Metastatic renal cell carcinoma masquerading as a primary ovarian mass in a post-operative case of meningioma and renal cell carcinoma

Sangita Bohara,1 Biswajit Dey,1 Swapnil Agarwal,1 Jyotsna Naresh Bharti,1 Nita Khurana,1 Poonam Sachdeva2
Departments of 1Pathology and 2Obstetrics and Gynecology, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India

Abstract

The clinical presentation of metastatic renal cell carcinoma to ovary is extremely rare as well as confusing due to its close resemblance to primary ovarian tumors, especially clear cell carcinoma. We present a case of metastatic renal cell carcinoma diagnosed in a 48-year-old female, who had renal cell carcinoma of the right kidney and right sphenoid wing meningioma of transitional type.

Introduction

Metastatic tumors to the ovary present a significant diagnostic problem in its interpretation. Renal cell carcinoma (RCC) metastasizes rarely to the ovaries. There are few documented cases in the English literature of the ovarian metastasis developing from RCC, which has been confirmed by immunohistochemistry, discovered during follow up of the primary.1 Metastatic renal cell carcinoma is often mistaken with primary clear cell tumors of the ovary. It is very important to differentiate between the two because of the different therapeutic and prognostic implications.

Case Report

A 48-year-old female attended the gynecology outpatient department for abnormal uterine bleeding. The patient was a follow up case of right-sided clear cell RCC that had been operated 3 years back by the procedure of radical nephrectomy. She had also been operated for meningioma right sphenoid wing (Figure 1A) by the procedure of craniotomy 6 years back following which, the patient developed recurrence. The removal of residual tumor was done by gamma knife therapy. On histopathological examination, the tumor showed features of transitional meningioma (WHO grade I). During follow up, the patient started developing right-sided lumbar pain for 3 months. Ultrasoundography revealed a hypeochoic lesion measuring 6.7×6.9 cm in the middle pole of right kidney with displacement of the pelvicoperitoneal system. CT scan revealed features suggestive of RCC (Figure 1B) which was proven on histopathology, when the tumor was removed by the procedure of radical nephrectomy. A Technetium99 MDP bone scan revealed no metastatic foci. Also VHL gene sequencing studies did not show any evidence of mutation.

Patient has been under constant follow up since then, when she started developing abnormal uterine bleeding. On ultrasonography, an echogenic lesion was identified on the right side of pelvis. Intra-operatively, a 5×4×3 cm ovarian mass was identified. The ovarian mass was solid with yellowish-grey and hemorrhagic areas with tiny cystic spaces (Figure 2A).

A frozen section examination was done along with intra-operative cytology in the form of imprints and scrape smears. Cytological smears showed cells dispersed singly along with focal clusters of clear cells. There was mild nuclear pleomorphism and presence of prominent nucleoli in some of the cells, however no mitosis or necrosis was identified. Frozen sections showed clear cells arranged in cords, nests as well as tubular pattern with mild nuclear atypia. A diagnosis of malignant epithelial tumor was given. A Total abdominal hysterectomy with bilateral salpingoophorectomy was performed. Histopathology of the right ovarian mass revealed a tumor composed of sheets, nests and glandular structures consisting of cells with abundant clear cytoplasm and small nuclei. Sections showed nests of clear, polygonal tumor cells arranged in sheets or nests surrounded by delicate, thin-walled vascular septa (Figure 2B). Nuclei were bland and without mitoses or pleomorphism.

Many areas showed tubules lined by attenuated tumor cells and filled with serous fluid or blood. Desmoplasia was absent in the surrounding stroma. There was no evidence of lymphovascular invasion at the periphery of either ovary or of metastatic spread to uterus, fallopian tubes or to the contralateral ovary. The tumor cells showed positive staining with periodic acid Schiff (PAS) and oil red O stain (Figure 2C). On immunohistochemistry, the tumor cells expressed epithelial membrane antigen (EMA) and CD 10 (Figure 2D) and were negative for Thyroglobulin and Inhibin. The uterus showed adenomyosis along with presence of intramural leiomyomas ranging in size from 1-2 cm in diameter. The cervix and left sided ovary as well as bilateral tubes were unremarkable. On histopathology, a final diagnosis of clear cell RCC grade II metastasizing to the ovary was given. The post-operative recovery of the patient was normal and she has been kept under follow up since then.

Discussion and Conclusions

Ovaries are a common site for intra-abdominal metastasis. About 6% of ovarian cancers found at laparotomy are secondary from other sites, commonly stomach, colon, breast, lymphoma.2 The metastasis of RCC has been rarely reported. This may be due to the vascular sclerosis of postmenopausal ovaries, in which age group the renal cell cancer is common and some of the metastatic lesions being mistaken for primary ovarian tumor.3 Metastasis to ovaries is thought to occur by retrograde venous embolization through the renal vein to the ovarian vessels.4 Some autopsy studies have demonstrated that 0.5% of women with RCC showed ovarian metastasis which are often undiagnosed, and 4.2% of secondary ovarian lesions were of renal origin.4

Sometimes there is no history of a primary renal neoplasm and the ovarian metastasis is the first presentation. The most common renal tumor to metastasize to the ovary is the typical clear cell carcinoma.2 In the ovary, the differential diagnosis of clear cell neoplasms includes primary clear cell carcinoma, steroid cell tumor, and dysgerminoma. However, careful gross and microscopic examination combined with immunohistochemical analyses can aid...
Primary clear cell carcinoma of the ovary occurs in women between 50 and 70 years of age with bilateral involvement. The gross appearance may mimic metastatic RCC, with predominantly cystic mass and focal solid areas. The microscopic appearance of clear cell carcinoma shows clear cells or hobnail cells lining cysts and tubules. The clear cells may line complex papillae. Clear cells may also be arranged in solid nests or masses, closely resembling the pattern of a clear cell carcinoma of renal origin. Immunohistochemically, tumor cells express cytokeratin, EMA, and CA 125.7

Steroid cell tumors usually occur in perimenopausal or postmenopausal women who typically present with androgenic or estrogenic symptoms. Steroid cell tumor— not otherwise specified is a differential diagnosis of clear cell carcinoma of renal origin. These tumors are rarely bilateral. Grossly, they are solid, well-circumscribed tumors of variable color with occasional hemorrhage and cystic degeneration. Microscopic examination reveals lipid-rich tumor cells with clear intracytoplasmic vacuoles arranged in solid sheets, thin cords, or columns. Immunohistochemical staining is usually positive for inhibin and negative for EMA and keratin.7

Dysgerminomas occur in women 20 to 40 years of age and present clinically with symptoms related to an abdominal mass. Although usually unilateral, these tumors may be bilateral in up to 20% of cases. Grossly, they are solid, fleshy, and lobulated mass with cystic degeneration and hemorrhage. Microscopically, the tumor cells are uniform, with clear cytoplasm and large round nuclei, and are arranged in a diffuse, trabecular, insular, or cordlike pattern. The fibrous stroma includes numerous mature lymphocytes. Dysgerminomas generally display immunoreactivity for placental alkaline phosphatase and do not typically stain for cytokeratin or EMA.7

Bilateral involvement of the ovaries by tumor should always raise the possibility of metastatic disease. Nearly 10% of bilateral ovarian tumors are metastatic, most commonly from the gastrointestinal tract and breast, but this does not apply in case of metastasis from RCC.7 Recognition of the metastatic nature of an ovarian tumor depends on an adequate clinical history, but a panel of immunohistochemical markers may play an important role if the primary lesion is unknown.

A panel of immunohistochemical markers as AE1/3, CK7, EMA, Inhibin, PLAP, RCC antigen, CD 10 and CA 125 can reliably distinguish primary ovarian neoplasms as clear cell carcinoma, dysgerminoma and steroid cell tumors from metastatic RCC.6

The presence of meningioma has been found only in a single case reported by Han et al., where the patient had undergone left radical nephrectomy for RCC seven years back. The meningothelial meningioma in this case was infiltrated by metastatic RCC of clear cell type.8 Though meningioma has been found to be the most common tumor to show the phenomena of tumor to tumor metastasis,9 in our case, meningioma was the first presentation followed by development of RCC, and no evidence of a metastatic RCC was found on histopathology.

Renal carcinomas are noted for unpredictable clinical behavior and long life history with metastases appearing many years later. So although rare, the possibility of metastatic RCC should be considered in the differential diagnosis of all cases of clear cell tumors of the ovary. Careful attention should be paid to characteristic morphological features and immunohistochemical profile.
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