) was observed in correspondence with the dense cystic portion (arrow).





(c)

Fig. 4 – Pathology (hematoxylin and eosin staining). (A) The teratoma lumen, composed of squamous epithelium with hair (thin arrow) and sebaceous glands (arrow), was seen adjacent to the mucous cavity (stars). (B) The mucous cavities consisted of 1 layer of high columnar (mucous) epithelium, corresponding to mucinous adenoma. (C) A part of the mucus cavity consisted of densely packed atypical cells, corresponding to mucinous carcinoma.

Table 1 – Tumor markers in mucinous carcinoma arising from mature teratomas reported to date.					
	Age	CEA (ng/mL)	CA125 (U/mL)	CA19-9 (U/mL)	
Reference range		<5.0	0-35	0-37	
Gaiko [2]	62	N.A.	N.A.	N.A.	
Fishman [8]	38	40	80	N.A.	
Hershkovitz [9]	13	5.5	268	162	
Clark [10]	42	1.2	20	349	
Takai [11]	49	6.9	20	3.8	
Wan [12]	58	2	14	58	
Kushima [13]	58	N.A.	36	106	
Yan [14]	51	W.N.L	W.N.L	41.9	
Our case	40s	1.8	51.4	41.2	

ponent except for a 7-mm nodule regarded as a Rokitansky protuberance on subtraction images (Fig. 1B, arrow), and an imaging diagnosis of mature teratoma was made. Recent pelvic MRI showed a multilocular cystic lesion of approximately 143 \times 319 \times 264 mm³ extending into the upper abdomen. A portion of the cysts contained adipose tissue (Fig. 2). Another part of the mass consisted of dense cysts (Fig. 2B, arrow). The dense cysts showed weak contrast enhancement on subtraction images (Fig. 2D, arrow) and a slightly high signal on diffusion-weighted images (b = 1000 s/mm²; TR/TE, 6255/78 ms) (Fig. 3A, arrow). On 18F-fluorodeoxyglucose (FDG) PET/CT, they showed abnormal FDG uptake [maximum standardized uptake value (SUVmax): 13.2] (Fig. 3B, arrow). No other abnormal FDG uptake was found in other organs, including the upper and lower gastrointestinal tract. Based on the imaging findings and medical history, a preoperative diagnosis of malignant transformation of mature teratoma was made. The patient was treated by abdominal modified radical hysterectomy, bilateral adnexectomy, pelvic and para-aortic lymph node dissection, and omentectomy.

Histopathologic examination revealed that the tumor in the left ovary had a teratoma component composed of squamous epithelium with hairs and sebaceous glands (Fig. 4A). In addition, examination revealed a mucinous cavity composed of a layer of tall columnar (mucinous) epithelium (Fig. 4B), mucinous borderline malignant tissue composed of mucinous epithelium with disorganized cell arrangement, and mucinous carcinoma tissue composed of dense dysplastic cells (Fig. 4C) juxtaposed to each other as well as the teratoma component. Thus, the diagnosis of mucinous carcinoma arising from a mature teratoma was made. These mucinous components were immunohistochemically positive for CK7 and CK20 and negative for caudal type homeobox transcription factor 2 (CDX-2) and paired box 8 (PAX8).

Discussion and conclusions

Because teratomas are derived from a tridermic component, any of the other constituent tissues can undergo malignant transformation. Adenocarcinomas arising from mature teratomas rarely occur, with an incidence of only 6.8% [2], and mucinous adenocarcinoma is the most common type (33%) among them [3]. Other less frequent adenocarcinomas include adenocarcinoma arising from sebaceous, thyroid, sweat, mammary, salivary, and prostate tissues.

Findings associated with malignant transformation compared with mature teratoma include patient age at diagnosis, tumor diameter, and tumor markers. The mean age at diagnosis of malignant transformation is older than that at diagnosis of mature teratoma (55.0 vs 37.5 years, respectively). In 1 study, the average tumor size in cases of malignant transformation of squamous cell carcinoma was larger than that for mature teratoma (152 vs 88 mm, respectively) [4]. Another study showed that the sensitivity of the SCC antigen level for malignant transformation in patients with squamous cell carcinoma was 80%, with a cutoff SCC antigen level of 2.5 ng/mL; if the combination of 2 criteria was applied (patient age of < 40 years and serum SCC antigen level of < 2.5 ng/mL), the specificity for mature teratoma was 94% [5]. In the present case, both patient age and tumor size satisfied the condition for malignant transformation. Although the SCC antigen level did not increase because of the nonsquamous histological type, both the CA125 and CA19-9 levels increased during the 3year period and exceeded their respective reference ranges. By contrast, the CEA level remained within the reference range. Among previous reports of mucinous carcinoma arising from a mature teratoma [2,6-12], elevation of the CEA level was seen in only half of the cases (3/6), whereas the CA19-9 level was elTable 2 – Immunostaining showing CK7/CK20 positivity in mucinous carcinoma arising from mature teratomas reported to date.

	CK7	CK20
Gaiko [2]	N.A.	N.A.
Fishman [8]	N.A.	N.A.
Hershkovitz [9]	_	+
Clark [10]	_	+
Takai [11]	_	+
Wan [12]	Focally+	+
Kushima [13]	_	+
Yan [14]	-	+
Our case	+	+

evated in most cases (5/6); however, the CA19-9 level may not be a useful guide because it can also be increased in a mature teratoma (Table 1).

Mucinous carcinomas of lower gastrointestinal tract origin are known to show a CK7–/CK20+ expression profile. Most previous reports of mucinous carcinoma due to malignant transformation of a mature teratoma showed CK7–/CK20+ immunostaining (Table 2), corresponding to the lower gastrointestinal tract, and these reports focused on the pathology of each case without coherent, detailed imaging features [7–9,11,12]. To the best of our knowledge, no report has focused on the imaging features of mucinous carcinoma arising from a mature teratoma and showing a CK7+/CK20+ expression profile.

The sonographic, CT, and macroscopic findings of mucinous carcinoma of lower gastrointestinal tract type arising from a mature teratoma have been previously described as a multiseptated cystic mass measuring 8.5 \times 13.9 cm² with small calcifications [10]; a well-defined mixed-density mass measuring 10 \times 14 \times 9.5 cm and containing solid, cystic, and fat density components and eccentric nodular foci of calcification [13]; a well-circumscribed heterogeneous solid mass measuring 7×10 cm with solid and cystic components [6]; complicated masses measuring 20 \times 13 \times 8.5 cm with a mixture of solid and cystic components [7]; large multilocular cystic lesions measuring 17-35 cm with numerous internal papillary ridges [2,8]; and large teratomas measuring 9-17 cm with a 4mm-3-cm mural solid component [9-11]. As described above, mucinous carcinoma of lower gastrointestinal tract type arising from a mature teratoma tends to be a large multilocular cystic mass that is sometimes accompanied by a solid or papillary component, although the morphology may vary. Our patient had a large multilocular cystic mass with densely packed cysts, and it was morphologically similar to primary ovarian mucinous carcinoma. Therefore, a mass with a component of densely packed cysts should be investigated, even when a solid component is not present, in a patient with a large mature teratoma.

The SUVmax of FDG-PET/CT of mucinous and clear cell carcinomas occurring in the ovary is lower than that of other histologic types (median values of 3.42 and 3.52, respectively) [14,15]; however, the tumor in this case showed a very high SUVmax of 13.2 on FDG-PET/CT. Yokoyama et al. [16] reported that the median SUVmax values for malignant transformation of mature teratomas were significantly higher than those of mature teratomas [18.3 (range, 5.3-23.3) vs 1.1 (range, 1.0-15.5), respectively]. Although the histological type in the malignant area was squamous carcinoma or a mixture of squamous carcinoma and adenocarcinoma in that study, the malignant area in a mature teratoma may show a very high SUVmax. FDG-PET/CT can also be useful in distinguishing between benign and malignant ovarian teratomas, especially in cases without solid components.

In conclusion, mucinous carcinoma arising from a mature teratoma showing a CK7+/CK20+ expression profile can take the form of densely packed multilocular cysts, similar to primary ovarian epithelial mucinous carcinoma within a teratoma on MRI as well as on pathologic examination, despite showing a much higher SUVmax than that of primary ovarian mucinous carcinoma. When a large ovarian teratoma contains a large multilocular cyst, the presence of densely packed multilocular cysts should not be missed even in tumors without solid components. Clinicians should consider the possibility of mucinous carcinoma showing a CK7+/CK20+ profile arising from a mature teratoma in such cases. Accumulation of further cases will provide more details on this condition.

Patient consent

Written informed consent was obtained from the patient for publication of this case report, any associated images and clinical details.

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