INTRODUCTION

Ovarian and appendicular tumors may have similar patterns of dissemination, so initial diagnosis is not easy.

The behavior of appendicular tumors differs depending on their histology (adenocarcinoma and ovarian metastasis), so it is very interesting to know about immunohistochemistry to discern both. Also, Hypertermic Intraperitoneal Chemotherapy (HIPEC) can offer a benefit in these tumors [1].

CLINICAL CASE

A 67 year old woman with no personal background went to the Emergency Room in December 2013 for epigastralgia and loss of 4 kg in 3 months. No alterations in physical examination. Gynecological ultrasound showed right and left ovary with heterogeneous image, Negative cervico-vaginal cytology. With these findings, we performed a pelvis MRI: bilateral anexal tumor suggestive of malignancy of 56 × 40 mm (right) and 38 × 49 mm (left).

Peritoneal surfaces suggested of peritoneal carcinomatosis as well as thickening of the cecal appendix.

Additional tests:

• Tumor markers CA125 443.6 U/mL (0-35), CA19.9 23 IU/mL (0-35), CEA 4.9 (0-6.3) (Figure 1)
• Thoracoabdominopelvic CT: No lung lesions, abdomen with no new findings regarding MRI (Figure 2).
• Colonoscopy (because of cecal thickening): extrin
• sic sigma compression, thickened ileocecal valve.

Figure 1. Tumor markers evolution.
So, our differential diagnosis in the presence of a bilateral anexial tumor with thickening of the cecal appendix and ascites is an ovarian cancer (or less likely appendix) with peritoneal carcinomatosis. Bilateral ovarian involvement is more common as metastatic disease (Krukenberg's Syndrome). However, elevation of CA 125 can occur in ovarian cancer although it also can rise in the presence of ascites.

In fact, it is essential to perform an exploratory laparoscopy to differentiate ovarian cancer versus appendix (March 2014); objectifying also an infiltration of both diaphragmatic domes to what was described. Peritoneal biopsies: Ring cell adenocarcinoma without alteration of mismatch repair (MMR). KRAS NRAS Native \[2,3\]. New colonoscopy: area of erythematous ileum with the same histological result than peritoneum one.

Because optimal cytoreduction could not be achieved and adenocarcinoma appendix was confirmed, neoadjuvant chemotherapy was decided.

Neoadjuvant chemotherapy (FOLFOX 6+Panitumumab) is initiatedx4 cycles with partial response in CT (May 2014): reduction of bilateral ovarian masses and appendicular lesion. Second laparoscopy was decided in June 2014, observing an important peritoneal disease (Peritoneal Cancer Index=PCI 25), discarding cytoreduction. 4 more cycles of 5FU+Panitumumab (stopping oxaliplatin because of grade 2 neuropathy and asthenia), observed an increase in the extent of carcinomatosis in September 2014.

Within a progression disease, we decided to change treatment to 5FU+Bevacizumabx5 cycles with tumor stability (Figure 3), so new laparoscopy was proposed (January 2015): excellent response, Implants only in omentum. PCI 2-3.
February 2015: Cytoreduction+HIPEC with Paclitaxel at 42º 60 min. Initial PCI: 12. Final PCI: 0. CC-0.

Histology: Appendicular ring cell carcinoma over carcinoid cells, bilateral ovarian metastases from an appendicular ring cell carcinoma (krukenberg tumor).

Staging pT4b N1 (1/6) L1V0 M1b Immunohistochemistry: CK20+, CDX 2+(in favour of colorectal origin and against ovarian origin that would express CK7+), MUC2 and focal positive with chromogranin, synaptophysin (in favor of neuroendocrine).

Adjuvant chemotherapy continued (5FU+Bevacizumab × 12 cycles) until July 2015, with CT reassessment in July and September 2015 without evidence of disease.

However, in January 2016, a sub occlusive CT scan showed signs of duodenal obstruction, ascites, and a 15 mm nodule in the right iliac fossa (Figure 4). Surgical intervention was planned aiming at an adhesion syndrome, so intestinal resection was performed with ring cell adenocarcinoma implant and positive cytology.

After resecting peritoneal recurrence 5FU+Bevacizumab (the same chemo than used 8 months before with tumor response) was maintained until April 2016 when she presented a new intestinal sub occlusion. Disease progression was assumed and chemotherapy regimen (3rd line) was modified with FOLFIRI+Aflibercept (6 cycles) with the last CT in July 2016 without tumor recurrence. However, in October, she was admitted with a new intestinal sub occlusion and finally died after 34 months from diagnosis.

![Intestinal obstruction in duodenum, ascites and 15 mm nodule in right iliac fossa (January 2016).](image)

**DISCUSSION**

In the presence of a bilateral anexial tumor with thickening of the cecal appendix and ascites, it is suspected that it is ovarian or appendix cancer with peritoneal carcinomatosis.

Bilateral ovarian involvement is more common than metastatic (Krukenberg's Syndrome) [2,3].

As for the elevation of CA 125 to the diagnosis can occur in ovarian cancer although also occurs in the presence of ascites, so you do not have to make us assume that it is a gynecological tumor. In addition, tumor markers offer lower sensitivity and negative predictive value in appendicular tumors [3].

For the differential diagnosis of ovarian cancer versus appendix, as well as to decide the initial therapeutic management, it is essential to perform laparoscopy to assess the degree of cytoreduction and to propose surgery of entry or after neoadjuvant chemotherapy. The chemotherapy chosen is the standard of a tumor of native KRAS digestive origin [4].

Both colon cancer and gynecological origin are being considered HIPEC added to cytoreduction when the peritoneal disease can be totally resectable. For this, laparoscopy is performed prior to surgery and peritoneal involvement is measured in the form of quadrants and nodule size in each. If PCI (Peritoneal Carcinomatosis Index) >22 in general, a non-optimal degree of cytoreduction is assumed and not raised. Survival has been shown to be superior to >number of surgeries if the highest degree of cytoreduction is achieved (in this case no evidence of disease at 32 months) [5].

In multivariate analyzes the two most important prognostic factors are tumor stage and degree of cytoreduction, although the research routes are oriented towards molecular factors [7].
CONCLUSION

Bilateral and appendicular ovarian involvement is more likely from an appendicular origin and not from an ovarian cancer with bilateral affectation, since >50% of the appendix tumors begin with ovarian metastases.

Immunohistochemistry is key: CK7- and CDX2+ in digestive tumors, CK7+ and CDX2- in ovarian ones. Chromogranin, synaptophysin support a neuroendocrine origin.

Tumor markers offer lower sensitivity and negative predictive value in appendicular tumors.

HIPEC+ cytoreduction are essential in treatment of appendicular metastatic tumors, achieving overall survival greater than 34 months.

The two most important prognostic factors are tumor stage and degree of cytoreduction, although research pathways are oriented towards molecular factors.

REFERENCES