Journal of Medical & Surgical Pathology

Mil-Saga et al., J Med Surg Pathol 2018, 3:3
DOI: 10.4172/2472-4971.1000164

Case Report Open Access

Long Survival Colon Cancer: The Key is Multidisciplinary Treatment

Mil-Saga G[1*], Meri-Abad M[2], Safont-Aguilera MJ[2], Calabuig-Farinas S[3,4], Hernandez-Machancoses A[5] and Camps-Herrero C[6]

[1]*Medical Oncology Department, Hospital General de Requena, Valencia, Spain*

[2]*Medical Oncology Department, Hospital General Universitario de Valencia, Valencia, Spain*

[3]*Molecular Oncology Laboratory, Fundacion Investigacion Hospital General Universitario de Valencia, CIBERONC, Valencia, Spain*

[4]*Department of Pathology, Universitat de València, Valencia, Spain*

[5]*Radiotherapy Oncology Department, Eresa, Hospital General Universitario de Valencia, Valencia, Spain*

[6]*Department of Medicine, CIBERONC, Universitat de Valencia, Valencia, Spain*

[*]**Corresponding author:** Mil-Saga G, Medical Oncology Department, Hospital General de Requena, Valencia, Spain, E-mail: mir_gil@hotmail.com

Received date: August 24, 2018; **Accepted date:** August 30, 2018; **Published date:** September 3, 2018

Keywords: Metastatic colorectal cancer; Long survival; Multidisciplinary team

Introduction

Colorectal cancer is one of the most common diseases of the Western countries. The incidence of colorectal cancer (CRC) in Spain in 2012 was 19261 cases in males and 12979 in females, and it was the second largest cause of cancer mortality in both sexes. More than 25% of patients are diagnosed with advanced disease, and 25% of patients with early stages have a relapse during the follow-up. Of these, 80%-90% have unresectable liver metastatic disease. Despite the significant improvement in the prognosis over the last decade, metastatic CRC (mCRC) is considered incurable in most cases with a median global survival of 30 months. Among the factors that have contributed to improving survival, we can highlight the improvement in the effectiveness of systemic treatments, the increase in the number of patients whose objective is the resectability of metastases and the implementation of support treatments in the therapeutic strategy. The clinical case presented below is a metastatic patient with a long history of oncology due to the combination of multiple local and systemic treatments.

Anamnesis

40-year-old woman with no medical-surgical history of interest and ex-smoker of 4.5 packs/year. She consults in March 2012 for a 7-month history of abdominal pain in the right upper quadrant. In the last month she refers nausea, hyporexia and hematochezia.

As a family history, she refers to a father with prostate cancer at age 60 and a paternal grandmother with colon cancer at 83 years of age.

Physical Examination

Good general condition (Performance status 0). Skin pale without signs of dehydration. Abdominal examination revealed a painful hepatomegaly 4 cm below the costal margin. Rest of exploration without pathological findings.

Complementary Tests

-Hemogram: Hemoglobin=10.5 g/dl, rest normal

-Biochemistry: An increase in the numbers of aspartate transaminase=54 U/L, alkaline phosphatase=171 U/L and gamma-glutamyltransferase=105 U/L.

-Tumor markers: Carcinoembryonic antigen (CEA) 1526.4. Carbohydrate antigen 19.98645.

-Toraco-abdomino-Pelvic computed axial tomography (TAP CT): highlights hepatomegaly with 6 Lesions in parenchyma suggestive of metastasis, the largest located in segments VI and VII of 113 × 70 mm of diameter.

-Colonoscopy: At 30 cm there is a vegetative, hard and friable tumor, preventing passage of the endoscope, a biopsy is taken. Otherwise normal exploration.

-Pathological anatomy: Well-differentiated, adenocarcinoma.

-Clinical molecular diagnostic tissue: Undetected mutations of gene *KRAS* (native status) analysed by Biocartis' fully automated, real-time polymerase chain reaction (Idylla™).

-Gastroscopy: Within normality.

Diagnosis

Colon adenocarcinoma IV (liver metastases), native KRAS.

Treatment

The patient was included in the PLANET clinical trial, being randomly assigned to the FOLFIRI/panitumumab branch.

Evolution

The patient showed a partial response (PR) maintained after 4, 8 and 12 cycles. The main toxicity was diarrhea and alopecia grade 1. The case was discussed in a multidisciplinary team, which decided surgery for liver metastases. On 5/11/2012 a limited resection of the metastases was performed in segments 2, 2-3, 3 and 4b with right portal ligation and on 11/12/2012 right hepatectomy with resection of the metastases in segment 4. The anatomopathological result confirmed metastasis of adenocarcinoma, one of the lesions with an affected margin. Subsequently, the patient completed 3 months of chemotherapy (CT) with FOLFIRI regimen.

In April 2013, laparoscopic sigmoidectomy was performed with pathological anatomy result of adenocarcinoma grade 1 pT3 N0 (12 adenopathies analysed) according to the seventh TNM classification.

In July 2013, it was observed liver disease progression in positron emission tomography-computed tomography (PET-CT) with elevation of CEA. It was decided to start a second line of treatment with FOLFOX/bevacizumab scheme. After 6 cycles the patient shows partial response with good tolerance (neurophaty grade 1). The case was presented again in a multidisciplinary team and the decision was treatment with hepatic stereotactic body radiation therapy (SBRT). She received a total dose of 45 Gy in 7 sessions (3 sessions per week), suffering asthenia grade 1 after treatment for 2 w. Then, it was started follow-up.

In April 2014, the patient presented a new unresectable hepatic progression with CEA=296 ng/ml. It was decided to start again chemotherapy with FOLFIRI/panitumumab. After 6 cycles, she showed a complete response maintained after 12 cycles and in September 2014 treatment was stopped.

In January 2015, the patient suffered a new hepatic and retroperitoneal progression. It was restarted FOLFIRI/panitumumab, showing after 12 cycles complete metabolic response. In June 2015 treatment was stopped.

In September of the same year, there was a new pulmonary and hepatic progression with hypermetabolic anexial image, with CEA 318. FOLFIRI/panitumumab was reinitiated. After 6 cycles, metabolic complete response was shown maintained after 12 cycles, with CEA normalization, persisting right adnexial uptake, so it was decided to suspend the chemotherapy. In May 2016, double adnexectomy and laparoscopic hysterectomy was performed, with an anatomopathological finding of intestinal adenocarcinoma metastasis with bilateral ovarian involvement. The molecular study of tissue by real-time polymerase chain reaction showed a native KRAS (exons 2-4), NRAS (exons 2-4) and BRAF (V600E) status. Normal expression of MLH1, MSH2, MSH6 y PMS2 proteins was detected by immunohistochemistry.

In June 2016, PET-CT showed pulmonary, hepatic, interaortocaval lymph node and hepatic hilar recurrence, with CEA>1000. Treatment with FOLFIRI/Panitumumab was restarted obtaining a partial response after 6 cycles. After 12 cycles, we obtained pulmonary and ganglionic complete response with persistence of 2 liver lesions and in multidisciplinary team it was decided SBRT on the hepatic lesions. However, in PET-CT requested during the planning of SBRT, there was an increase in metabolic activity of known pulmonary nodules and new-onset infradiaphragmatic and supraventricular lymph nodes. Given this findings, it was decided to suspend SBRT on the liver lesions and start chemotherapy with FOLFOX/Bevacizumab.

The patient showed partial response maintained after 12 cycles, oxaliplatin being suspended due to neurotoxicity from cycle 11. After 18 cycles, she maintained pulmonary and lymph node response and presented hepatic progression; therefore, the multidisciplinary team decided treatment with hepatic SBRT (total dose of 45 Gy). The main toxicity was hypertransaminasemia grade 1.

In February 2018 she showed hepatic, pulmonary and paraaortic progression and it was started TAS 102 treatment.

After 1 month of treatment, frank worsening of liver function secondary to hepatic progression was observed. It was performed RAS status in peripheral blood (liquid bipsy) by BEAMing Digital PCR technology, showing native result so it was decided, given the rapid progression, to modify the treatment scheme to irinotecan/cetuximab. She has currently received 4 cycles with good tolerance (except cutaneous rash grade 1) with decreased transaminases, alkaline phosphatase and gamma-glutamyltransferase.

Discussion

This case illustrates the importance of the multidisciplinary approach to establish the optimal treatment strategy in the mCRC. In this sense, several observational studies have shown a favorable impact on survival when patients are managed within a multidisciplinary team. Today, the choice of the optimal CT treatment as part of a multimodal strategy of continuity is based mainly on: the objective of the treatment, the general state of the patient, and the mutational state of *RAS* and *BRAF* genes. In those "fit" patients with liver disease considered unresectable at onset, intensive chemotherapy schemes with doublet or triplet associated with a biologic agent have shown to be effective as conversion therapies [1]. On the other hand, the combination of hepatic surgery with local treatments such as SBRT or ablative techniques is offering the possibility of prolonging survival in these patients [2].

However, the optimal sequence of CT treatment combined with an inhibitor of the epidermal growth factor receptor (EGFR) *vs.* antiangiogenic drug in patients with native RAS, BRAF tumors located on the right side, is not clearly established [3]. The inclusion of the patient within a clinical trial as in this case allows us to continue advancing in the knowledge of the disease. In any case, what seems to be clearly established is the survival benefit of patients when they receive all available drugs.

Another interesting aspect of the case is the concept of treatment discontinuation and maintenance therapy. After induction therapy, there is the possibility of performing an active maintenance treatment and planning discontinuation of treatment of the initial combination scheme. When we use the FOLFOX-bevacizumab induction schedule, the most common maintenance therapy is the combination of a fluoropyrimidine (capecitabine) with bevacizumab [4]. In patients receiving CT based on irinotecan, the optimal maintenance therapy is not so clear. It is generally recommended to maintain the treatment until progression or unacceptable tolerance. However, intermittent treatment is also a valid option in multi-treated patients who wish to rest from CT without a clear impact on the efficacy of the treatment as shown in the case presented [5]. An essential component is to individualize each case and discuss expectations with the patient.

Conclusion

In conclusion, the case presented shows a sequence in the regimens used, showing responses during the successive relapses of the disease to EGFR inhibitors and with multiple local treatments with radical intention on the metastases decided in a multidisciplinary team. This shows us that the approach and multidisciplinary vision of patients is vital to increasing survival.

References

1. GLOBOCAN (2012) International Agency for Research on Cancer (World Health Organization) (Internet).
2. Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, et al. (2016) ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol 27: 1386-1422.
3. Arnold D, Lueza B, Douillard JY, Peeters M, Lenz HJ, et al. (2017) Prognostic and predictive value of primary tumour side in patients with RAS wild-type metastatic colorectal cancer treated with chemotherapy

and EGFR directed antibodies in six randomized trials. Ann Oncol 28: 1-17.

4. Koopman M, Antonini NF, Douma J, Wals J, Honkoop AH, et al. (2007) Sequential versus combination chemotherapy with capecitabine, irinotecan, and oxaliplatin in advanced colorectal cancer (CAIRO): a phase III randomised controlled trial. Lancet 370: 135-142.

5. Labianca R, Sobrero A, Isa L, Cortesi E, Barni S, et al. (2011) Intermittent versus continuous chemotherapy in advanced colorectal cancer: a randomised 'GISCAD' trial. Ann Oncol 22: 1236-1242.