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Case Report

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A Case Report of Colon Cancer Succeeding Long Survival Without Chemotherapy, Msi-H, Braf Mutated

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Introduction

Immunotherapy is now indicated in the first line setting in metastatic colon cancer, while it is generally indicated in MSI-H tumors. A similar BRAFm V600E mutation is a poor prognostic indicator, while there is approved treatment in the 2nd line. The tolerance profile of these treatments may be the same or even better compared to chemotherapy and their use has gained considerable priority. The aim with this report is to highlight the possibility of successfully treating a patient with metastatic colon cancer without chemotherapy in the first two lines, especially when it ought to a frail patient. The patient is monitored in our department from the beginning of her diagnosis until the moment of this publication.

Case Report

A 72-year-old patient visited a gastroenterologist, due to diarrhea and blood loss from the stool, who scheduled a colonoscopy. A mass was found in her anion whose biopsy showed low-grade adenocarcinoma. A right hemicolectomy was performed with a difficult but subsequent postoperative course, as the wound did not heal easily, and the patient had lost significant body weight. From her personal history, the patient had heart failure with EF = 40%, diabetes mellitus, hypercholesterolemia and hypothyroidism. The rest of the imaging tests showed peripheral pulmonary embolism in sections of the left pulmonary artery, pulmonary metastases and a few hepatic foci, findings that were diagnosed 3 months after colectomy.

Due to the poor overall performance status of the patient, molecular testing was requested from the surgical preparation, the results of which were as follows:

a) mutation BRAF V600E/E2/D

b) MLH1, PMS2, no presence of activity, diagnosis of MSI-H tumor

It was therefore decided after a tumor board that the patient was not able to receive aggressive chemotherapy so we decided to initiate capecitabine monotherapy. However, the very poor tolerance in the first days of treatment, even after reducing the dose, forced us to stop it. We decided to start Pembrolizumab, with close monitoring of any complications. The patient received the immunotherapy well, without side effects for 14 months during which time she had a significant response to pulmonary and hepatic foci with a clear improvement in her clinical picture. The worsening of the disease involved new lung lesions, so it was considered progressive disease. It was then decided to change treatment to a target agent with encorafenib + cetuximab, which has been taking a total of 7 months so far. The only side effect was low fever in the first month of treatment, but with antipyretics it subsided without new side effects. The patient is now PS = 1, has regained weight and comes normally for her treatment and regular monitoring.

Discussion

Microsatellite stability (MS) consists of repeated sequences of 1-6 nucleotides [1]. The distribution characteristics differs from 15 to 65 nucleotides tandem repeats of small satellite DNA, which is mainly located near the ends of chromosomes. MS frequently is located near the coding region. MSI (microsatellite instability) can be distinguished into three types: high microsatellite instability (MSI-H), low microsatellite instability (MSI-L) and microsatellite stability (MSS) [2]. At present, clinical research inclines to classify MSS-L and MSS as one entity. According to the different molecular mechanisms of MSI in colorectal cancer, it can be divided into colorectal cancer (CRC) with no obvious family genetic history and Lynch syndrome with non-polyposis, with family genetic history. Because of the limitation of early MSI detection and the vagueness of early MSI mechanism, only specific chemotherapy drugs can be used as therapy to MSI patients. Later studies revealed weak response of locally advanced MSI-High CRC tumors to 5-FU-based regimens in adjuvant therapy,[3] indicating no benefit from single-agent fluoropyrimidine therapy in MMR-deficient CRC tumors [4,5]. Furthermore, some studies indicate not only resistance of patients with MSI-H colorectal cancer to treatment with 5-FU, but also lower survival rates of them after receiving 5-FU compared with the patients who did not receive 5-FU [5]. With the recent development of MSI detection technology and immunosuppressant in tumor therapy, researchers found that MSI-H tumors have good response rates to immunotherapy. FDA approved PD-L1 blockade pembrolizumab to treat MSI-H/MMR patients [6].

The next important section as for this case report is BRAF targeted therapy. The BRAF protooncogene, which encodes for the BRAF protein kinase, is located on chromosome 7 (q34) and is composed out of 18 exons. There have been more than 30 BRAF mutations identified to date, occurring in various frequencies. The most common is BRAF V600E mutation (MT)[7]. BRAF V600E-mutated tumors more often arise from serrated adenomas, mainly in the right colon, with a higher incidence in women and elderly patients and are usually poorly differentiated and present a mucinous histotype [8].

The therapeutic approach to BRAF-mutated CRC has always been considered challenging, given its resistance to chemotherapy. Some phase III trials showed a survival advantage with chemotherapy, such as FOLFOXIRI, plus bevacizumab as compared to the FOLFIRI plus bevacizumab for first line treatment. In second line treatment, some trials showed that aflibercept or ramucirumab plus FOLFIRI had a relevant improvement in OS compared to the BRAF-WT population, although data did not reach statistical significance. In addition, the use of anti-EGFR cetuximab and panitumumab in BRAF-mutated/ RAS WT CRC has no therapeutic restrictions. BRAF inhibitors such as vemurafenib, encorafenib, dabrafenib, showed promising results for the treatment of metastatic melanoma, NSCLC, cholangiocarcinoma and anaplastic thyroid cancer, although they are not as effective in CRC because of different resistance mechanisms [9,10]. Furthermore, many trials investigated the role of iBRAF in association with EGFR, MEK and PI3K inhibitors, particularly in second-line therapy and beyond, highlighting only a partial activity[7]. In cases of MSI, the presence of the $BRAF^{V600E}$ hotspot mutation practically excludes the possibility of Lynch Syndrome, and the clinical utility of the combination of these two markers is well established. $BRAF^{V600E}$ shows an independent negative prognostic association with survival in MSS CRC, but associations with the combination of MSI and *BRAF* have not been thoroughly investigated. Recent findings indicate that the prognostic potential of MSI slide over the negative prognostic potential of $BRAF^{V600E}$, though eliminating the deleterious role of $BRAF^{V600E}$ within the MSI subgroup. In this case report we used BRAF inhibitor in combination with pembrolizumab rushed by the recommend of International guidelines, which suggests using both MSI and *BRAF* immunohistochemical (IHC) staining for LS screening algorithms [4]. Although the negative prognostic association with survival, in coexistence of MSI-H and BRAF V600E mutation, our patient, has a good outcome after receiving BRAF inhibitor (encorafenib) in combination with pembrolizumab and cetuximab (Figure 1).

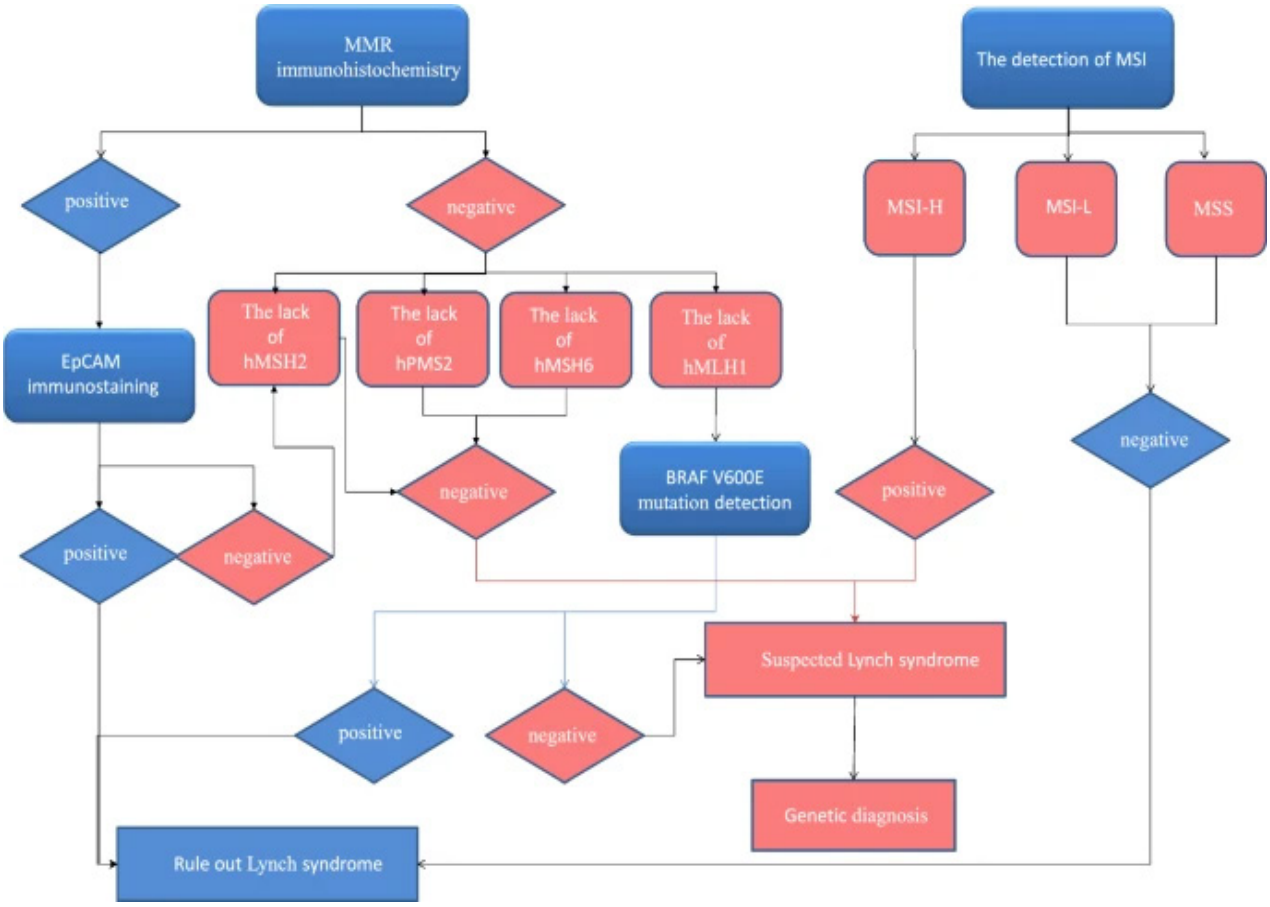

Figure 1: Microsatellite stability process, the method of suspected Lynch syndrome, through BRAF and MSI examination **[11].**

References

1. Garrido-Ramos MA (2017) Satellite DNA: an evolving topic. Genes (Basel) 8: 230-235.
2. Bonneville R, Krook MA, Chen HZ, Smith A,Samorodnitsky E, et al. (2020) Detection of microsatellite instability biomarkers via next-generation sequencing. Methods Mol Biol 2055: 119-132.
3. Sargent DJ, Marsoni S, Monges G, Thibodeau SN, Labianca R, Hamilton SR, et al. (2010) Defective mismatch repair as a predictive marker for lack of efficacy of fluorouracil-based adjuvant therapy in colon cancer. J Clin Oncol 28: 3219-3226.
4. Li K, Luo H, Huang L, Luo H, Zhu X (2020) Microsatellite instability: a review of what the oncologist should know. Cancer Cell Int 20:16.
5. Zeinalian M, Hashemzadeh-Chaleshtori M, Salehi R, Emami MH (2018) Clinical Aspects of Microsatellite Instability Testing in Colorectal Cancer. Adv Biomed Res 7: 28.
6. Seppala T, Böhm J, Friman M, Lahtinen L, Väyrynen VMJ, et al. (2015) Combination of microsatellite instability and BRAF mutation status for subtyping colorectal cancer. Br J Cancer 112:1966-1975.
7. Caputo F, Santini C, Bardasi C, Cerma K, Casadei-Gardini A, et al. (2019) BRAF-Mutated Colorectal Cancer: Clinical and Molecular Insights. Int J Mol Sci. 20: 5369.
8. Tran B, Kopetz S, Tie J, Gibbs P, Jiang ZQ, et al. (2011) Impact of BRAF mutation and microsatellite instability on the pattern of metastatic spread and prognosis in metastatic colorectal cancer. Cancer 117: 4623-4632.
9. Hyman DM, Puzanov I, Subbiah V, Faris JE, Chau I, et al. (2015) Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. N Engl J Med 373: 726-736.
10. Kopetz S, Desai J, Chan E, Hecht JR, O'Dwyer PJ, et al. (2015) Phase II pilot study of vemurafenib in patients with metastatic BRAF-mutated colorectal cancer. J Clin Oncol 33: 4032-4038.
11. Kai Li, Haiqing Luo,Huang L,Luo H,Zhu X (2010) Microsatellite instability: a review of what the oncologist should know. Cancer Cell Int 20: 16.