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A case report and review of the literature

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Solitary liver metastasis of chromophobe renal cell carcinoma 17 years after nephrectomy. A case report and review of the literature

The prognosis for renal metastatic carcinoma is poor: in fact only a small portion of patients have metastases surgically treatable for their number and sizes with often a multiorgan involvement.
We present a case in whit a solitary liver metastasis was incidentaly detected 17 years after nephrectomy for renal clear cell carcinoma. during a staging computed tomography performed for colonic cancer. We discuss the main feature of this rare condition.

KEY WORDS: Hepatic resection, Liver metastasis, Renal cell carcinoma

Introduction

Patients with renal carcinoma will presents at the diagnosis with synchronous metastasis in 25-30% of the times [1,2], while 50% of the them will develop local recurrence or metastasis during follow-up period after surgical resection of the primary tumour. [3]
The most common sites of metastasis are the lungs (50-60%), lymph nodes (50%), bones (3-4%), liver (30-40%) and brain (5%) [4]; other rare sites of metastases include pancreas, adrenal glands, the parotid gland, pharynx. and skin [5]. The prognosis for renal metastatic carcinoma is poor: the median survival is about 16 months and 1-year survival is 73%, while only 10% reaches the 5-year survival [6]. This is grim result is explained by the fact that only a small portion of patients have metastases surgically treatable for their number and sizes with often a multiorgan involvement.
Chemotherapy, hormone therapy and radiotherapy have proved generally ineffective, while an increase in survival has been recorded with immunotherapy, and more specifically with the use of interleukins and interferon [7].
Nephrectomy and resection of solitary metastases, when possible, is the first treatment to offer to these patients. We report a case of a patient with cancer of the colon, in which a renal metastasis was find and treated after 17 years from nephrectomy.

Case report

M.F, 64 years old male, was admitted in our surgical division for descending colon adenocarcinoma, diagnosed by means of a colonoscopy after a positive occult fecal blood test. His past medical history showed a left nephrectomy for clear cell carcinoma in 1995, and a

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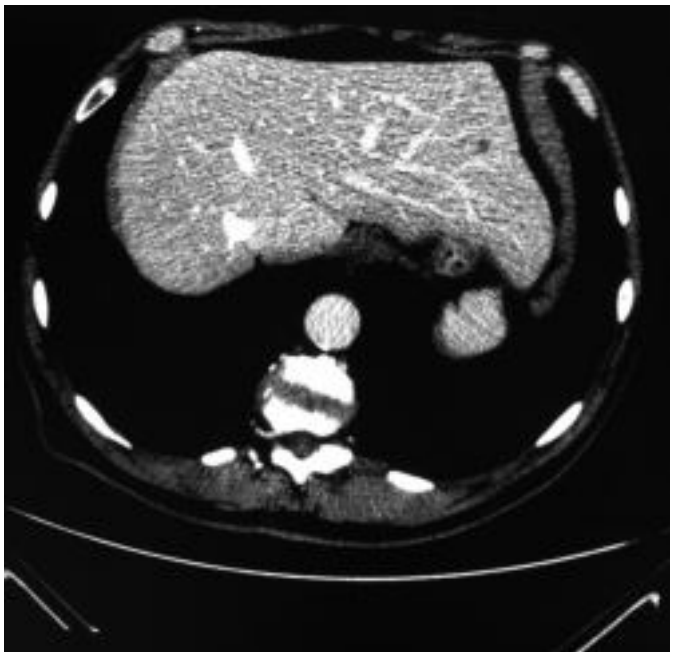

Fig. 1: Ct scan showing a 2 cm hypodense lesion in the III liver segmnet.

bilateral hernia repair in 1998 and 2007. Physical examination showed abdomen soft not tender, no mass were palpable. CT scan showed a diffuse thickening of the splenic flexure, with diffuse linphonode enlargment; a 2 cm hypodense image, was diagnosed in the III hepatic segment. (figure 1). Blood test and oncomarker were normal. The patient underwent to left hemicolectomy and wedge resection of the lesion in the III segment.
Pathological study of the specimen showed an infiltrating carcinoma of the discending colon (T3N0M0). The liver speciment was studied by immunohistochemestry and was found to be positive to vimentine and keratine 7 thus this lesion was associated with a metastasis of the clear cell carcinoma for which the patient underwent nephrectomy 17 years before. Post operative period was uneventful, the patient is alive and disease free at 9 month follow up.

Discussion

Only 2-4% of patients with renal carcinoma have treatable hepatic metastasis [8]. In fact in most of the patients these metastasis are multiple and often associated with extrahepatic disease, so that only 13% of patients reach 5 year survival [9]. Maldazys stated that the site of the metastasis is a prognostic factor since lung and bone localizations have median survival longer than liver and cerebral ones (62 months vs 22 months).[10]. Thus more than 40% of patients with single lung metastasis present a long disease free interval (>5 years) [11]. Different author in clinical studies stated an important clinical evidence: patient with sinchronous metastasis have a much worse survival compared to those with metachronous ones [12]. Synchronous metastasis not treated are associated with a very low median survival 4 month and only 10% of this group of patients reach a 12 month survival [13], consequently all the possible effort should be made to secure the treatment of both primitive and metastatic disease [14,15].
Other clinical studies stated that the survival in patients with metacrhonous metastasis that presented whitin a year from the nephrectomy is scanty (median survival 33 months), if compared to that of patient with metastasis that arised later (median survival 55 months) [16,17].
Autopsies series showed that 41% of patients with a metastatic renal cancer have liver involvement, and only 5% of this group have a single metacrhonos one. Metachronous liver metastasis develop in half of patients affected by renal cell carcinoma without macroscopic intraoperative finding [18].
Even though it seems obvious from data collected in literature that surgical treatment consisting in nephrectomy and liver metastasectomy is the base of the treatment of these patients, the real value of this approach is not completely assessed. This is probably due to the exiguous number of patients reported and to the difference in the variable assessed. Middleton reported a three year and five years overall survival of 45% an 34% after surgical removal of a single metastasis [19]; Giuliani described his experience with 41 patients and reported a 5 year overall survival of 29% and a median survival of 11 months [6]. Postoperative mortality varies from 3-6% (20) to 31% (10) depending on the number and dimensions of the metastasis and consequent type of liver resection.
Recently postoperative follow up has been established: an ultrasound scan should be performed every 3 months for the first postoperative year, every 4 months for the second and third postoperative years, every 6 months in the IV and V years, then yearly. A yearly thoracic and abdominal CT scan should be associated to ultrasound [21].
In the last year a growing interest in the medical therapy of metastasic renal cancer has been registered. Different studies showed that the results in term of survival are significantly better when nephrectomy is associated with Interferon Alfa and interleukin 2, rather than interleukine [22]; with this treatment the patient reach a 5 year survival of 19.6% with a 5,8 month increase in median survival (median survival 16.7 months) [23].
The role of inhibitor of tyrosin kinase receptor has been assessed: Sorafenib, Sunitinib, Bevacizumab have prove their efficacy in randomized trial for metastastic clear cell renal carcinoma [24]. There is a long list of chemotherapic drug used in clinical trial to assess the efficacy on hepatic metastasis of renal carcinoma. Only three agent (floxuridina, 5 FU, and vinblastin) have showed objective, but marginal results; in fact in a group o 4094 patient only 6% showed objective response [25].
The adjuvant or neo-adjuvant role of radiotherapy has been assessed in different studies. None of these showed

a real advantage in survival, on the contrary three of these point out that radiotherapy may be associated with a worse survival [26]. Radiotherapy is a palliative treatment, in case of non operable renal carcinoma o neoplastic relapse, with a local control in 90-98% of the cases [27].

Mean disease free period after nephrectomy reported is 37 months (1-108 months) [28]; in our case the time elapsed from the first operation to the development of liver metastasis was 215 months (17 years an 9 months). This is, to the best of our knowledge, the second long lasting disease free period for a presentation on a synchronous metastasis In fact in literature it is registered only one case, decribed by Lordan et al [30] in which the time from nephrectomy to the presentation of the metastasis was 20 years [29]. As in our case the liver metastasis was an accidental finding, so it is difficult to determinate how long it had been present, anyway this tumour has acted contradictory to the published finding, as it did not disseminate within the liver or to extrahepatic organs. The decision whether to perform postoperative chemotherapy in this particular subset of patients is very difficult since there is no evidence in literature.

Riassunto

La prognosi dei pazienti affetti da carcinoma renale metastatico è molto grave. Solo una piccola percentuale di pazienti può essere sottoposta a chirurgia in quanto alla diagnosi spesso le metastasi sono multiple e multiorgano. Presentiamo un caso clinico nel quale una metastasi epatica singola è stata diagnosticata incidentalmente 17 anni dopo una nefrectomia eseguita per carcinoma renale a cellule chiare, e discutiamo le peculiarità di questa rara situazione.

References

1. Cohen HT, McGovern FJ: *Renal cell carcinoma*. N Engl J Med, 2005; 353(23):2477-490.

2. Mulders P, Figlin R, deKernion JB, Wiltrout R, Linehan M, Parkinson D, deWolf W, Belldegrun A: *Renal cell carcinoma: Recent progress and future directions*. Cancer Res, 1997; 57(22):5189-95.

3. Matveev VB, Gurari LL, Began-Bogatskii KM: *Surgical treatment of late metastases of kidney cancer.* Urol Nefrol (Mosk), 1999; 2:51-52.

4. Ritchie AW, Chisholm GD: *The natural history of renal carcinoma*. Semin Oncol, 1983; 10(4):390-400.

5. Canizzaro MA, Veroux M, Cavallaro A, Costanzo M, Galasso MG, Veroux PF: *Skin metastasis from renal cell carcinoma: Epidemiological and clinical aspect.* Ann Ital Chir, 2002; 73:305-08.

6. Giuliani L, Giberti C, Martorana G, Rovida S: *Radical extensive surgery for renal cell carcinoma: Long-term results and prognostic factors*. J Urol, 1990; 143(3):468-73.

7. Flanigan RC, Salmon SE, Blumenstein BA, Bearman SI, Roy V, McGrath PC, Caton JR Jr, Munshi N, Crawford ED: *Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer*. N Engl J Med, 2001; 345:1655-659.

8. Kozlowski JM: *Management of distant solitary recurrence in the patient with renal cancer. Contralateral kidney and other sites*. Urol Clin North Am, 1994; 21(4):601-24.

9. Stief CG, Jáhne J, Hagemann JH, Kuczyk M, Jonas U: *Surgery for metachronous solitary liver metastases of renal cell carcinoma.* J Urol, 1997; 158(2):375-77.

10. Maldazys JD, deKernion JB: *Prognostic factors in metastatic renal carcinoma*. J Urol, 1986; 136(2):376-79.

11. Kavolius JP, Mastorakos DP, Pavlovich C, Russo P, Burt ME, Brady MS: *Resection of metastatic renal cell carcinoma*. J Clin Oncol, 1998; 16(6):2261-266.

13. Rafla S: *Renal cell carcinoma: Natural history and results of treatment*. Cancer 1970; 25:26-40.

14. O'dea MJ, Zincke H, Utz DC, Bernatz PE: *The treatment if renal cell carcinoma with solitary metastasis*. J Urol, 1978; 120:540-42.

15. Talarico F, Buli P, Iusco D, Sangiorgi A: *Synchronous right nephrectomy, left kindey tumorectomy, right lateral hepatic sectorectomy and inferior vena cava thrombectomy for metastastic clear cell renal carcinoma Report of a case and review of the literature*. Ann Ital Chir, 2013; 84:209-12.

16. Talarico F, Buli P, Iusco D, Sangiorgi A, Jovine E: *Synchronous nephrectomy and right hepatectomy for metastatic chromophobe renal cell carcinoma: Report of a case and review of the literature*. Chir Ital, 2007; 59(2):257-61.

17. Skinner DG, Colvin RB, Vermillion CD, Pfister RC, Leadbetter WF: *Diagnosis and management of renal cell carcinoma. A clinical and pathologic study of 309 cases*. Cancer, 1971; 28:1165-177.

18. Tongaonkar HB, Kulkarni JN, Kamat MR: *Solitary metastases from renal cell carcinoma*. J Surg Oncol, 1992; 49(1):45-48.

19. Tolia BM, Whitmore WF Jr: *Solitary metastases from renal cell carcinoma* J Urol, 1975; 114(6):836-38.

20. Middleton RG: *Surgery for metastatic renal cell carcinoma*. Urol, 1967; 97:973-77.

21. Iwatsuki S, Shaw BW, Starzl TE: *Experience with 150 liver resections.* Ann Surg, 1983; 197:247.

22. Skolarikos A, Alivizatos G, Laguna P, de la Rosette J: *A review on follow-up strategies for renal cell carcinoma after nephrectomy*. Eur Urol, 2007; 51(6):1490-500.

23. Mickisch GH, Garin A, van Poppel H, de Prijck L, Sylvester R: European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group: *Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: A randomised trial*. Lancet, 2001; 358(9286):966-70.

24. Pantuck AJ, Belldegrun AS, Figlin RA: *Nephrectomy and interleukin-2 for metastatic renal-cell carcinoma*. N Engl J Med, 2001; 345(23):1711-712.

25. Bellmunt J, Guix M: *The medical management of metastatic renal cell carcinoma: Integrating new guidelines and recommendations*. BJU Int, 2009; 103(5):572-77.

26. Yagoda A, Abi-Rached B, Petrylak D: *Chemotherapy for advanced renal-cell carcinoma: 1983-1993*. Semin Oncol, 1995; 22(1):42-60.

27. Kortmann RD, Becker G, Classen J, Bamberg M: *Future strategies in external radiation therapy of renal cell carcinoma.* Anticancer Res, 1999; 19(2C):1601-603.

28. Wersäll PJ, Blomgren H, Lax I, Kälkner KM, Linder C, Lundell G, Nilsson B, Nilsson S, Näslund I, Pisa P, Svedman C: *Extracranial stereotactic radiotherapy for primary and metastatic renal cell carcinoma*. Radiother Oncol, 2005; 77(1):88-95.

29. Alves A, Adam R, Majno P, Delvart V, Azoulay D, Castaing D, Bismuth H: *Hepatic resection for metastatic renal tumors: Is it worthwhile?* Ann Surg Oncol, 2003; 10(6):705-10.

30. Lordan JT, Fawcett WJ, Karanjia ND: *Solitary liver metastasis of chromophobe renal cell carcinoma 20 years after nephrectomy treated by hepatic resection*. Urology, 2008; 72:230.e5-6.