



Case Report

Prolonged Remission After Radiotherapy in a Patient with BRAF V600E Mutated Colon Cancer with Latero-Aortic Lymph Node Involvement

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Citation: Canova CH, Troussier I, Klausner G (2022) Prolonged Remission After Radiotherapy in a Patient with BRAF V600E Mutated Colon Cancer with Latero-Aortic Lymph Node Involvement. Ann Case Report. 7: 1082. DOI: 10.29011/2574-7754.101082

Received Date: 06 December 2022; Accepted Date: 10 December 2022; Published Date: 13 December 2022

Introduction

Colorectal cancer is the second Leading cause of cancer mortality in Europe [1].

Among patients with locally advanced disease, 20 to 30% will develop metastatic disease [2]. Management has expanded over time since the advent of immunotherapy for patients with microsatellite instability [3] and some targeted therapies such as anti-BRAF molecules combined with anti-EGFR in case of BRAF V600E mutation [4].

There are few data in the literature on para-aortic oligometastatic lymph node involvement and the prevalence of this isolated involvement is estimated at 1.7% [5].

Case report

51 years old patient with no notable medical history. The patient underwent surgery on 19/01/2018 for a poorly differentiated right colonic adenocarcinoma, MSS, RAS unmutated but with a BRAF V600E mutation, with an initial stage of T4 N2, with a postoperative CT scan that found coelio mesenteric lymphadenopathy of 35 X 25 mm.

Chemotherapy with FOLFOX-Bevacizumab was started, followed by LV5 FU2 maintenance with Bevacizumab from February to October 2018.

Despite a good initial response, progression was noted on PET-CT of november 2018 at the inter-aortic-caval lymph node level (Figure 1).

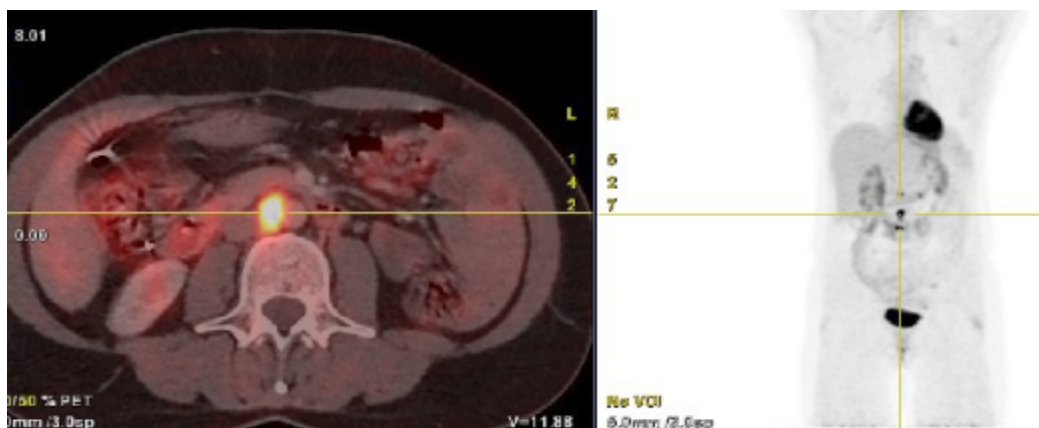


Figure 1: PET-CT after FOLFOX chemotherapy (November 2018).

A treatment with FOLFIRI bevacizumab was proposed in second line.

A stability of lymphadenopathy was noted on the dosimetric scanner.

Bevacizumab treatment was interrupted 6 weeks before the beginning of the irradiation in order not to increase the risk of bowel toxicity.

Para-aortic radio-chemotherapy was performed with capecitabine at a dose of 45 Gy in 25 fractionations of 1.8 Gy and a simultaneous integrated boost at a dose of 54 Gy was delivered in 25 fractionations of 2.16 Gy (Figure 2).

This irradiation was performed with a VMAT technique on a VERSA HD using 6 MV energy beams.

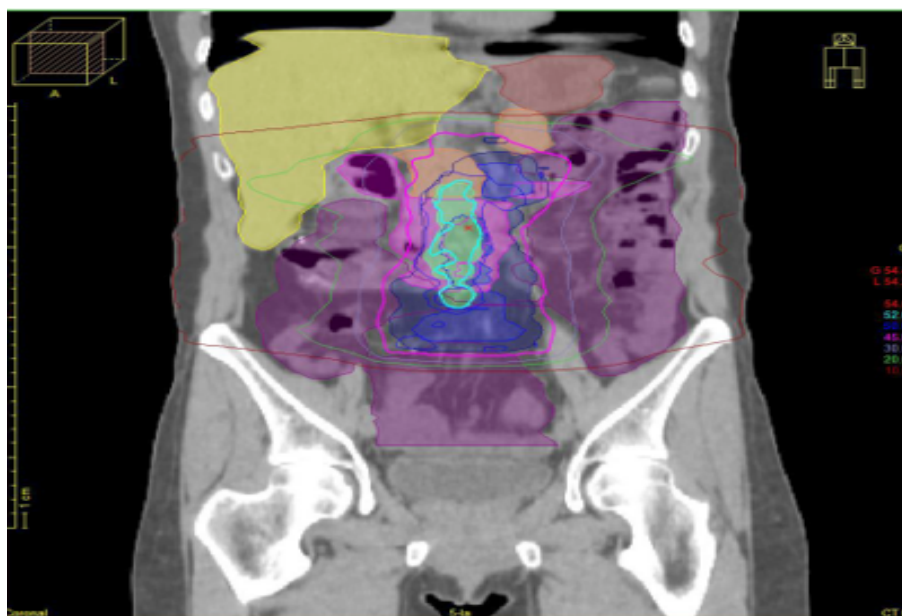


Figure 2: Radiation planning of para-aortic treatment

Chemo-radiation was complicated by nausea, grade 3 vomiting requiring a short 48h hospitalization for rehydration and hydro-electrolytic rebalancing.

FOLFIRI protocol was completed for a total of 6 cycles on April 2019 and continuation with LV5FU2 interrupted on 05/29/2019.

Early PET-CT evaluation on 03/21/2019 found complete remission (Figure 3).

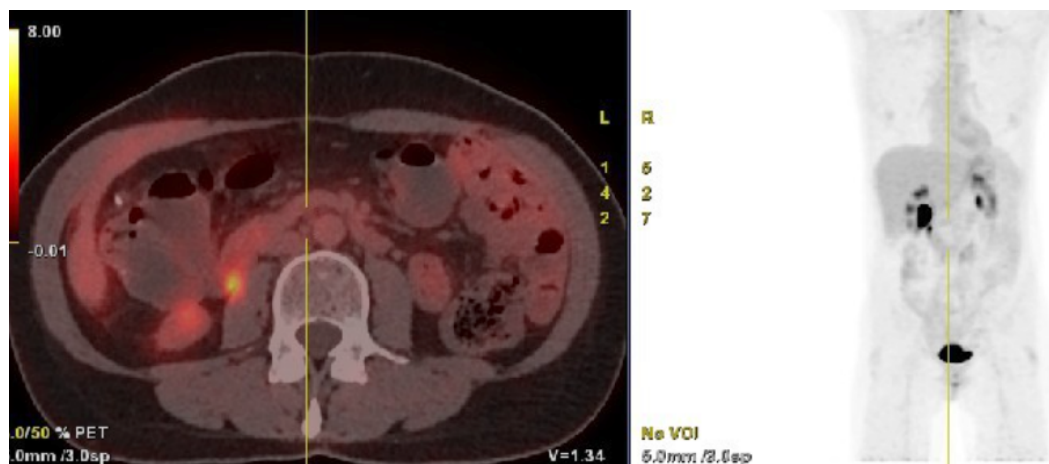


Figure 3: PET-CT of March 2019 showing early complete response

The examinations were normal until December 2020 or it appeared an infracentimetric retroesophageal node with a SUV max of 5.

A close follow-up on 01/03/2021 found a morpho-metabolic progression and a biopsy under EBUS confirmed the progression of colonic origin (Figure 4).

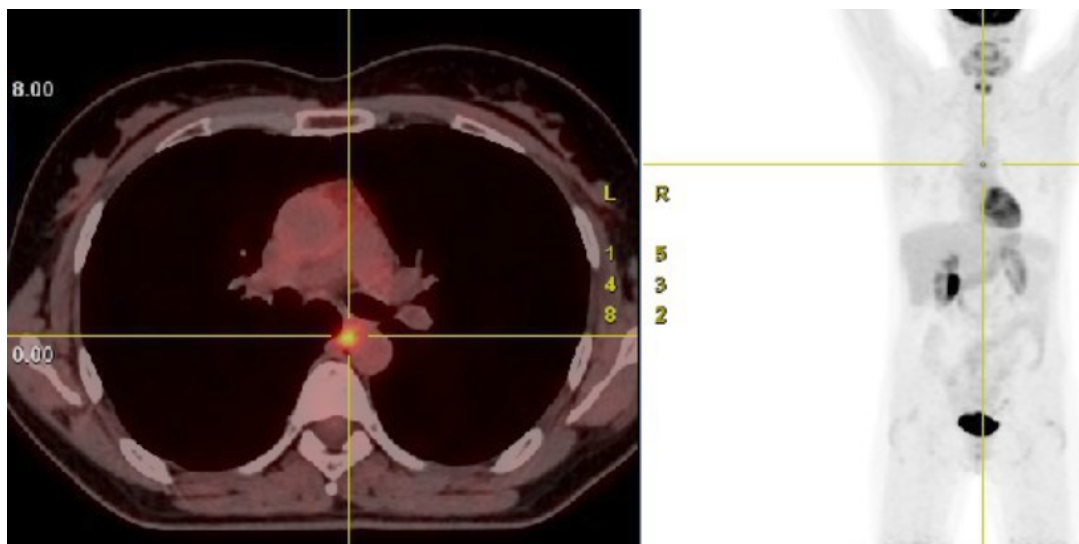


Figure 4: PET-CT of March 2021 finding infracentimetric retroesophageal node

FOLFIRI regimen was administered on 03/05/2021 with poor tolerance for three courses followed by three courses of LV5FU2 with concomitant irradiation of the retroesophageal lymphadenopathy at a dose of 55 Gy in 25 fractionations of 2.2 Gy from 07/06/21 to 13/07/21. Chemotherapy was discontinued on 07/12/21.

Tolerance was excellent with no toxicity of grade 2 or more related to radiation therapy (Figure 5).

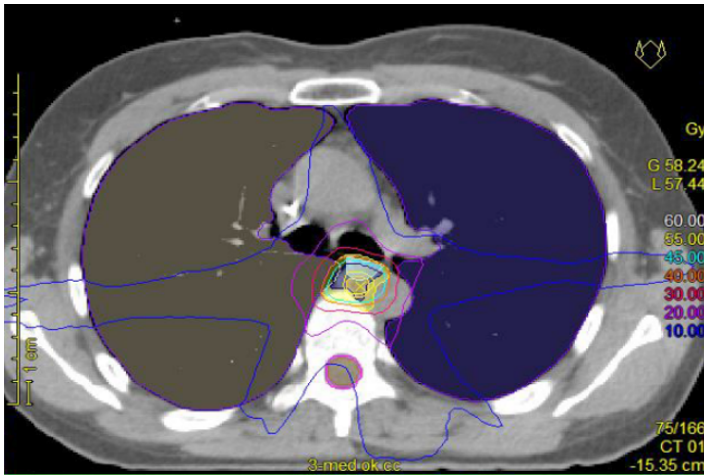


Figure 5: Radiation planning of retroesophageal treatment

The patient is still in complete remission one year later with a normal PET-CT done in december 2022.

Discussion

Radiotherapy in this oncological setting allowed sterilization of the initially involved lymph node sites.

An oligoprogression almost 2 years later was treated with only 3 months of chemotherapy and radiotherapy which again allowed a durable tumor control over time and a major quality of life for the patient who presents a 90% performance status almost 4 years after the onset of the disease.

This result is all the more interesting since there is a BRAF V600E mutation which is a poor prognostic factor in the studies.

The median progression survival after first-line treatment in the BEACON trial was 9.3 months with Encorafenib and Cetuximab [6].

This type of approach should be discussed more often in multidisciplinary tumor boards.

Benny Johnson et al. [7] published a study of 65 patients with para-aortic and/or mesenteric lymph node involvement treated in the United States with chemotherapy, radiotherapy at a dose of 50 Gy followed by lymph node dissection with intraoperative radiotherapy to deliver an additional dose of 12.5 Gy. With a follow-up of 77.6 months, 40% of the patients did not develop distant recurrence and are still free of recurrence.

Compared to this approach, ours was less invasive including only external beam radiotherapy and chemotherapy.

The extent of lymph node involvement did not suggest treatment under stereotactic conditions. A prospective cohort was published in this oligo metastatic setting with superior outcomes for lymph node involvement versus visceral involvement (hepatic and lung metastases mainly). In this series, local control at 1 year

was 90% for lymph node irradiation versus 75% for visceral lesions [8].

It is the same reasoning for the surgical approach, here the involvement was multiple latero-aortic, inter-aortico-cava. The surgical approach when it is feasible, can bring an interesting benefit but its positioning is difficult and more invasive. A recent review finds a potential benefit in certain situations without being able to establish recommendations [9].

Conclusion

It is important to leave room for the discussion of radical treatments such as surgery or radiotherapy in situations of isolated distant lymph node.

To date, no systemic treatment or targeted therapy can permanently sterilize macroscopic tumor cells outside of immunotherapy in this situation.

A combined approach is very promising for the therapeutic management of these patients.

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