



LAPAROSCOPIC METASTASECTOMY OF ADRENAL MASS: A THERAPEUTIC OPTION. CASE REPORT AND LITERATURE REVIEW.

Beatriz Gutierrez*	Urology Department, Clinico San Carlos Hospital, Madrid, Spain. *Corresponding Author
Alvaro Serrano	Urology Department, Clinico San Carlos Hospital, Madrid, Spain.
Jeronimo Barrera	Radiodiagnosis Department, Clínico San Carlos Hospital, Madrid, Spain.
Irene de la Parra	Urology Department, Clínico San Carlos Hospital, Madrid, Spain.
Jose Antonio Cortes	Anatomopathology Department. Clínico San Carlos Hospital. Madrid. Spain.
Jesus Moreno	Urology Department, Clínico San Carlos Hospital, Medicine Faculty, Complutense University, Madrid, Spain.

ABSTRACT Invasive ductal breast carcinoma (IDC) metastasizes to several organs, but it does not usually affect the adrenal glands. In our knowledge, the cases described in the literature are few. A 60-year-old woman diagnosed with ductal breast carcinoma, was found to have adrenal metachronous metastasis during follow-up. While treatment is unclear, laparoscopic adrenalectomy could be a treatment option with curative intention. In our patient, we decided transperitoneal laparoscopic adrenalectomy, with favourable evolution after surgery.

KEYWORDS : Adrenal metastasis, ductal breast cancer, transperitoneal laparoscopic adrenalectomy.

INTRODUCTION:

Breast cancer is the most common tumor in women. Its most frequent histological type is ductal invasive carcinoma. In spite of multidisciplinary treatment of breast cancer (surgery, chemotherapy, radiotherapy, hormonal therapy and molecular therapy), tumoral relapses have been reported in 30 to 80% of patients with breast cancer [1]. This tumor can metastasize in multiple organs, such as lung, liver, bone and brain [2], but adrenal metastatic affection is uncommon, with few cases described in the literature [2-6].

The progress in diagnosis and therapeutic techniques is allowing a safer surgical approach in patients with metastatic disease of breast cancer. Nevertheless, due to the infrequency of metastatic disease in the adrenal gland because of breast cancer, more multicentric studies are needed for establish a therapeutic attitude to follow. We report a case of a large adrenal metastatic tumor of breast ductal carcinoma, and perform a literature review.

Case report:

We are presenting the clinical case of a 60-year old woman, diagnosed with breast cancer in 1998, treated by tumorectomy with right linfadenectomy and intraoperative radiotherapy (total dose 12 Gy). The pathological anatomy corresponds to an invasive ductal carcinoma with intraductal component grade III/III pT2N1M0, with positive hormonal receptors. Vascular invasion was confirmed and the axillary lymph nodes were 1/16 positive.

The patient received adjuvant radiotherapy (fractional dose 2 Gy/day until total dose of 50 Gy + fractional dose 2 Gy/day until 60 Gy above the surgical scar). Subsequently, in March 1998 she was treated for 3 months with systemic chemotherapy with adriamycin (50 mg iv two doses), 5- fluorouracil (800mg iv two doses), and cyclophosphamide (160 mg vo 14 days). Treatment with Tamoxifen started in 1998 and lasted 5 years.

In 2014 recidivation signs in the thoracic and abdominal TC scan were found, consisting of a 8x5 cm pulmonary mass, with growth towards the soft parts of the sternal region. Ensuing biopsy shows metastasis from breast cancer. On the same year, an isotope bone scanning showed a peripheral osteoblastic lesion in the sternal body and in the right ileopubic branch. With this findings, treatment with radiotherapy to the sternal lesion was decided (fractional dose 2 Gy/day until 40 Gy dose) and chemotherapy (Paclitaxel + Bevacizumab). Treatment with Letrozol was started on the same year and was given until January 2018.

During the follow-up, the 2018 abdominal TC scan showed a right adrenal mass of 5.1 x 3.8 cm, with SUVmax of 6.2, compatible with metastasis. The lesion presented anomalous FDG uptake and no diagnostic fine-needle aspiration biopsy was performed. The patient started treatment with Fulvestrant (250 mg im 2 doses) + m-Tor inhibitor MLN0128 (30mg/week), for a total 10 cycles, changing the treatment later to Exemestane (25mg/day) + Everolimus (10mg/day) due to radiological progression, receiving a total 4 cycles. During follow-up with TC scan, the adrenal mass was seen to have increased in size up to 8.5 x 4.3 cms (shown in Fig. 1, 2), in spite of having received several lines of treatment, changing in October 2019 to Ribociclib (600mg/day during 7-21 days, depending on the cycle) + Anastrozole (1 mg/day), receiving a total 4 cycles.

Due to progressive increase in size of the right adrenal mass and appearance of pain in the right hypochondrium, surgical treatment of the lesion was decided. The patient had a good renal function and no hormonal alterations of adrenal origin were found in the analysis. Metastatic bone disease was stable and, in that moment, the patient was being treated with Ribociclib y Anastrozole.

A right laparoscopic adrenalectomy transperitoneal approach was performed in February 2020 (shown in Fig. 3). Histological analysis of the adrenal mass was compatible with adrenal metastasis of mammary origin (shown in Fig. 4). Hormonal and Herceptest receptors were negative, with ki67 of 70%. Immunophenotype showed CKAE1 AE3+, MELan A-, Calretinin -, Synaptophysin +, Chromogranin -, CD56-, TTF1 -. The resection edges of the mass were free of tumoral disease.

The patient did not present complications in the immediate postoperative period, and started adjuvant chemotherapy with 3 cycles of Capecitabin. In May 2020 she presented with fever and abdominal pain, whereupon an urgent TC showed a collection in the hepatorenal recess and liver subcapsular region that disappeared in posterior radiological controls after antibiotic therapy.

Currently the patient is being treated with Docetaxel, having received to date 3 cycles of treatment. Abdominal TC control done in August 2020 did not show local signs of tumor relapse (shown in Fig. 5).

Discussion:

When an adrenal mass is found, it is important to differentiate between primary adrenal tumor and metastatic disease. It is estimated that in patients with a previous oncological history, between 30 to 70 % of the adrenal gland injuries are finally metastatic, depending on the series

[7-8]. Nevertheless, it is essential to dismiss mass functionality; this is why it is necessary to perform a hormonal study in all the patients [9]. In our case, the hormonal study did not show any alterations.

Due to their significant blood flow, the adrenal glands are a frequent site of metastasis of primary tumors, and concerning frequency lung, breast, colon, kidney and skin (melanoma) stand out [9].

Although breast cancer causes metastasis in said organs (especially lobular invasive carcinoma), ductal carcinoma is infrequent as a cause of adrenal metastasis, as is the case that we are describing. In our knowledge, there are few cases described in the literature. Liu et al (2010) [4] published the case of a woman with ductal breast carcinoma with diagnosis of adrenal metastasis during the follow up, which prompted them to decide surgical treatment with laparoscopic adrenalectomy, with favourable evolution. Tang et al [2] published another case of a woman with ductal carcinoma and later finding during follow up of adrenal and gastric metastasis. In this case surgical treatment was not considered because it was not a solitary lesion; the publication does not describe the patient's subsequent evolution.

Monitoring patients with breast cancer with imaging techniques entails an increased finding of metastatic lesions, including adrenal glands. Most of the time, these metastatic lesions are asymptomatic. Adrenal insufficiency is uncommon, and it is caused by a major destruction or replacement of the gland [2,7].

The most widely accepted imaging technique for the diagnosis of adrenal metastasis is abdominal CT [7], with a sensitivity that varies between 20 and 50% depending on the series, and a specificity of 99% in some studies [7,10,11]. Nevertheless, both RMI and TC are suitable methods for differentiating between primary tumour and metastatic disease [4,12], although definitive diagnosis will be given by fine needle biopsy or a histopathology study after metastasectomy [4]. In a sample of 443 patients with non-small cell lung cancer, Porte et al [13] observed that the sensitivity and the specificity of the CT combined with RMI for adrenal metastasis diagnosis is 100 % and 80% respectively. PET-CT allows satisfactory identification of adrenal metastasis, due to an increased uptake of FDG by the lesion [2,6]. Finally, some authors advocate the use of PAAF in cases of unresectable adrenal masses or upon clinical suspicion with unclear image in PET-CT [9,14,15]. Our patient presented anomalous FDG uptake, and no diagnostic PAAF was done.

The prognostic factors that can influence survival are not clearly established. Several studies have assessed as prognostic factors chemotherapy, histological type, grade of differentiation, lesion size or time elapsed from primary surgery to metastasis diagnosis (DFI). However, the small size of the sample of several studies makes interpretation of the results difficult [4,9,16,17].

Regarding treatment, increased survival has been seen in patients with adrenal metastasis who received surgical treatment, as compared to other type of treatments [2,7,9,18-20].

As to the approach route, there are several complications associated with the open approach, such as increased postoperative pain, risk of surgical wound infection, risk of incisional hernia and longer hospital stay [21]. The laparoscopic approach is associated with lower morbidity and shorter hospital stay compared to open approach, without clear differences in survival [4,16,21].

While laparoscopic adrenalectomy is clearly the treatment of choice of benign adrenal lesions, is not fully established as treatment of malignant lesions. Over time, the laparoscopic treatment has been chosen as a treatment of patients with single adrenal metastasis, [2,7,9,21] with good results and the possibility to prolong survival in these cases. This is why there is an increasing tendency to treat these patients with the laparoscopic approach. In our case, we decided to perform a laparoscopic adrenalectomy transperitoneal approach to avoid complications associated with the open technique. Although we were aware that, due to the adrenal metastasis size and its intimate contact with the vena cava, there was the possibility of reconverting to open surgery to remove the metastasis, an eventuality that did not occur.

Conclusions:

The existence of metastasis of ductal breast carcinoma in the adrenal

gland is very rare. We consider that early diagnosis is essential and that removal of the metastasis by laparoscopic transperitoneal surgery is a therapeutic option to be considered, as it is able to improve survival in these patients.

Disclosure of interest:

The authors have no conflicts of interest to declare.

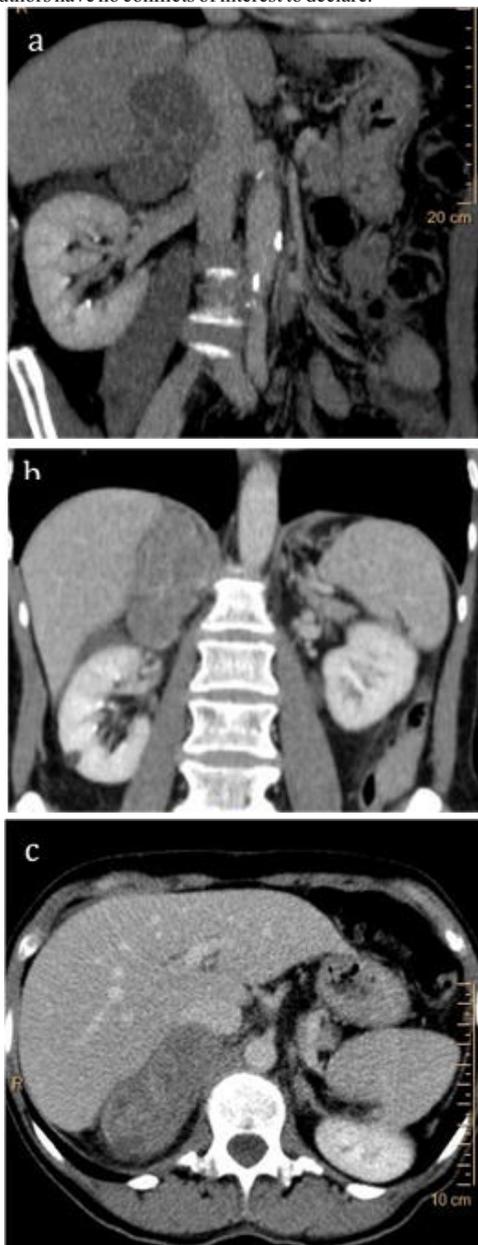


Fig. 1: Right adrenal mass of 8,5 x 4,3 cm in TC scan images, that displaces the inferior vena cava laterally and is inserted behind it until it exceeds it. Coronal section (a,b), transverse section (c).



a.- Anterior view



b.- Posterior view

Fig.2: Three-dimensional reconstruction of a right adrenal metastatic mass of breast cancer. Note the broad relation between the inferior vena cava and the adrenal mass. Anterior view (a), posterior view (b).

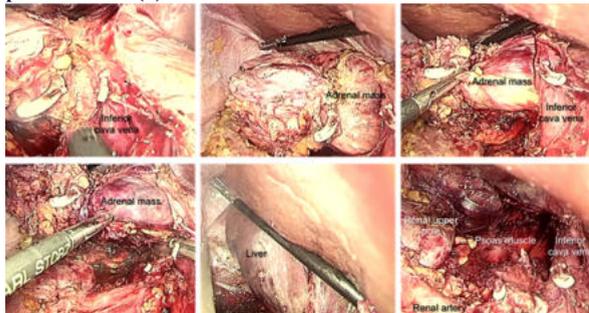


Fig.3: Sequencing the adrenalectomy technique of a large adrenal mass. Beginning of adrenal mass excision after right decoliation, Kocher maneuver, renal pedicle release and separation of the adrenal mass from the upper pole of the kidney and the inferior vena cava (a). Laparoscopic image showing the sectioned adrenal vein, prior placement of Hem-o-lok (b). Adrenal mass release from the adhesions to inferior vena cava (c). Last separation of adrenal mass from inferior vena cava, section of adhesions with Harmonic scalpel (d). Separation of firm attachments of the adrenal mass to the liver (e). Laparoscopic image of the retroperitoneal site where the adrenal mass was located (f).

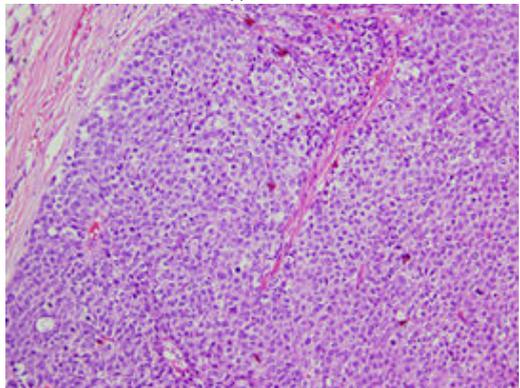


Fig.4: Histopathological image of breast cancer metastasis. H&E stain.



Fig.5: Abdominal CT performed 6 months after right

adrenalectomy, where no evidence of metastatic recurrence can be seen.

REFERENCES:

1. Signorelli, C., Pomponi-Formiconi, D., Nelli, F., & Pollera, C. F. (2005). Single colon metastasis from breast cancer: a clinical case report. *Tumori*, 91(5), 424–427.
2. Tang, T., Zhang, L., Li, C., & Zhou, T. (2020). Gastric and adrenal metastasis from breast cancer: Case report and review of literature. *Medicine*, 99(3), e18812.
3. Fernández Sarabia, M. T., Rodríguez García, J. M., Cardenal Escarcena, A., Serrano Vicente, J., & García Bernardo, L. (2008). Adrenal metastasis of breast cancer with involvement of the inferior vena cava. *Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico*, 10(11), 761–763.
4. Liu, X. J., Shen, P., Wang, X. F., Sun, K., & Sun, F. F. (2010). Solitary adrenal metastasis from invasive ductal breast cancer: an uncommon finding. *World journal of surgical oncology*, 8, 7.
5. Borst, M. J., & Ingold, J. A. (1993). Metastatic patterns of invasive lobular versus invasive ductal carcinoma of the breast. *Surgery*, 114(4), 637–642.
6. Demirci, U., Buyukberber, S., Cakir, T., Poyraz, A., Baykara, M., Karakus, E., Tufan, G., Benekli, M., & Coskun, U. (2011). Isolated mucinous adrenal metastasis in a breast cancer patient. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners*, 17(4), 444–447.
7. Spartalis, E., Drikos, I., Ioannidis, A., Chrysikos, D., Athanasiadis, D. I., Spartalis, M., & Avgerinos, D. (2019). Metastatic Carcinomas of the Adrenal Glands: From Diagnosis to Treatment. *Anticancer research*, 39(6), 2699–2710.
8. Kutikov A, Crispen PL, Uzzo RG. Pathophysiology, Evaluation, and Medical Management of Adrenal Disorders. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA. Campbell-Walsh Urology. Vol 2. 11th Edit. Elsevier. Philadelphia. 2016. pp. 1528-1576.
9. de la Quintana Basarrate, A., Martínez Fernández, G., Arana González, A., Prieto, M., Alvarez, I., Martínez Indart, L., García González, J. M., Perdigó Bilbao, L. F., & Colina Alonso, A. (2012). Cirugía de las metástasis en la glándula suprarrenal: resultados de una serie de 35 pacientes [Surgical treatment of adrenal gland metastases: results in a series of 35 patients]. *Cirugía española*, 90(10), 634–640.
10. Allard, P., Yankaskas, B. C., Fletcher, R. H., Parker, L. A., & Halvorsen, R. A., Jr (1990). Sensitivity and specificity of computed tomography for the detection of adrenal metastatic lesions among 91 antineoplastic lung cancer patients. *Cancer*, 66(3), 457–462.
11. Antonelli, A., Cozzoli, A., Simeone, C., Zani, D., Zanotelli, T., Portesi, E., & Cosciani Cunico, S. (2006). Surgical treatment of adrenal metastasis from renal cell carcinoma: a single-centre experience of 45 patients. *BJU international*, 97(3), 505–508.
12. Fassnacht, M., Kenn, W., & Allolio, B. (2004). Adrenal tumors: how to establish malignancy? *Journal of endocrinological investigation*, 27(4), 387–399.
13. Porte, H. L., Ernst, O. J., Delebecq, T., Métois, D., Lemaitre, L. G., & Wurtz, A. J. (1999). Is computed tomography guided biopsy still necessary for the diagnosis of adrenal masses in patients with resectable non-small-cell lung cancer?. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*, 15(5), 597–601.
14. Castillo, O. A., Vitagliano, G., Kerkebe, M., Parma, P., Pinto, I., & Diaz, M. (2007). Laparoscopic adrenalectomy for suspected metastasis of adrenal glands: our experience. *Urology*, 69(4), 637–641.
15. Villar Del Moral, J. M., Muñoz Pérez, N., Rodríguez Fernández, A., Olmos Juárez, E., Moreno Cortés, C., Rodríguez González, R., Martín Cano, F. J., Sánchez Sánchez, R., & Ferrón Orihuela, J. A. (2010). Efectividad diagnóstica de la tomografía por emisión de positrones con (18)fluorodeoxiglucosa asociada a tomografía axial en la discriminación de benignidad o malignidad de las lesiones suprarrenales [Diagnostic efficacy and discriminatory capacity of positron emission tomography combined with axial tomography of adrenal lesions]. *Cirugía española*, 88(4), 247–252.
16. Strong, V. E., D'Angelica, M., Tang, L., Prete, F., Gönen, M., Coit, D., Touijer, K. A., Fong, Y., & Brennan, M. F. (2007). Laparoscopic adrenalectomy for isolated adrenal metastasis. *Annals of surgical oncology*, 14(12), 3392–3400.
17. Sebag, F., Calzolari, F., Harding, J., Sierra, M., Palazzo, F. F., & Henry, J. F. (2006). Isolated adrenal metastasis: the role of laparoscopic surgery. *World journal of surgery*, 30(5), 888–892.
18. Higashiyama, M., Doi, O., Kodama, K., Yokouchi, H., Imaoka, S., & Koyama, H. (1994). Surgical treatment of adrenal metastasis following pulmonary resection for lung cancer: comparison of adrenalectomy with palliative therapy. *International surgery*, 79(2), 124–129.
19. Branum, G. D., Epstein, R. E., Leight, G. S., & Seigler, H. F. (1991). The role of resection in the management of melanoma metastatic to the adrenal gland. *Surgery*, 109(2), 127–131.
20. Kim, S. H., Brennan, M. F., Russo, P., Burt, M. E., & Coit, D. G. (1998). The role of surgery in the treatment of clinically isolated adrenal metastasis. *Cancer*, 82(2), 389–394.
21. Feliciotti, F., Paganini, A. M., Guerrieri, M., Baldarelli, M., De Sanctis, A., Campagnacci, R., & Lezoche, E. (2003). Laparoscopic anterior adrenalectomy for the treatment of adrenal metastases. *Surgical laparoscopy, endoscopy & percutaneous techniques*, 13(5), 328–333.