Primary Retroperitoneal Mucinous Cystadenocarcinoma in a Twenty-nine year old Pregnant Woman

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ABSTRACT

Primary retroperitoneal mucinous cystadenocarcinoma (PRMCAC) is rare. Approximately 50 cases have been reported in the English literature, and 2 cases were associated with pregnancy. Here we report the third case of PRMCAC in a woman during pregnancy. The 29-year-old woman was asymptomatic when a routine ultrasound examination at the 28th week of gestation revealed a suspected right ovarian cyst. A caesarean section delivery was performed at the 38th week of gestation, during which a large tumor was found intra-operatively in the right-retroperitoneal space. Laparotomic tumor resection was performed 2 months later, and the PRMCAC diagnosis was made.

Unlike ovarian cancers, primary retroperitoneal mucinous cystadenocarcinoma (PRMCAC) is rare [1]. We review the clinical presentation and the prognosis of PRMCAC from the literature, and discuss its proposed etiology and management. We systematically describe useful imaging features for diagnosing primary retroperitoneal tumors, and analyzed the reports of the gross appearance of PRMCAC in the literature to identify possible imaging features. The accurate preoperative diagnosis and malignancy prediction of PRMCAC is difficult. Thus, imaging may be helpful in delineating the lesion, and provides useful information for preoperative assessment.

CASE REPORT

A 29-year-old pregnant woman (G1P0) was admitted to Shin-Kong Hospital at 38 weeks of gestation for a pre-arranged cesarean section due to cephalopelvic disproportion. She had no significant medical history, except hematuria and frequency of micturition from a suspected urinary tract infection. At 28 weeks of gestation, a large cystic lesion was noted during a routine ultrasound (US) examination, and a right ovarian cyst was suspected. Despite the size of the lesion depicted in the sonograph (11 × 8 cm), she was asymptomatic, and the remaining pregnancy was uneventful. The cesarean section was performed on the day of admission, and a 2785-g infant was delivered. However, a large retroperitoneal tumor (10 × 10 cm) was discovered intra-operatively.

A contrast-enhanced computed tomography (CT) scan was performed the following day, revealing a well circumscribed, cystic mass in the right-retroperitoneal space with a diameter of 12.3 cm, uneven wall thickness, and several minimally-enhancing mural nodules. The tumor was located superior to the right ovary, displacing the ascending colon anteriomedially. The tissue planes between the tumor, the lower surface of right kidney, part of the lateral margin of psoas muscle and segment 6 of liver, were obliterated. But the tumor and the organs appeared separable (Fig. 1). Lymph node sizes did not indicate pathology. Initial differential diagnosis was tumor of sarcoma group or neurogenic tumor. The tumor was screened for CEA, CA-125, and CA 19-9 markers, and the results showed elevated CA-125 (106.1

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U/mL). The patient was discharged 4 days post-delivery to recover from the caesarean section.

Two months later, laparotomic tumor resection was performed, and the large cystic mass with mural nodules was excised. The mass was 12 cm in diameter, and was not connected to the surrounding organs. It was step-wise dissected, and removed with the capsule intact. The post-operative recovery was uneventful, and the patient was discharged 4 days following laparotomy. Under gross inspection, the cystic tumor had a smooth external surface, and measured 14 × 7 cm. The cystic cavity contained multiple solid nodules that were tan to light brown in color, measuring up to 3.7 × 3.0 × 2.0 cm in size (Fig. 2). The nodules were firm with a gritty and mucous covered surface.

Figure 1. Post-contrast computed tomography demonstrated a well-defined cystic mass with enhancing nodules. (a) The mass displaced the ascending colon anteriomedially and obliterates the margin at the right psoas muscle. (b) The mass compresses on the right kidney.

Figure 2. Gross features of the primary retroperitoneal mucinous cystadenocarcinoma. (a) Intra-operative identification of the lack of a connection between the mass and the viscera allowed complete removal of the large, well-encapsulated cystic tumor with the capsule intact. (b) The cut section after the removal of the mucinous content revealed multiple solid nodules over the inner surface, which was compatible with the CT findings.
The histological examination showed variable glandular or cystic spaces with florid papillary tufting lined with stratified mucous cells. Most of the tumor cells exhibited nuclear hyperchromatism and variable nuclear pleomorphism. Focal lining cells displayed bland-looking basally located nuclei. However, stromal invasion with a micropapillary pattern was noted focally. The lesions measured approximately 0.6 × 0.4 cm. A thin fibrous wall with adjacent fat tissue surrounded the tumor. No visible residual organ tissue was found. An intestinal type mucinous cystadenocarcinoma was considered, but the origin of the tumor was unclear. Immunohistochemical screening for CK7, CK20, and CDX2 showed that the tumor cells exhibited diffuse reactivity for CK7, and that only scattered cells reacted with CK20. Foci of CDX2 reactivity were also noted. Thus, the immunohistochemical analysis indicated an ovarian origin. However, because all the possible sites of origin appeared negative, including the ovary, the gastrointestinal tract, and the pancreaticobiliary system, PRMCAC was diagnosed. No evidence of recurrence of the PRMCAC was observed during a 4-month follow-up period to the date of this report.

DISCUSSION

The number of PRMCAC cases that have been reported in the English literature range from 52 [1] to 49 [2]. Two cases of PRMCAC were associated with pregnancy [3]. The first-reported patient underwent tumor resection at the 31st week of gestation, and vaginal delivery at 38 weeks was unremarkable. In the second case, the tumor was resected during caesarean section at the 38th week of gestation. Therefore, our case is the third reported case of PRMCAC associated with pregnancy, and represents the first case that was managed with a fertility-sparing surgery following delivery. Based on radiologic findings of cystic masses in the retroperitoneal region, PRMCAC is not a common differential diagnoses because of its rarity. Here, we analyze the clinical features and imaging characteristics of PRMCAC, and discuss a proposed etiology.

The mean age of PRMCAC patients is 43.7 years, with a range of 17 to 86 years [2]. PRMCAC is most frequently reported in females. Only 4 male PRMCAC patients have been reported [1]. Most patients are asymptomatic on presentation, and the tumor is either self-detected or discovered during a routine examination [3]. However, flank pain with abdominal distension has been reported in some PRMCAC patients [1, 3]. Among the pregnant PRMCAC patients, one was referred at the 12th week of gestation based on pelvic pain [3], and the remaining 2 patients were asymptomatic, with detection occurring during routine US examination [3, 4].

Perhaps based on its accessibility, US is often the first imaging method used in the diagnosis of intra-abdominal tumors. However, CT and magnetic resonance imaging (MRI) can provide a better understanding of the involved structures, the site of origin, and the extent of the lesion. The soft tissue resolution in CT and MRI may also be useful for estimating malignancy. CT is most often chosen over MRI as the second choice for imaging investigation, despite its poorer soft tissue resolution and the associated risk of radiation exposure in CT.

To consider PRMCAC as a differential diagnoses, evidence of a retroperitoneal origin is required. Nishino et al suggested first identifying the displacement of normal anatomic structures of the retroperitoneum, such as the kidneys, the adrenal glands, the ureters, the ascending and descending colon, the pancreas, and duodenal segments [5]. Foshager et al also suggested the use of several similar CT and MRI imaging signs to differentiate retroperitoneal masses from intraperitoneal disease. In our patient, the retroperitoneal location of the PRMCAC was indicated by the displacement of the ascending colon anteriomedially, mild compression of the anterior surface of right kidney, and the obliteration of the plane of the right psoas muscle (Fig. 1).

Before a retroperitoneal tumor can be described as primary, the possibility that a tumor originated from an abdominal organ must be excluded. Also, as mucinous tumor may occur in 2 different organs concurrently, a careful search of the ovaries, pancreas, gallbladder, and so on should be performed. Nishino et al described several radiologic signs that are helpful in determining the organ of origin for a retroperitoneal tumor, including the beak sign, the phantom- (invisible) organ sign, the embedded-organ sign, and the prominent-feeding-artery sign. Only when there is no definite sign that suggests an organ of origin, the diagnosis of primary retroperitoneal tumor becomes likely. Our patient’s mucinous tumor was described as primary because no involvement of associated abdominal organs was identified and no radiologic signs were observed that indicated it resulted from metastasis elsewhere.

Possible differential diagnoses can be proposed based on the cystic description of a tumor, which is often discernible during US examination. Yang et al classified retroperitoneal cystic tumor as either neoplastic or non-neoplastic [7]. Despite overlapping appearances in CT images, a diagnosis can be estimated through a combination of clinical and imaging features. Our case is a homogeneous, unilocular cystic mass at CT, which, in combination with its clinical feature of an asymptomatic woman, should make the diagnosis of at least mucinous cystadenoma possible.

The next step is to understand the nature and thus the possible image presentation of this disease. Primary retroperitoneal mucinous (PRM) tumors can be classified as cystadenomas, cystadenoma with borderline or low malignancy potential, or cystadenocarcinoma [3]. Because the imaging characteristics are similar to ovarian mucinous cystadenomas, the malignancy potential of PRM
cystadenomas may be evaluated using the same imaging criteria. Jung et al described several imaging features that may suggest malignancy in ovarian epithelial neoplasms, such as thick septa, papillary projections, a large soft-tissue component with necrosis, and thick, irregular walls. However, imaging features, such as wall thickening, septa, and multilocularity, are less reliable indicators of malignancy especially in ovarian mucinous cystadenoma [8]. Our case demonstrated uneven wall thickness with papillary projections. Thus, malignancy is indicated based on the criteria for ovarian epithelial neoplasms.

Although the number of images of PRM tumors in the literature is limited, one can perhaps assume that their image appearance would resemble those of their gross appearance. Roma et al reviewed 18 cases of PRM tumors, and 4 patterns in gross appearance were identified: (1) unilocular cyst with a thin wall, (2) predominantly cystic with papillary areas or nodules, (3) multiloculated cyst with or without nodules, and (4) predominantly solid with cystic areas. The tumors were all unilateral, ranging in size from 7 to 26 cm, with a mean diameter of 13.2 cm [3]. The gross appearance of all the PRM cystadenomas was described as a thin-walled, unilocular cyst. Whereas all PRMCACs appeared as either a uni- or multi-locular cyst with nodules or papilla or as solid masses with cystic areas. However, the PRM cystadenomas with borderline or low malignancy potential had a more variable gross appearance.

The macroscopic description in our case fits the pattern of gross appearance described for PRMCACs because it was a predominantly cystic tumor with papillary areas or nodules, which also fits well with the imaging findings as a large, unilocular cystic mass with several enhancing interior nodules. Because a PRMCAC is often comprised of a cystic mass with interior nodules, malignancy may be estimated prior to obtaining pathology findings. In our case, an estimation of malignancy based on imaging findings and gross appearance of the tumor would have accurately indicated PRMCAC. Therefore, the high resolution of CT and MRI nowadays with the combination of contrast agents should be useful for the differentiation of soft tissues, allowing patterns in imaging features to be used as diagnostic tools for identifying PRM tumors and estimating their malignancy.

Four hypotheses [1, 2, 3] regarding the etiology of PRM tumors have been formulated: (1) heterotopic ovarian tissue, (2) monodermal teratomas, (3) enterogenous genesis, and (4) coelomic metaplasia. The first hypothesis is largely based on the histological similarities between ovarian and PRM tumors. However, this does not explain the 4 reports of this malignancy in male patients with phenotypically normal gonads. In addition, most of the female patients with PRM tumors have normal ovaries and no ovarian stroma around the PRM tumor. The second hypothesis proposes that PRM tumors arise from either an ovarian teratoma or primary teratoma of retroperitoneum in which the mucinous epithelium has obliterated all other components, becoming the only identifiable tissue. This hypothesis may hold true in some cases, however there is usually lack of other tissue types or typical structures of teratoma. The hypothesis of enterogenous genesis from intestinal duplication is less persuasive because of the lack of a connection to the bowel and the lack of well-developed intestinal mucosa and muscular layers.

The most widely accepted theory is coelomic metaplasia. During embryogenesis, the coelomic epithelium gives rise to the peritoneum and the germinal epithelium of the ovary. The peritoneal epithelium maintains the same potential for Müllerian differentiation as the epithelial tumor cells of the ovary. Therefore, the retroperitoneum functions as a type of secondary Müllerian system. Deposits of small clusters of coelomic epithelial cells of the peritoneum invaginate and develop into inclusion cysts [9]. The mesothelium of these cysts may subsequently undergo metaplasia, much like the neoplastic development in the primary Müllerian system of the ovary.

The clinical course and prognosis of patients with PRM tumors are variable. Although most patients have no recurrence of disease or metastasis following tumor resection, some appear to have more aggressive clinical courses. According to their study of 18 cases of PRM tumors [3], Roma et al identified 3 main patterns of clinical courses: (1) the patient dies within 18 months of follow-up, (2) the patient develops metastasis, with or without chemotherapy, with survival ranging from 18 months to 5 years, and (3) no development of further disease [3]. The last group accounts for most patients, including those with PRMCAC. However, the follow-up period used by Roma et al was highly variable, with a mean of 40 months and median of 22 months. In another review of 33 cases, only 3 patients had died as the result of the PRM tumor [9]. The mean follow-up was, however, only 22 months, ranging from 3 to 60 months. Therefore, these tumors generally have a good prognosis following complete surgical removal. However, studies using longer follow-up periods and greater numbers of cases are needed.

Tumor markers are not useful for differentiating the exact origin of the lesion because CA-125 and CA19-9 may not be elevated. However, it is possible that tumor markers may help in detecting recurrent tumors, like in ovarian cancer or colon cancer [10].

The management of PRMCAC is controversial given its rarity and the limited experience of clinicians in its management. The range of clinical courses may also be confounding. Fertility preservation is another concern because 20 of the 49 reported patients (41%) were of reproductive age (< 40 years) [2]. Two main schools of thought have developed regarding the maintenance of female patients’ reproductive status [2, 4]. One promotes tumor resection alone, and the other recommends tumor resection with total abdominal hysterectomy (TAH) and bilateral
salpingo-oophorectomy (BSO). Dierickx et al proposed that treatment of PRMCAC, especially the malignant and mixed type, should include TAH and BSO in women who have completed their child bearing or are postmenopausal [2]. Kashima et al recommended PRMCAC excision alone, especially in young patients who wish to preserve their fertility, if an intact capsule and no dissemination are present, indicating a good prognosis [4]. Therefore, thorough examinations of both the pelvis and the abdominal organs are required. Nonetheless, discussions with patients regarding treatment options should focus primarily on the uncertainty of the disease, its clinical course, and possible management plans to aid them in making informed decisions regarding treatment.

In conclusion, PRMCAC is a rare disease entity. Here we present the third reported case associated with pregnancy. Although pre-operative diagnosis is difficult, there are certain imaging clues that may help in estimating the location of the tumor, its extent, the origin, and the potential for malignancy. Although approaches to treatment remain controversial, the resection of the entire tumor with an intact capsule is recommended as a conservative treatment. Because the benefits of additional surgical intervention and/or chemotherapy are unclear, the uncertainty of prognosis must be discussed with patients to enable them to make informed decisions regarding treatment.

REFERENCE

9. Tjalma WA, Vaneerdeweg W. Primary retroperitoneal mucinous cystadenocarcinomas are distinct entity. Int J Gynecol Cancer 2008; 18: 184-188