



Rectal Adenocarcinoma in Brca 2 Carrier Case Report

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Keywords: Case report; BRCA2 protein; Rectal neoplasms; Hereditary cancer syndromes.

Abbreviations: IBMCC: Institute Of Cancer Molecular And Cellular Biology; BRCA: Breast Cancer Gene; DNA: Deoxyribonucleic Acid; ADC: Adenocarcinoma; MRI: Magnetic Resonance Imaging; CT: Computed Tomography.

Background

We present the case of a Spaniard male who was carrier of a pathogenic germline mutation in the BRCA2 gene. The proteins synthesized by these genes are part of the DNA damage detection and repair mechanisms. However, even though the genetic alteration is present in all the cells of the carriers, the factors that modulate tissue-specific modulation to promote carcinogenesis in a specific organ are still unknown.

Abstract

Background: The relationship of mutations in the BRCA 2 gene has been established with some types of tumors, especially breast, ovarian, prostate, or pancreatic cancer. However, the relationship between the development of colorectal tumors and type of genetic alteration is not entirely clear.

Case Presentation: We present the case of a 64-year-old Spaniard male carrier of a BRCA 2 germline mutation, with family history of several types of cancer, who developed locally advanced rectal adenocarcinoma, treated with neoadjuvant chemoradiotherapy with capecitabine, underwent surgery and received adjuvant capecitabine and oxaliplatin. Finally, complete response maintained since June 2016 until today.

Conclusions: This is an infrequent case that provides relevant information on the link between the germline BRCA mutations and this type of tumors. Although not confirmed yet, this relationship would make us consider the possibility of taking advantage of the diagnostic opportunity screening these patients for colorectal cancer.

Case presentation

The patient is a 64-year-old man with a germline mutation in the BRCA2 gene and a personal history of atrial fibrillation, vasomotor rhinitis, dyslipidemia, and intestinal dysrhythmia (**Figure 1**).

His family history includes breast cancer in 2 of his sisters, one of whom was the index case that raised suspicion of hereditary cancer predisposition syndrome. A test revealed a deletion in BRCA2 c.9026_9030delATCATp. (Tyr3009fs). Three paternal aunts and 4 paternal cousins had developed breast cancer. In



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addition, he had 2 daughters under 45 years old who were carriers for the same mutation and had a diagnosis of breast cancer, and a son who was healthy carrier.

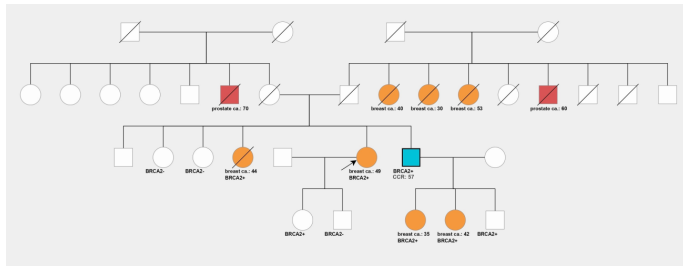


Figure 1: Index case and family members carrying the mutation. The patient presented with rectum ADC and the age and type of tumors diagnosed.

He was admitted with pinkish mucus in stool without any other associated symptoms; the abdomen was soft and depressible, not painful on palpation with no masses. No lymph nodes were palpable. Absence of hepatomegaly or splenomegaly at the first visit to general practitioner in July 2015.

A fecal occult blood test was conducted in August 2015 and was positive, without signs of anemia. The colonoscopy revealed an ulcerated cancer in the upper-middle rectum, 10-15 cm diameter occupying half of the circumference. Biopsy showed histological confirmation of poorly differentiated ADC not expanded, without involvement of the mismatch repair system in the immunohistochemical study.

The pelvic MRI showed thickening of the proximal rectal wall that was compatible with cT3-4N1, Stage IIIB [1] rectal cancer (**Figure 2**) with several adenopathies in meso-rectal fat up to 0.6 cm.

The extension study with CT was negative, without any metastatic lesion. Liver of normal size and morpho-structural characteristics; no mesenteric, retroperitoneal, iliac, or inguinal nodes of pathological size were evident. Pancreas, spleen, adrenal glands and both kidneys were free of pathology.



Figure 2: MRI of cT3-4N1 locally advanced rectal cancer.

Initial neoadjuvant treatment was administered with capecitabine together with radiotherapy on the primary tumor and lymphatic drainage chains, which ended on November 9, 2015, and was well tolerated. On January 21, 2016, the patient underwent laparoscopic anterior resection with mechanical anastomosis and protective ileostomy achieving a complete resection (R0). The results from the anatomopathological analysis were compatible with ypT1N0 rectal adenocarcinoma (Stage I) [1].

Then, the patient started adjuvant chemotherapy with capecitabine plus oxaliplatin for 6 cycles which ended in June 2016. The patient attained complete response and has been monitored since then without reappearance of the disease.

Summarizing, we described a case of locally advanced rectal cancer in a patient with germline BRCA2 mutation. Diagnosed in August 2015, after completing neoadjuvant chemoradiotherapy, he underwent surgery in January 2016, followed by 6 cycles of adjuvant chemotherapy combination (oxaliplatin and capecitabine), which ended in June of the same year.

Since then, he has started regular check-ups every 3 months for 1 year, then every 6 months for 2 years, and annually from 2019. The last consultation was in January 2023, with no signs of recurrence in colonoscopy or CT scan and normality of tumor markers (regular CEA tests every 6 months).

Discussion

The risk of breast cancer in men with the BRCA2 mutation is higher than in the general population. There is also a proven association between BRCA2 mutation and other tumors, such as prostate, pancreas, larynx, or malignant melanoma. On the other hand, the increased risk of developing colorectal cancer in this population has not yet been accurately described [2].

Colorectal cancers are currently one of the most common types of cancer, and it is expected to be the most diagnosed cancer in Spain in 2023. In locally advanced rectal cancer, such as the case described above, the use of neoadjuvant treatment with chemoradiotherapy prior to surgery followed by 5-fluorouracil chemotherapy based, has shown very beneficial results; reducing the risk of local recurrence to 7.6% in 5 years, reaching 11.4% of pathological complete responses and overall survival rates close to 80% [3]. In our case, 7 years have passed since surgery with no signs of relapse. The postoperative histopathological features (TNM stage, T substage, the number/proportion of involved lymph nodes) and the quality of the mesorectal excision have an impact on the risk of local recurrence.

Although most cases related to an inherited genetic predisposition appear in the context of Lynch syndrome, some recent studies have reported a higher probability of developing colorectal cancers in the context of BRCA1 and BRCA2 mutations as well [2].

There have been attempts to establish this correlation for quite some time, initially in the community of Ashkenazi Jews (with a high prevalence of BRCA mutations) with colorectal cancer, which showed high mutation levels suggesting a potential association [4]. The characteristics of carriers who develop colon tumors generally include a younger phenotype on diagnosis, with a more common involvement of the left colon.

One of the largest case series researched to date included approximately 7000 women with colon cancer and BRCA1/BRCA2 involvement, and it showed an increased risk of colorec-

tal cancer in patients under 50 years old with BRCA1 mutation, but not in patients with BRCA2 mutation or patients over that age [5].

However, there are several published meta-analyses that provide contradictory results regarding BRCA1/BRCA2 involvement in the risk of developing colorectal cancer. It seems that BRCA1 involvement could be a risk factor according to these results, but the evidence for BRCA2 remains inconclusive [6].

Another recent study published in 2020 by Sun P et al. [7], which compares the incidence of colorectal cancer in men who are carriers of the mutation, showed a higher incidence than what was observed in patients without BRCA mutations and higher than women who were carriers of the mutation. More specifically, most cases of colorectal cancer appeared in men with BRCA2 mutation. In addition, the mutational status of BRCA could have prognostic and therapeutic implications, although there are no conclusive results in this regard to date [8].

Conclusions

✓ BRCA mutations show phenotypic heterogeneity in men, probably with histopathological characteristics.

✓ We present this case to emphasize the relevance of studying men in families with BRCA1- and BRCA2-associated breast and ovarian cancer syndrome.

✓ Given the potential of colorectal cancer screening programs, this could be an opportunity to reinforce the early detection protocols in carriers of the BRCA mutation, despite the controversial evidence.

Declarations

Ethics approval and consent to participate

There wasn't any human participants, human data or human tissue included in the present reported case. The patient accepted and signed the required consent to participate.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

All the material and data is recovered in the Oncology System from Hospital Universitario de Salamanca.

Competing interests

There wasn't any competing of interest.

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Authors' contributions

The present work was developed with the unconditional help of the cited co-authors.

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References

- O'Sullivan B, Brierley J, Byrd D, Bosman F, Kehoe S, Kossary C, et al. The TNM classification of malignant tumours—towards common understanding and reasonable expectations. *Lancet Oncol*. 2017; 18: 849–851.
- Maccaroni E, Giampieri R, Lenci E, Scortichini L, Bianchi F, Belvederesi L, et al. BRCA mutations and gastrointestinal cancers: When to expect the unexpected? *World J Clin Oncol* [Internet]. 2021 Jul 7 [cited 2023 Mar 29]; 12: 565. Available from: /pmc/articles/PMC8317649/
- Ali F, Keshinro A, Wesiser MR. Advances in the treatment of locally advanced rectal cancer. *Annals of Gastroenterological Surgery*. Blackwell Publishing Ltd; 2021; 5: 32–38.
- Kirchhoff T, Satagopan JM, Kauff ND, Huang H, Kolachana P, Palmer C, et al. Frequency of BRCA1 and BRCA2 mutation in unselected Ashkenazi Jewish patients with colorectal cancer. *J Natl Cancer Inst*. 2004; 96: 68–70.
- Phelan CM, Iqbal J, Lynch HT, Lubinski J, Gronwald J, Moller P, et al. Incidence of colorectal cancer in BRCA1 and BRCA2 mutation carriers: Results from a follow-up study. *Br J Cancer* [Internet]. 2014; 110: 530–534. Available from: <https://pubmed.ncbi.nlm.nih.gov/24292448/>
- Oh M, McBride A, Yun S, Bhattacharjee S, Slack M, Martin JR, et al. BRCA1 and BRCA2 Gene Mutations and Colorectal Cancer Risk: Systematic Review and Meta-analysis. *J Natl Cancer Inst* [Internet]. 2018; 110. Available from: <https://pubmed.ncbi.nlm.nih.gov/30380096/>
- Sun P, Li Y, Chao X, Li J, Luo R, Li M, et al. Clinical characteristics and prognostic implications of BRCA-associated tumors in males: A pan-tumor survey. *BMC Cancer* [Internet]. 2020; 20. Available from: /pmc/articles/PMC7556962/
- Kupfer SS, Gupta S, Weitzel JN, Samadder J. AGA Clinical Practice Update on Colorectal and Pancreatic Cancer Risk and Screening in BRCA1 and BRCA2 Carriers: Commentary. *Gastroenterology*. 2020; 159: 760–764.