



Ovarian metastasis of renal cell carcinoma: Clinical and pathological presentation of a case

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ABSTRACT

A 82-year-old woman was referred to our hospital with complaints of weight loss, loss of appetite, abdominal pain and a palpable pelvic mass. Abdominal imaging revealed a tumour at the upper pole of the right kidney with a maximum diameter of 8 cm and a second tumour in the pelvis, mostly solid, with a maximum diameter of 16 cm, that seemed to originate from the left ovary. As she was initially considered to have two distinct tumours, through a single transabdominal incision, she simultaneously underwent right radical nephrectomy and also bilateral salpingo-oophorectomy for the tumour that originated from the left ovary. Histopathological examination showed that the tumour in the right kidney was a clear-cell renal cell carcinoma (RCC) (stage pT3a, Fuhrman grade 2). The ovarian tumour proved to be an ovarian fibroma that included a circumscribed focus with a diameter of 0.7 cm which was a metastasis from the kidney tumour. Immunohistochemistry contributed significantly to the diagnosis, as the focus showed strong and diffuse expression of CD10 and RCC antigen, which are reliable markers of RCC. With less than 30 reported cases in the literature, it is very important to differentiate ovarian metastasis of RCC from primary ovarian tumour due to different treatment alternatives and prognosis.

Keywords: Immunohistochemistry; renal cell carcinoma; ovarian metastasis.

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Introduction

Although many intraabdominal cancers frequently metastasize to ovaries, renal cell carcinoma rarely metastasizes to the ovary. Moreover, metastatic tumours of the ovary may induce significant diagnostic problems, especially when metastasis occurs from tumours which are histologically similar to primary tumours of the ovary. A case of renal cell carcinoma with a simultaneous left ovarian metastasis in a postmenopausal woman is presented and the appropriate immunohistochemical tools that aided in the confirmation of the diagnosis are analyzed.

Case presentation

A 82-year-old woman was referred to our hospital with complaints of weight loss and abdominal pain. Physical examination revealed a palpable mass at the lower abdomen. Complete blood count and other routine laboratory test results were within normal limits, whereas her CA 125 serum level was moderately elevated (103.3 U/mL, normal range: 5-30 U/mL). A magnetic resonance imaging (MRI) of the abdomen was performed that showed a solid tumour at the upper pole of the right kidney with a maximum diameter of 8cm (Figure 1) and an extensive solid and partly multicystic tumour in



Figure 1. Coronal section of MRI shows upper pole tumour of the right kidney

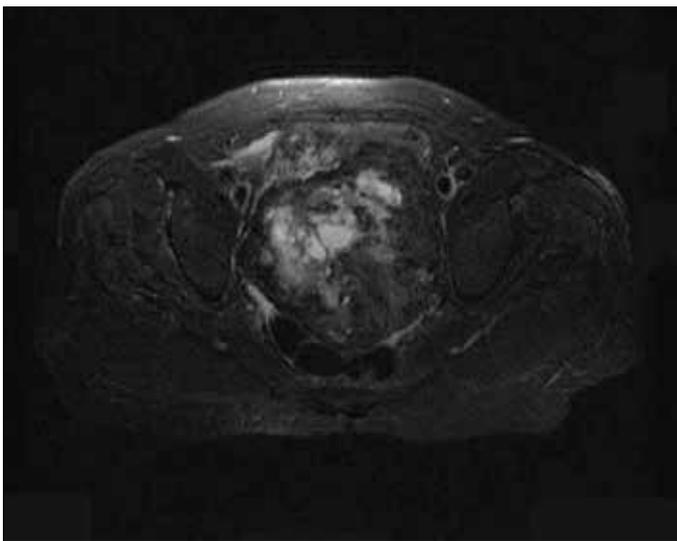


Figure 2. Axial section of MRI shows large pelvic tumour originating from left ovary

the pelvis with a maximum diameter of 16 cm (Figure 2). A preoperative X-ray of the thorax could not detect pulmonary metastases. As she was assumed to have two distinct tumours, and she underwent through a transabdominal approach right radical nephrectomy, resection of the left ovarian tumour and bilateral salpingo-oophorectomy. Apart from the fact that post-operatively she had a mild renal insufficiency, her recovery was uncomplicated and she was discharged from the hospital at the sixth postoperative day.

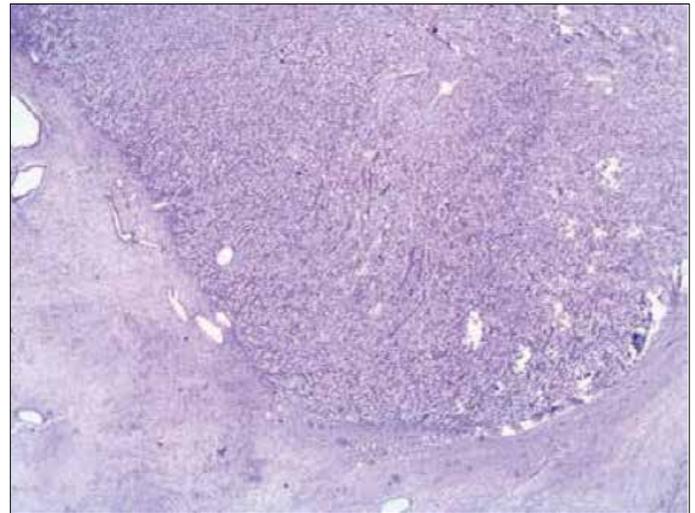


Figure 3. The metastatic focus is seen as a well circumscribed lesion consisting of epithelial cells with clear cytoplasm and a compact growth pattern (upper right). The bundles of spindle cells recognized peripherally (lower left) correspond to the ovarian fibroma. H&E x20.

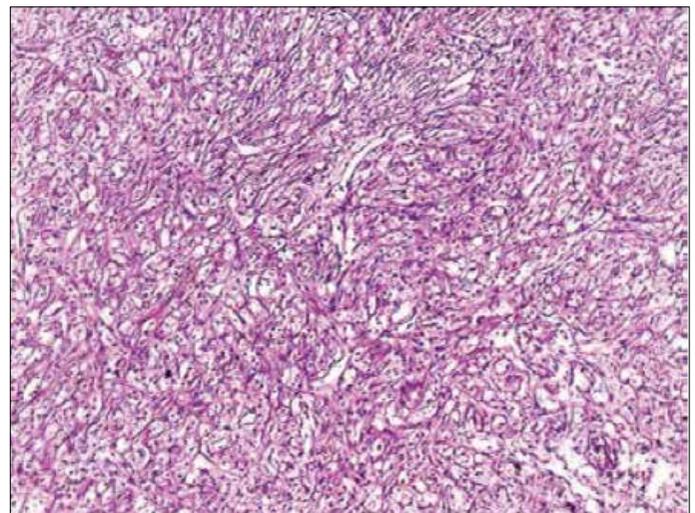


Figure 4. Higher magnification of the metastatic cells showing cellular features of clear cell renal cell carcinoma. H&E x200

Histopathological examination verified the tumour in the kidney as a clear-cell renal cell carcinoma (RCC). The grade 2, stage pT3a (Fuhrman's classification system tumour extended into the renal vein, and invaded the perirenal it should be fat). The tumour in the left ovary was an ovarian fibroma that stained positively with inhibin, calretinin and vimentin. A well-circumscribed metastatic lesion of 0.7 cm in diameter, consisting of epithelial cells with clear cytoplasm presenting with a solid and a compact growth pattern was discovered inside the fibroma (Figure 3). The cellular

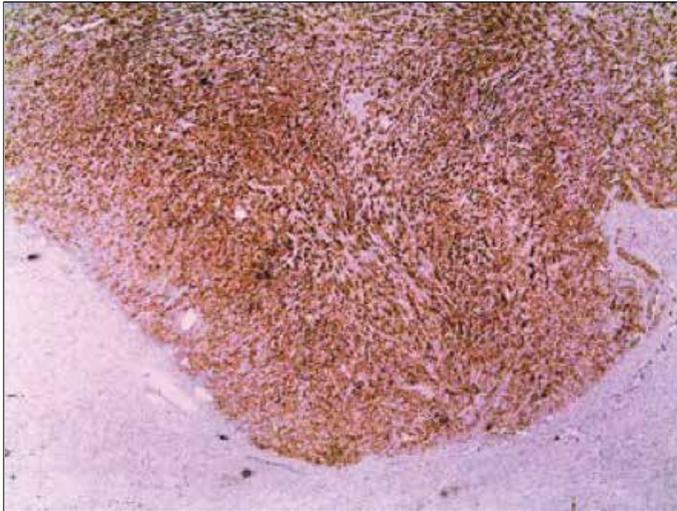


Figure 5. Strong and diffuse expression of CD10, a sensitive clear cell renal cell carcinoma marker. CD10 immunostain x20

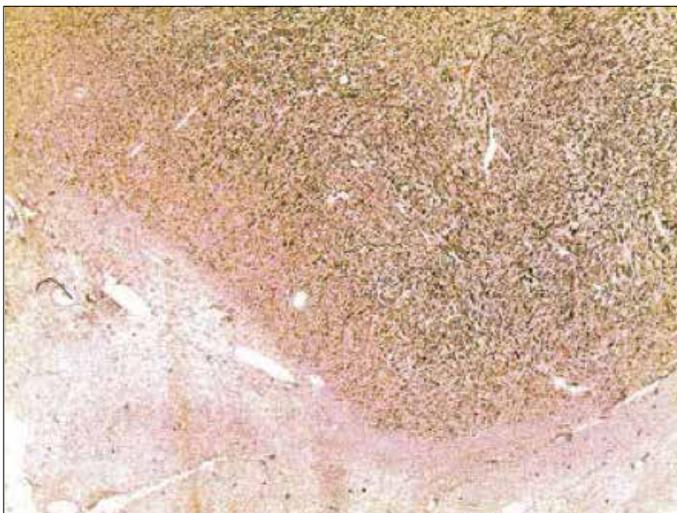


Figure 6. Strong and diffuse expression of RCC antigen, a fairly specific marker for renal cell carcinomas. RCC immunostain x20

features of this lesion suggested that it had originated from a RCC (Figure 4). Immunohistochemically, these cells presented a strong and diffuse expression of CD10, which is a sensitive clear-cell RCC marker (Figure 5) and a strong and diffuse expression of RCC antigen, a fairly specific marker for RCCs (Figure 6).

The patient was informed about the results and gave her consent to us to further analyze and use them for scientific purposes. She was referred to an oncologist for further treatment. To the extent of our knowledge, she is still alive and is being followed up for recurrence of the tumour, but she has not received any adjuvant treatment.

Discussion

Renal cell carcinoma (RCC) represents 2-3% of all types of cancers with a 1.5:1 male predominance and a peak incidence between 60 and 70 years. Renal cell carcinoma most frequently metastasizes via lymphatic and haematogenous route to the lungs (50-60%), lymph nodes (36%), bones (30-40%), liver (30-40%) and brain (5%)^[1], but it is also known to metastasize to unusual sites in rare cases. On the other hand, the ovaries are common sites for intraabdominal metastasis and about 6% of ovarian tumours found at laparotomy are secondary tumours originating from other organs, as stomach, colon, breast and lymphoma.^[2] Ovarian metastasis from renal cell carcinoma is extremely rare, as fewer than 30 cases have been reported in the English literature. In one autopsy study, ovarian metastasis was found in 0.5% of the cases with renal cell cancer.^[3]

A proposed pathophysiologic mechanism of ovarian metastasis from RCC is the retrograde venous embolization through the renal vein to the ovarian vessels, the so called renal-ovarian axis. This hypothesis would explain the slight predominance of left-sided ovarian metastases and partly the rarity of ovarian metastases from RCC. Postmenopausal women represent the peak age group affected by RCC, the ovaries have already undergone fibrotic change and vascular sclerosis, and therefore fewer tumour emboli would be carried to an ovary. Male predominance of RCC and the difficulty in differentiating a metastatic ovarian tumour from clear-cell RCC and a primary ovarian clear cell carcinoma are causes of its rarity in women.^[3]

As its differential diagnosis includes entities like primary ovarian clear cell carcinoma, steroid cell tumour and dysgerminoma, histological differentiation may be challenging. The presence of clear cells in some areas showing a tubulocystic pattern with the characteristic “hob-nail” appearance of the lining epithelium and extracellular mucin are more typical of the clear-cell carcinoma of the ovary. On the contrary, a solid and tubular growth pattern with bland cells that contain numerous lipid vacuoles and long slender microvilli devoid of rough endoplasmic reticulum, with prominent vascularity, raises the possibility of clear-cell RCC.^[4,5] Immunohistochemical analyses can be useful in the distinction of a metastatic lesion. Cytokeratin 7 expressed by most adenocarcinomas of ovarian origin, is typically negative in RCC.^[5] CA 125 is a marker expressed by epithelial ovarian tumours (including clear cell carcinomas) but is negative in RCC.^[5] Ovarian clear cell carcinomas are positively stained for HMWCK, whereas clear cell RCC are rarely stained for this biomarker.^[6] CD10 and RCC antigens are strongly expressed in all clear-cell RCCs, while CD10 is not expressed in all and RCC antigen negativity is detected in most ovarian tumours.^[7] Kato

et al.^[8] considered a panel of immunohistochemical markers consisting of HMWCK, CD10, CK7, RCC antigen and CA 125 to be very useful in the differentiation of a clear-cell carcinoma of the kidney and the ovary.

Renal cell carcinomas are known to have unpredictable clinical behavior and can metastasize to unusual sites. Although rare, an ovarian tumour should be suspected to be a metastasis of a renal tumor even if appears several years later, if there is a history of primary renal tumour. Pathologists should be aware of this rare entity and look for its characteristic morphological features and immunohistochemical profile.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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