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Metastases of renal clear cell carcinoma to ovary – case report and review of the literature

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Summary

In the literature the renal-ovarian axis has been demonstrated. Although, kidney and ovary are in a very distant anatomic position, they are supposed to have a lot of in common. This unusual connection begins from embryology, vascularization, and metastasizing tumors to each other. In the present systemic review the authors showed 24 case reports published in the literature, describing the metastases of primary renal cancer to ovary and only four cases reporting primary ovarian cancer metastases to kidney. Finding primary origin of the tumor is crucial in diagnostic process and subsequent therapy. The present case is a 25th case of renal cell carcinoma (RCC) metastasizing to ovary. The authors report the case of 51-year old woman with a four-year history of metastatic renal clear cell carcinoma (MRCC) presented in the present hospital with contralateral metastasis in right ovary.

Key words: Renal clear cell carcinoma; Ovarian metastases.

Introduction

Renal cell carcinomas (RCCs) most often metastasize to bones, lungs, central nervous system, liver, lymph nodes, adrenal glands, and contralateral kidney. Other sites of metastases are rare [1, 2]. Moreover, ovarian cancer metastasize mainly to contralateral ovary, lymph nodes in minor pelvis, para-aortical nodes, distant mediastinal or supraclavicular nodes. and characteristic intraperitoneal seeding. Hematogenous metastases are seen in lungs, bones or vagina [1, 2].

About 6% of ovarian cancers found at laparotomy are secondary from other sites like stomach, breast, fallopian tube, bowel cancer or contralateral ovarian cancer [2, 3]. Kidney cancer rarely disseminates to ovary, which may cause a misdiagnosis of the cancer's primary origin and lead to inappropriate subsequent adjuvant treatment.

In the literature there were published 24 case reports describing the metastases of primary renal cancer to the ovary and only four cases reporting primary ovarian cancer metastases to kidney. The present is the 25th case of RCC metastasizing to the ovary.

Case Report

A 51-year old woman with a four-year history of metastatic RCC was admitted to Department of Gynecology and Oncological Gynecology, because of suspected tumor in right ovary which was revealed during follow-up positron emission tomography computed tomography (PET/CT) examination. In March 2013 PET examination showed a hyperactive, 15-mm diameter focus in pelvis SUV 8.2mm, which corresponded to right ovary (Figure 1). Inguinal right-sided lymph nodes were also hyperactive SUV 2.7 and enlarged to 14 mm. The renal clear cell carcinoma was primary diagnosed in September 2009, after left nephrectomy. The patient was admitted to hospital that time with a short history of back pain and irregular, unreactive for typical treatment arterial hypertension for six years. Histopathologic examination revealed tumor in left kidney 85 x 75 x 70 mm in size, pTx Nx Mx. A year after that, the patient was complaining of headaches and progressive narrowing right-sided field of view. MRI examination in July 2010 showed a tumor in left occipital lobe. Left occipital craniectomy confirmed metastasis of clear cell carcinoma from kidney. The adjuvant radiotherapy was performed. In December 2012 the biopsy of thyroid gland demonstrated the metastasis. Thyroidectomy revealed the metastasis of clear cell carcinoma from kidney. (CKAE1/AE3+, CD10+).

On admission to the present hospital, transvaginal ultrasonography was performed and confirmed the presence of hyperechogenic, well vascularised (RI-0.51 PI=0.75), 16 x 14 mm in size focus in right ovary. Because of the patient's medical history and postmenopausal age, she qualified to undergo laparotomy with panhysterectomy.

The initial result of extemporaneous histological examination of right ovary was not conclusive. Detailed microscopic examination demonstrated the clear cell carcinoma metastasis from kidney. The patient was discharged in good general condition. Control follow-up transvaginal ultrasonography in two months after laparotomy did not reveal any pathological lesions in the pelvis minor.

Discussion

Our patient and most of patients reported in the literature (Table 1) presented multifocal metastasizing renal cell carcinoma (MRCC) and was treated by nephrectomy and

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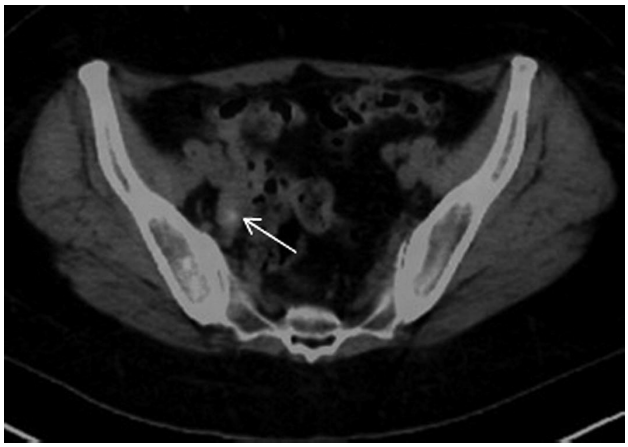

Figure 1. — PET/CT scan showing hyperactive focus in pelvis SUV-8.2 mm, corresponding to right ovary.

metastasectomy. Typical treatment for RCCs is nephrectomy. In the past several years, immunotherapy consisting of recombinant interleukin-2 (rIL-2) and recombinant interferon-alpha (rIFN-alpha) has been considered standard first-line treatment for patients with MRCC. Moreover, following metastastasectomy is nowadays recommended in MRCC [4, 5]. Metastasectomy (even incomplete) is thought to be an independent prognostic factor for survival. (P1⁄40.01, HR 0.297) [4]. Alt *et al.* examined 887 patients with MRCCs treated by nephrectomy and revealed that complete metastasectomy was associated with a significant prolongation of median cancer-specific survival (4.8 years *vs* 1.3 years; $P < 0.001$). A survival advantage from complete metastasectomy was also observed among patients with multiple, non-lung-only metastases, who had a five-year cancer-specific survival rate of 32.5% with complete resection *vs* 12.4% without complete resection ($p < 0.001$) [5].

Autopsy studies revealed that less than 1% of RCC metastases are directed to ovaries. However, up to 4.2% of secondary ovarian tumors are of renal origin [6]. Metastatic tumors of the ovary are a significant diagnostic problem in the identification of ovarian tumors. It is very confusing in differential diagnosis especially when metastasis occurs from tumors which are histologically similar to primary tumors of the ovary.

In presented systemic review (Table 1) 24 out of 25 cases (including the present), metastatic ovarian tumors were clear cell carcinomas from kidney. In 3/25 cases first diagnosed localization of the tumor was ovary and in 7/25 tumors were localized simultaneously in both organs. In the

Table 1. — *Reported cases of renal cell carcinoma metastases to ovary.*

N.	Year	Age	Primary detection	Renal Localisation	Ovarian Localisation	Time to metastases	Other metastases	Histopathology	Author
1	1949	57	Kidney	Left	Left	8M	Vagina	RCC	Martzloff *et al.* [16]
2	1957	64	Kidney	Right	Bilateral	11Y	Lung	RCC	Vorder Bruegge *et al.* [10]
3	1981	68	Kidney	Right	Left	3M	No	RCC	Stefani *et al.* [17]
4	1983	52	Simultaneous	Left	Left	No	RCC	Buller *et al.* [18]	
5	1992	48	Ovary	Right	Left	8Y	No	RCC	Young *et al.* [7]
6	1992	62	Kidney	Left	Right	1Y	Thyroid/Lung	RCC	Young *et al.* [7]
7	1992	48	Simultaneous	Left	Left	No	RCC	Young *et al.* [7]	
8	1992	28	Kidney	Right	Left	7M	Bone	RCC	Liu *et al.* [19]
9	1993	40	Ovary	Left	Bilateral	7M	Skin, parotid, brain	RCC	Spencer *et al.* [20]
10	1994	46	Kidney	Left	Bilateral	3Y	No	RCC	Adachi *et al.* [21]
11	1996	54	Kidney	Right	Left	3 Y	No	RCC	Fields et al. [22]
12	1996	66	Kidney	Right	Bilateral	11Y	Skin	RCC	Vara et al. [23]
13	2001	47	Kidney	Left	Left	4Y	No	RCC	Shinojima *et al.* [24]
14	2003	50	Kidney	Right	Right	1Y	No	RCC	Insabato *et al.* [25]
15	2003	49	Kidney	Right	Not available	14M	Bone, visceral	RCC	Insabato *et al.* [25]
16	2003	17	Kidney	Left	Left	2Y	No	RCC	Insabato *et al.* [25]
17	2003	48	Simultaneous	Left	Right	Bone	RCC	Hammock *et al.* [26]	
18	2004	61	Kidney	Left	Bilateral	7Y para-aortic	Skin, omentum,	RCC	Valappil *et al.* [8]
19	2006	52	Simultaneous	Left	Right	Simultaneous	Bone	RCC	Kato *et al.* [27]
20	2007	73	Ovary	No available	Left	No inf.	No	PRCC	Stolnicu *et al.* [28]
21	2008	52	Simultaneous	Left	Left	No inf.	Lymphatic nodes	RCC	Monzon *et al.* [29]
22	2009	54	Simultaneous	Left	Left	6M	Bone, lung	RCC	Toquero *et al.* [30]
23	2010	54	Kidney	No data	Bilateral	39M	No	RCC	Guney *et al.* [31]
24	2013	50	Simultaneous	Right	Bilateral	No inf.	No	RCC	Hołody-Zaręba *et al.* [32]
25	Our 2013	51	Kidney	Left	Right	10M	Brain/thyroid	RCC	

RCC: renal cell carcinoma; PRCC: papillary cell carcinoma; Y: year; M: month.

Table 2. — *Reported cases of metastases from ovarian carcinoma to kidney.*

N.	Year	Age	Primary origin	Renal Localisation	Ovarian Localisation	Time to metastases	Other metastases	Histological type	Author
1	1974		Ovary	No data available	No data available	9Y	No data available	Epithelial ovarian carcinoma	Friedman *et al.* [33]
2	1986	49	Ovary	Left	Left	Simultaneous	No	Serous adenocarcinoma	Cortes *et al.* [15]
3	2003	62	Ovary	Left	Left	5Y	No	Serous adenocarcinoma	Gavallos *et al.* [9]
4	2008	70	Ovary	Abdominal mass	Left	2Y	Lung	Papillary serous carcinoma	Sthyagaraja-nand *et al.* [34]

Y: year; M: month.

rest of reported cases, 10/25 tumors primary localization was in kidney. Although, it is extremely rare for ovarian cancer to metastasize to kidney, the four cases are described in the literature (Table 2). Due to this fact, interpretation of primary origin of the tumor is crucial in diagnostic process and treatment, particularly in simultaneous localization of the lesions. This process may be difficult, because the RCCs predominate in males, in females occur in post-menopausal age when vascular sclerosis is most common in ovaries, and some of metastatic tumors may be mistaken as a primary ovarian tumor [7, 8].

There are some histological differences between RCC and ovarian clear cell carcinoma.The tubules and papillae of primary clear cell carcinoma of the ovary are lined with hobnail cells, positive for Ca 125, and contain intraluminal mucin: findings rarely seen in RCCs. In the present case, Ca 125 blood levels were normal [7-9].

There are some theories about renal-ovarian axis, explaining the etiology of renal-ovarian metastases. One of them bases on anatomic relations between these organs.

Current literature shows that in most of cases 10/25 (40%) metastases arose from left-sided primary renal cancer ipsilaterally to left ovary. In 8/25 (32%) cases, RCCs disseminate to contralateral ovary. According to primary ovarian cancer, probably in all cases ipsilateral left-sided ovarian cancer and left-sided renal metastases occurred. This make a suspicion of hematogenous retrograde venous dissemination by way of left ovarian vein [7,10].

It is known that there is anatomic vessel relation between left kidney and left ovary. The kidney is vascularised by renal artery, ovary by ovarian artery, and ovarian branch from uterine artery. Venous correlation seems to be connected. Left ovary vein goes to left renal vein, and right ovarian vein to vena cava inferior. That is why the anatomy of left renal and ovarian veins may lead incompetent left ovarian vein to retrograde venous flow and enable dissemination of the cancer [11]. Moreover, it is generally known that kidney cancer may disseminate by renal vein forming tumor thrombus (TT). This fact may give rise to the theory that anatomic venous connection between left kidney and left ovary allows metastasizing to ovary. Unfortunately, there is no data available, which describe the presence of TT in renal vein, in cases of MRCC to ovary. The neoplastic TT in renal vein is found in 4-23% cases of RCCs. It is proved that TT in RCCs often occurs in malignant, higher grade tumors with metastases to lymph nodes. However, comparing the prognosis of the kidney tumors with TT and without TT in the group with the same tumor grading and staging is comparable. This is why, nowadays it is claimed that only the presence of TT is not a risk factor influencing prognosis, but also prognosis of RCCs mainly depends on oncologic features of the tumor. On the other hand, RCC with risk factors and TT has much worse prognosis [12-14].

Anatomic correlation between kidney and ovary seems to be distant. Extraperitoneal localisation of the kidney and intraperitoneal ovarian localisation probably excludes peritoneal seeding between kidney and ovary, which is typical for ovarian cancer oppositely to renal cancer. Hematogenous spread is typical for RCC, which may explain the cause of most metastases from renal RCC cancer to the ovary especially from right kidney, which may explain the way of metastasizing in the present case [9, 15].

Hematogenous way of metastasizing between oncologic lesions in kidney and ovary may have justification in embryology. Embryology of final kidney, Wolffian body, and gonad is strictly connected. Until seventh week of prenatal life, the kidney is vascularised by urogenital plexus and by abdominal aorta branches. The final kidney is formed in fifth week of prenatal life, but its development depends on proper development of temporary organs like forekidney and Wolffian body. In prenatal life kidney, Wolffian body and gonad have common vessels, which is called genitourinary plexus (32-33 days of prenatal life). In 51-53 days of prenatal period the renal artery is formed, but there are still common arteries of Wolffian body and gonad. These common vessels create circumrenal plexus [11].

Although, kidney and ovary are in a very distant anatomic position, they have much in common. Beginning from embryology, vascularization, and metastasizing tu-

mors to each other. Even if metastases from kidney cancer to ovary and vice-versa are very rare, it is worth taking this phenomenon into consideration in diagnostic process and identification primary origin of the tumor.

References

[1] Kordek R. (ed). "Onkologia. Podręcznik dla studentów i lekarzy. Rak jajnika". Gdańsk: Via Medica, 2007, 244.

[2] Bręborowicz G.H. (ed). "Ginekologia i położnictwo. Nowotwory jajnika".Warszawa: Wydawnictwo Lekarskie PZWL, 2010, 845.

[3] Petru E., Pickel H., Heydarfadai M., Lahousen M., Haas J., Schaider H., Tamussino K.: "Nongenital cancers metastatic to ovary". *Gynecol. Oncol.*, 1992, *44*, 83.

[4] Vogl U.M., Zehetgruber H., Dominkus M., Hejna M., Zielinski C.C., Haitel A., Schmidinger M.: "Prognostic factors in metastatic renal cell carcinoma: metastasectomy as independent prognostic variable". *Br. J. Cancer*, 2006, *95*, 691

[5] Alt A.L., Boorjian S.A., Lohse C.M., Costello B.A., Leibovich B.C., Blute M.L.: 'Survival after complete surgical resection of multiple metastases from renal cell carcinoma". Cancer, 2011, *117*, 2873. doi: 10.1002/cncr.25836. Epub 2011 Jan 10.

[6] Karsh J.: "Secondary malignant disease of the ovaries: a study of 72 autopsies". *Am. J. Obstet. Gynecol.*, 1951, *61*, 154.

[7] Young R.H., Hart W.R.: "Renal cell carcinoma metastatic to ovary: a report of three cases possible confusion with ovarian clear cell adenocarcinoma". *Int. J. Gynecol. Pathol.*, 1992, *11*, 96.

[8] Valappil S.V., Toon P.G., Anandaram P.S.: "Ovarian metastasis from primary renal cell carcinoma: report of a case and review of literature". *Gynecol. Oncol.*, 2004, *94*, 846

[9] Gavallos G., Tawfik O., Herrell D., Langenstroer P.: "Renal-ovarian axis: a case report and review". *Urology*, 2003, *62*, 749

[10] Vorder Bruegge C.F., Hobbs J.E., Wegner C.R., Wintemute R.W.: "Bilateral ovarian metastasis from renal adenocarcinoma: report of a case and discussion of pathogenesis". *Obstet. Gynecol.*, 1957, *9*, 198.

[11] Dobruch J., Borówka A., Grotthuss G., Dzik T.: "Rozwoj unaczynienia tętniczego nerki w okresie zarodkowym człowieka". Urol. Pol., 2007, *60*, 1.

[12] Cieśliński P.: "Charakterystyka onkologogiczna guzów nerki wnikających do naczyń żylnych". *Urol. Pol.*, 2007, *60*, 1.

[13] Ficarra V., Righetti R., D´Amico A., Rubilotta E., Novella G., Malossini G., Mobilio G.: "Renal vein and vena cava involvement does not affect prognosis in patients with renal cell carcinoma". *Oncology*, 2001, *61*, 10.

[14] Kim H.L., Zisman A., Han K.R., Han K.R., Figlin R.A., Belldegrun A.S.: "Prognostic significance of venous thrombus in renal cell carcinoma. Are renal vein and inferior vena cava involvement different?" *J. Urol.*, 2004, *171*, 588

[15] Cortes J., Uriz A., Terrasa J., Rifá J., Rosselló J.J., Llompart M.: "Ovarian cancer metastatic to the kidney: case report". *Eur. J. Gynaecol. Oncol.*, 1986, *7*, 206.

[16] Martzloff K.H., Manlove C.H.: "Vaginal and ovarian metastases from hypernephroma; report of case and review of literature". *Surg. Gynecol. Obstet.*, 1949, *88*, 145.

[17] Stefani P., Selli C., Nicita G., Turini D.: "Angiographic aspects of renal cell carcinoma metastatic to the female genitalia". *Cardiovasc. Intervent. Radiol*., 1981, *4*, 183.

[18] Buller R.E., Braga C.A., Tanagho E.A., Miller T.: "Renal-cell carcinoma metastatic to the ovary. A case report". *J. Reprod. Med.*, 1983, *28*, 217.

[19] Liu F.S., Ho E.S., Lu F., Chang C.Y.: "Solitary metastasis of renal cell carcinoma to the ovaries: a case report". *Zhonghua Yi Xue Za Zhi (Taipei)*, 1992, *50*, 165.

[20] Spencer J.R., Eriksen B., Garnett J.E.: "Metastatic renal tumor presenting as ovarian clear cell carcinoma". *Urology*, 1993, *41*, 582.

[21] Adachi Y., Sasagawa I., Nakada T., Saitoh M., Mitobe K., Ohta T., Tanaka M.: "Bilateral ovarian metastasis from left renal cell carcinoma". *Urol. Int.*, 1994, *52*, 169.

[22] Fields S., Libson E., Lavie O., Beller U.: "Renal cell carcinoma metastatic to the ovary. Ultrasound and CT appearance". *Clin Imaging*, 1996, *20*, 42.

[23] Vara A., Madrigal B., Veiga M., Diaz A., García J., Calvo J.: "Bilateral ovarian metastases from renal clear cell carcinoma". *Acta Oncol.*, 1998, *37*, 379.

[24] Shinojima T., Nakajima Y., Kiguchi H.: "Renal cell carcinoma metastatic to the ovary: a case report". *Nihon Hinyokika Gakkai Zasshi*, 2001, *92*, 694.

[25] Insabato L., De Rosa G., Franco R., D'Onofrio V., Di Vizio D.: "Ovarian metastasis from renal cell carcinoma: a report of three cases". *Int. J. Surg. Pathol.*, 2003, *11*, 309.

[26] Hammock L., Ghorab Z., Gomez-Fernandez C.R.: "Metastatic renal cell carcinoma to the ovary: a case report and discussion of differential diagnoses". *Arch. Pathol. Lab. Med.*, 2003, *127*, e123

[27] Kato Y., Numata A., Wada N., Iwata T., Saga Y., Hashimoto H., Kakizaki H.: "A case of metastatic renal cell carcinoma to the ovary". *Acta Urol. Jpn.*, 2006, *52*, 923.

[28] Stolnicu S., Borda A., Radulescu D., Puscasiu L., Berger N., Nogales FF.: "Metastasis from papillary renal cell carcinoma masquerading as primary ovarian clear cell tumor". *Pathol. Res. Pract.*, 2007, *203*, 819.

[29] Jalón Monzón A., Alvarez Múgica M., Bulnes Vázquez V., González Alvarez R.C., García Rodríguez J., Martín Benito J.L., *et al.*: "Metástasis ovárica de carcinoma de células renales primario". *Arch. Esp. Urol.*, 2008, *61*, 534.

[30] Toquero L., Aboumarzouk O.M., Abbasi Z.: "Renal cell carcinoma metastasis to the ovary: a case report". *Cases J.*, 2009, *2*, 7472

[31] Guney S., Guney N., Ozcan D., Sayilgan T., Ozakin E.: "Ovarian metastasis of a primary renal cell carcinoma: case report and review of literature". *Eur. J. Gynaecol. Oncol.*, 2010, *31*, 339.

[32] Hołody-Zaręba J., Kinalski P., Sulkowski S., Kozłowski R., Kinalski M.: "Obustronne przerzuty raka jasnokomórkowego nerki do jajników – opis przypadku". *Ginekol. Pol.*, 2013, *84*, 650.

[33] Friedman M., Browde S., Rabin S., Murray J., Nissenbaum M.: "Late metastases of emphasizing ovarian carcinoma. A case report". *S. Afr. Med. J.*, 1984, *65*, 178.

[34] Sthyagarajanand M., Abdi S.: "Recurrent ovarian carcinoma presenting as a solitary metastasis to the kidney". *Br. J. Radiol.*, 2008, *81*, e293.

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