

## REVIEW ARTICLE

**Liver resection for hepatic metastases from adrenocortical carcinoma**ISIDORO DI CARLO<sup>1</sup>, ADRIANA TORO<sup>1</sup>, FRANCESCA SPARATORE<sup>1</sup> & STEFANO CORDIO<sup>2</sup><sup>1</sup>*Department of Surgical Sciences, Organ Transplantations and Advanced Technologies, University of Catania, Cannizzaro Hospital and* <sup>2</sup>*Department of Oncology, Garibaldi Hospital, Catania, Italy***Abstract**

Liver metastases from adrenocortical carcinoma are very rare and no clear indications for surgery exist. The aim of the present work was to define surgical indications for these neoplasms. All the patients submitted to hepatic resection for liver metastases from adrenal carcinoma reported in the literature (PubMed source) from 1978 to 2005 were considered for the present study. Forty-eight patients were found in the period of study, but it was only possible to obtain certain data for nine patients (18.7%). The data investigated suggest that metachronous metastases, developed after a minimum of 1 year from the primary tumor, and completely removable, may represent an indication for surgery – although this still needs to be proved.

**Key Words:** *Liver metastases, adrenocortical carcinoma, hepatic surgery*

**Introduction**

With an incidence of 0.5–2 cases per million population each year, adrenocortical carcinoma represents a very rare tumor [1]. Isolated liver metastases are even more rare, since only about 50 cases have been reported in the literature. The majority of these cases have been comprehensively discussed in association with other noncolorectal nonneuroendocrine liver metastases.

The aim of this study was to analyze exclusively liver metastases from adrenal carcinoma in order to determine indications for surgery.

**Patients and methods**

All the patients submitted to hepatic resection for liver metastases from adrenal carcinoma reported in literature (PubMed source) from 1978 to 2005 were considered for the present study. The following details were considered for each publication: the number of patients, sex, age, time of metastases presentation in relation to primary tumor, number of metastases, size of the tumor, localization in the liver, extent of resection (according to Couinaud [2] classification

of minor hepatic resection is defined as less than two segments, major hepatic resection as three or more segments), adjuvant chemotherapeutic treatment, disease-free interval (DFI), survival after liver resection and outcome. Literature with incomplete data was investigated by an e-mail request addressed to the authors of the original reports.

**Results**

Patients considered for this study are listed in Table I [3–15]. Forty-eight patients were found in the period of study, but it was only possible to obtain certain data for nine patients (18.7%).

A case of a female patient aged 36 years, affected by adrenal carcinoma and developing a single liver metastasis 3 years after primary tumor resection, has been reported by our group [13]. The lesion was located in segment 6 of the liver and a segmentectomy was performed. The patient is alive without any relapse. No chemotherapy has been administered.

Williams et al. reported the case of a male patient submitted to a two-stage subtotal hepatectomy 20 months after an adrenalectomy for bilobar liver metastases [12]. A metastasis of 9 cm in diameter

Table I. Liver metastases from adrenocortical carcinoma reported in the literature\*.

References	Year	Number of patients	Sex	Age (years)	Time from primary tumor	Number of metastases	Site	Size (cm)	Extension of resection	Chemotherapy	DFI	Survival	Outcome
Foster [3]	1978	2	–	–	–	–	–	–	–	–	–	–	–
Cobourn et al. [4]	1987	2	–	–	–	–	–	–	–	–	–	–	–
Iwatsuki & Starzl [5]	1988	4	–	–	–	–	–	–	–	–	–	–	–
Harrison et al. [6]	1997	7	–	–	–	–	–	–	–	–	–	–	–
Berney et al. [7]	1998	1	Female	27	Met (36 months)	2	Segment 4	2.8–6	Minor	Yes (mitotane)	135 months	135 months	Alive
Lang et al. [8]	1999	6	–	–	–	–	–	–	–	–	–	–	–
Hemming et al. [9]	2000	3	–	–	–	–	–	–	–	–	–	–	–
Laurent et al. [10]	2001	1	–	–	Met (22 months)	–	Bilobar	–	–	–	–	42 months	Dead
Langer et al. [11]	2000	2	–	–	Syn	1	–	–	Minor	–	–	1 months	Dead
–	–	–	–	–	Met	1	–	–	Minor	–	–	4 months	Dead
Williams et al. [12]	2002	1	–	–	Met (20 months)	3	Bilobar	9, 7, 5, respectively	Major	No	18 months	27 months	Dead
Di Carlo et al. [13]	2004	1	Female	32	Met (36 months)	1	Segment 6	7	Minor	No	38 months	38 months	Alive
Weitz et al. [14]	2005	15	–	–	–	–	–	–	–	–	–	–	–
Ercolani et al. [15]	2005	3	Male	18	Syn	4	–	12	–	–	–	11 months	Dead
–	–	–	Male	22	Met (6 months)	6	Right lobe	7	Major	No	6 months	10 months	Dead
–	–	–	Male	51	Syn	3	–	5	–	–	–	6 months	Dead
Total number of patients		48											

syn, synchronous; met, metachronous; DFI, disease-free interval.

\*Search of PubMed.

was located in the left lobe, and two lesions, measuring 7 and 5 cm, respectively, in the right lobe. A right hemihepatectomy and cryotherapy to the left lobe were performed at the first step; 4 months later the patient was submitted to a left lobectomy including the mass treated with cryotherapy. The patient was free from disease for 18 months, but he died 2 years and 3 months after the initial liver resection. The cause of death is not specified in the manuscript.

Langer et al. report the cases of two patients affected by hepatic metastases from adrenal carcinoma [11]. In one patient the metastasis was synchronous, so adrenalectomy, nephrectomy and resection of liver metastasis were performed at the same time. This patient died 1 month after surgical treatment. The second patient, after resection of primary tumor, developed a local recurrence and liver metastasis that were both resected, but the patient survived only 4 months. The single case reported by Berney et al. [7] has experienced an excellent survival of 135 months. In contrast, the patients in the report by Ercolani et al. had a poor outcome [15]. These patients were affected by synchronous metastases or had a limited DFI between the primary tumor and the liver metastases.

The remaining patients presented in the literature are reported comprehensively with other kinds of tumor, and data are incomplete.

## Discussion

Adrenal carcinoma is a rare malignancy with a poor prognosis. Different reports have been published with different conclusions about the appropriate treatment of this tumor. However, the basis of any treatment is the complete surgical ablation of the tumor and of the local or metastatic recurrence. Hepatic metastases from adrenal carcinoma are very rare and concern the field of noncolorectal nonneuroendocrine metastases.

The presented data are limited and details of only a few of these cases are complete. We have contacted the authors of the recent reports but, due to moving to other hospitals and consequent lack of access to the old data [8], or no reply to our requests [6,9], some reported cases remain incomplete. Of the data reported in the present study the best results were achieved in patients with metachronous metastases developed after a disease-free survival >1 year in which a complete resection was performed. The patients with synchronous metastases had poor results, recurrence occurred rapidly and the survival was short.

Surgery is the only choice of treatment for metastatic disease, because there is no definitive protocol for chemotherapy, and although therapy with mitotane is commonly used, its therapeutic value, alone or in combination with other chemotherapeutic agents, is still very controversial. In fact, the use of mitotane after surgical resection, as recommended by some

authors, to improve the survival, has not been proved to be effective [1,16]. Cryotherapy has been reported as a bridging therapy to prevent progression of the remaining tumor, in order to perform a two-stage subtotal hepatectomy for multiple metastases from adrenal carcinoma [12].

In conclusion, no guidelines can be given, but this study suggests that metachronous metastases, developed after a minimum of 1 year from the primary tumor, and completely removable, may represent an indication for surgery, although this has still to be proved. Cryotherapy or radiofrequency ablation can be used to make the metastases resectable.

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## References

- [1] Barzon L, Fallo F, Sonino N, Daniele O, Boscaro M. Adrenocortical carcinoma: experience in 45 patients. *Oncology* 1997;54:490–6.
- [2] Couinaud C. Liver anatomy: portal (and suprahepatic) or biliary segmentation. *Dig Surg* 1999;16:459–67.
- [3] Foster JH. Survival after liver resection for secondary tumors. *Am J Surg* 1978;135:389–94.
- [4] Cobourn CS, Makowka L, Langer B, Taylor BR, Falk RE. Examination of patient selection and outcome for hepatic resection for metastatic disease. *Surg Gynecol Obstet* 1987; 165:239–46.
- [5] Iwatsuki S, Starzl TE. Personal experience with 411 hepatic resections. *Ann Surg* 1988;208:421–34.
- [6] Harrison LE, Brennan MF, Newman E, Fortner JG, Picardo A, Blumgart LH, et al. Hepatic resection for noncolorectal, nonneuroendocrine metastases: a fifteen-year experience with ninety-six patients. *Surgery* 1997;121:625–32.
- [7] Berney T, Mentha G, Roth AD, Morel P. Results of surgical resection of liver metastases from non-colorectal primaries. *Br J Surg* 1998;85:1423–7.
- [8] Lang H, Nussbaum KT, Weimann A, Raab R. Liver resection for non-colorectal, non-neuroendocrine hepatic metastases. *Chirurg* 1999;70:439–46.
- [9] Hemming AW, Sielaff TD, Gallinger S, Cattral MS, Taylor BR, Greig PD, et al. Hepatic resection of noncolorectal nonneuroendocrine metastases. *Liver Transpl* 2000;6:97–100.
- [10] Laurent C, Rullier E, Feyler A, Masson B, Saric J. Resection of noncolorectal and nonneuroendocrine liver metastases: late metastases are the only chance of cure. *World J Surg* 2001;25: 1532–6.
- [11] Langer P, Bartsch D, Moebius E, Rothmund M, Nies C. Adrenocortical carcinoma – our experience with 11 cases. *Langenbecks Arch Surg* 2000;385:393–7.
- [12] Williams RN, White SA, Lloyd DM. Two stage subtotal hepatectomy for metastatic adrenal adenocarcinoma, a case report. *Hepatogastroenterology* 2002;49:535–7.
- [13] Di Carlo I, Barbagallo F, Toro A, Sofia M, Cordio S, Grasso G. Primary adrenocortical carcinoma and delayed metastasis:

- is the surgery alone the right treatment? Case report. *Hepatogastroenterology* 2004;51:343–5.
- [14] Weitz J, Blumgart LH, Fong Y, Jarnagin WR, D'Angelica M, Harrison LE, et al. Partial hepatectomy for metastases from noncolorectal, nonneuroendocrine carcinoma. *Ann Surg* 2005;241:269–76.
- [15] Ercolani G, Grazi GL, Ravaioli M, Ramacciato G, Cescon M, Varotti G, et al. The role of liver resections for noncolorectal, nonneuroendocrine metastases: experience with 142 observed cases. *Ann Surg Oncol* 2005;12:459–66.
- [16] Hahner S, Fassnacht M. Mitotane for adrenal carcinoma treatment. *Curr Opin Investig Drugs* 2005;4:386–94.