CASE REPORT

Renal metastasis of an ovarian granulosa cell tumour inducing growth of a cystic nephroma

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SUMMARY

A 44-year-old woman presented with a large pelvic mass. Pathology revealed a granulosa cell tumour of the left ovary. The patient was followed after surgery with inhibin B levels and interval imaging. Six years later, she began to experience severe back pain. A vertebral biopsy was positive for metastatic granulosa cell tumour. She underwent radiation to the spine. Inhibin B levels began to rise and, several months later, a CT scan showed a large heterogeneous mass essentially replacing the left kidney. She underwent an open left radical nephrectomy. Pathology revealed a 12 cm cystic nephroma with a 5 cm nodule of metastatic granulosa cell tumour. Immunohistochemistry demonstrated that the mass was inhibin and oestrogen receptor positive. This is a novel presentation of these coexisting pathologies. This unique case sheds light on the possibility of induction of cystic nephroma by the altered hormonal environment created by a granulosa cell tumour metastasis.

BACKGROUND

We describe the clinical, radiographic and pathological findings of a woman who developed a granulosa cell metastasis and a large cystic nephroma in the same kidney. This unique case of a hormonally active metastasis leading to the formation of an oestrogen-responsive tumour adds further insight into the pathogenesis of cystic nephroma.

CASE PRESENTATION

The patient is a 44-year-old woman who presented in June 2004 at the age of 36 with an acute abdomen. At that time, she underwent an exploratory laparotomy with left salpingo-oophorectomy, lymph node dissection and omentectomy. Pathology revealed a 20 cm granulosa cell tumour of the left ovary. The patient was followed after surgery with monitoring of inhibin B levels and interval imaging, which were initially normal. Adjuvant chemotherapy was planned but was postponed due to pregnancy. The patient went on to deliver without complications. The patient underwent continued surveillance until January 2010, when she began to experience severe lower back pain. A CT scan showed a lytic lesion at the L1 vertebral body. An MRI scan demonstrated that the lesion was consistent with metastatic disease. The patient then underwent a vertebral biopsy which was positive for metastatic granulosa cell tumour. A positron emission tomography (PET)/CT showed no other areas of recurrence. The patient then underwent radiation to the spine.

In October 2011, a PET/CT showed left-sided hydronephrosis and an increased density to the left renal pelvis. The patient underwent a technetium-99m mercaptoacetyltriglycine (MAG-3) renal scan which demonstrated decreased excretion on the left side. The patient then underwent ureteroscopy and renal pelvis biopsy which showed no evidence of malignancy. In April 2012, the inhibin B level was elevated to 104 pg/mL, however, a PET/CT showed no new abnormalities. Inhibin B levels continued to increase to 187 pg/mL and in July, the patient began experiencing vaginal bleeding and severe back pain. A CT scan showed a large lobulated heterogeneous mass essentially replacing the left kidney. At that time, the inhibin B level was 343 pg/mL.

The patient then underwent an open left radical nephrectomy. The mass appeared to be confined to the kidney. Pathology revealed a 12 cm cystic nephroma with a 5 cm solid nodule of metastatic granulosa cell tumour.

PATHOLOGICAL FINDINGS**Gross description**

Gross findings consisted of a left nephrectomy specimen weighing 1590 g. Multiple thin-walled cysts of varying size completely replaced the normal renal parenchyma. Thin, clear-to-yellow watery fluid was present in the majority of the cysts. A 5 cm smooth tan-yellow semifirm solid tumour was present in the upper pole. Areas of necrosis and haemorrhage were identified within the solid component (figure 1).

Figure 1 Gross pathology: bivalved nephrectomy specimen revealing multiple cysts replacing the renal parenchyma and distorting the architecture. A yellow-tan, haemorrhagic, solid component occupied the upper pole.

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Figure 2 Positive nuclear staining for oestrogen receptor in the ovarian-type stroma of the cystic nephroma (×20).

Microscopic findings

On H&E-stained slides, the cystic component showed multiple cysts with thin septations. The cysts were lined by flat, cuboidal and hobnail epithelium. Spindled stromal cells surrounding the cysts resembled ovarian-type stroma. The spindle cells displayed strong nuclear ER positivity on immunohistochemical staining (figure 2). The solid tumour consisted of diffuse and microfollicular patterns of round-to-oval-shaped cells with coffee bean nuclei. The nuclei of these cells were haphazardly oriented, round-to-oval with rare nuclear grooves and prominent nucleoli. Mitoses were present with up to 10/10 high-power fields. In the areas of microfollicular pattern, Call-Exner bodies were evident, characterised by small follicles with eosinophilic material with nuclear debris (figure 3). Immunohistochemically, the granulosa cell tumour cells were positive for inhibin (figure 4).

RADIOGRAPHIC FINDINGS

Multimodality imaging, including CT, MRI, PET and MAG-3 renal scans, was obtained over a period of 4 years chronicling the progression of the left renal mass. In November 2008, a contrast-enhanced CT of the abdomen and pelvis was obtained which demonstrated a normal left kidney and no evidence of tumour recurrence. In February 2010, an MRI of the lumbar spine was performed to further evaluate a destructive vertebral body lesion seen on an outside CT. This study partially imaged the left kidney and revealed a new small 1.7 cm simple cystic lesion compatible with a renal cyst (figure 5). In November

Figure 3 Metastatic granulosa cell tumour exhibiting microfollicular pattern and Call-Exner bodies (×20).

Figure 4 Metastatic granulosa cell tumour displaying inhibin positivity (×20).

2011, a PET/CT and a non-contrast CT of the abdomen were obtained and revealed interval enlargement of the upper pole cystic renal lesion, now measuring 3.5 cm. A MAG-3 renal scan was also performed at that time demonstrating an essentially non-functional left kidney. In February 2012, an MRI of the lumbar spine was performed to assess for change given the history of metastatic disease to the spine. This study demonstrated marked increase in the size of the left renal lesion, now measuring 6.8 cm. This mass was again cystic in appearance; however, multiple internal septations and herniation of the mass into the renal hilum were now appreciated, suggestive of a cystic nephroma. Finally, in July 2012, a non-contrast CT of the abdomen followed by an MRI of the lumbar spine were performed prior to left nephrectomy. These studies demonstrated further increase in size of the multiseptated cystic left renal mass, measuring 11.8 cm at that time (figure 6).

OUTCOME AND FOLLOW-UP

The patient recovered well from surgery and then underwent chemotherapy treatment with carboplatin and paclitaxel. After surgery and chemotherapy, the inhibin B level was normal at 14 pg/mL.

Figure 5 Axial T2-weighted MRI demonstrating a new small simple cyst in the upper pole of the left kidney.

Figure 6 Axial T2-weighted MRI demonstrating continued increase in size of the multiseptated left renal mass with herniation into the renal hilum.

DISCUSSION

Cystic nephroma is a rare, benign lesion that has a bimodal age distribution with peaks in the first few years of life (with a slight male predominance) and again in the fifth and sixth decades (with a strong female predominance). Adult cystic nephroma is a benign lesion of the kidney characterised by biphasic epithelial and stromal components. The cysts vary in size and are lined by flat, low cuboidal or hobnail epithelial cells. The septa are thin, less than 5 mm in size and with variable cellularity. Mixed epithelial and stromal tumours (MEST) are also benign biphasic tumours with epithelial and stromal components. MESTs have more complex and thicker cystic septa (>5 mm). In addition, a solid component may be present.¹ However, many similarities exist and it has been proposed that these two lesions represent two entities along the same spectrum of disease. Furthermore, since these tumours occur mostly in women, it has been proposed that their growth might be controlled by, or at least influenced by, oestrogens and progesterone. The stromal components of both are often oestrogen receptor and/or progesterone receptor positive.^{2–5} In summary, cystic nephromas and MESTs have been shown to possess similar clinical features, morphological features and gene profiles,⁶ but were distinct from other renal neoplasms.²

Granulosa cell tumours represent 2–5% of all ovarian cancers. Approximately 70% of granulosa cell tumours secrete oestrogen. The median time to relapse is 4–6 years after diagnosis, however, longer time periods have been documented.⁷ A common site of recurrence is the pelvis which has been reported in 30–40% of cases,⁸ although extrapelvic peritoneal and retroperitoneal recurrences have also been described.⁷

To our knowledge, the apparently synchronous development of a cystic nephroma (or MEST of the kidney) and a granulosa

cell metastasis in the same kidney has not been previously described. We propose that the primary event was the formation of the granulosa cell metastasis which then influenced the growth of the cystic nephroma via an oestrogen pathway. This is supported by the fact that the cystic nephroma is strongly ER-positive and that the tumours were spatially and temporally coexistent. Though this seems like a logical progression, it is possible that these tumours formed separately and their existence within the same location was coincidental. Rare presentations such as this may serve to further elucidate the pathogenesis of cystic nephroma.

Learning points

- ▶ Cystic nephroma is a rare, benign renal lesion that occurs predominantly in women in their 40s and 50s.
- ▶ The growth of cystic nephroma has been shown to be influenced by oestrogens and progesterone.
- ▶ Granulosa cell tumours secrete oestrogens in approximately 70% of cases.
- ▶ The rapid growth of a cystic nephroma in this case appears to have been induced by a granulosa cell metastasis to the kidney.

Contributors EMB developed the concept for this paper and wrote the manuscript. SAB provided histopathological interpretation and analysis. MMP provided radiographic interpretation and analysis. JSR revised the manuscript and approved the final version.

Competing interests None.

Patient consent Obtained.

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