Autologous Therapeutic Vaccine For Stage IV Metastatic Colon Cancer: A Case Report

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***Abstract*—This case report is of a 57-year old Caucasian male with a history of metastatic colon cancer to the liver failing multiple chemotherapeutic regimens. The addition of a novel autologous therapeutic vaccine (ATV) prepared from a hepatic metastectomy was employed as a last resort. The patient received 5 months of weekly ATV subcutaneous injections as his only form of therapy, and the tumor burden decreased. Additional chemotherapies, surgery, and radiation treatments were resumed after the 5-month ATV period to augment the possible immunological improvement from the ATV. Subsequently, the patient entered into remission. Based on this patient's outcome, ATVs could provide a new cell-based approach to augment the standard treatment of colon cancer.**

Introduction

This is a unique case of an ATV offering a therapeutic benefit in a stage IV colon cancer patient. One other such case has been documented with encouraging results.[1] The three year survival rate of stage IV colon cancer is 20.7%, a time scale which the patient has surpassed.[2]

Narrative:

Patient is a 57-year old Caucasian male with a family medical history of paternal grandfather with colon cancer, who died from leukemia. Further history is noncontributory (Surgeries, Social, Medications, past medical history). Patient was asymptomatic with colon cancer which was found on routine colonoscopy in September 2017. Patient was diagnosed with sigmoid colon adenocarcinoma categorized as grade 2, stage IV and KRAS/BRAF wild; microsatellite status MS stable with metastases to both lobes of the liver identified on PET scan. Tumor markers indicated progressive colon cancer with CEA elevated at 17.1 ng/mL and CA19-9 elevated at 180 U/mL (normal range: 0-3 ng/mL for CEA and 0-37 U/mL for CA19-9)[3] Patient underwent robotic-assisted left colectomy, and follow-up exploratory laparotomy which demonstrated hepatic bi-lobe involvement. Prior to ATV therapy the patient received three rounds of chemotherapy (mFOLFOX + Avastin, mFOLFOX6, FOLFIRI + Avastin), two Yttrium radioembolization (Y90), and one CT-guided radiofrequency ablation. During this time, imaging with MRI and PET/CT showed initial improvement in lesions of the liver, which later became unresponsive to therapy. Liver resection was scheduled, and intraoperatively abandoned after it revealed diffuse bi-lobe spread of metastases to multiple liver segments (2, 3, 4A, and 4B). Metastasectomy of liver segment 2 was performed and sent to Rutgers-NJMS for preparation of an experimental stage IV colon cancer ATV. After the failed resection, the patient was informed that there was nothing further the original oncology team could offer him, and he was referred to a tertiary cancer care center at Cleveland Clinic for further management.

During the 5-month period between Jan. 2019 and May 2019, the patient stopped all other cancer therapies and received only the ATV as a weekly 0.5cc subcutaneous injection in either shoulder for a total of 22 doses. After 5 doses of the ATV, labs showed an 83% drop in CEA from 3 to 0.5 and a 64% drop in CA19-9 from 150 to 54. After the initial drop in tumor markers, these markers began to gradually increase. A complete trend of CEA and CA19-9 are shown in figure 1. Imaging was generally favorable during this time period. After 7 doses, PET showed an overall decrease in tumor activity. After 13 doses PET showed slightly increased FDG uptake, and after 18 doses MRI showed no discrete mass or lymphadenopathy. There were complications of biloma, pancreatitis and ascites during this period likely secondary to the failed liver resection.

Cancer therapies were resumed after the ATV protocol was finished. The patient received a non-curative right lobe hepatectomy in June 2019, and tumor markers continued to trend upwards. In Nov. 2019 he received 1.) A biliary leak repair, biloma repair, and third Y90. The patient was informed that he was in remission in Dec. 2019. Vectibix and Irinotecan were started shortly after, and tumor markers trended down for nine months. Subsequent genetic analysis detected a tumor mutational burden greater than 10 Muts/Mb (meaning the tumor transformed into a more benign form) and the patient was switched to long-term Keytruda immunotherapy. Throughout the post-ATV time period, imaging was positive suspicious lesions and lymphadenopathy, but largely indeterminate of new neoplastic growth vs infectious/reactive changes secondary to liver/abdominal complications. The most recent MRI in Aug. 2021 showed shrinking lesions along with mildly increased tumor markers. There were a number of complications during this time; a lung right lower lobe thoracotomy was performed because of necrosis of the right lower lobe secondary to a chylothorax, likely a complication of a prior ventral hernia repair. At the time of publication, the patient has remained in remission and showed significant improvement in overall quality of life, inclusive of being able to return to prior occupation.

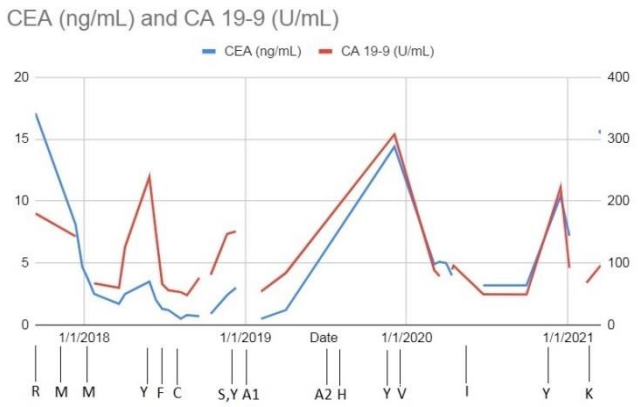

Figure 1: Trend of CEA and CA19-9 showing response to treatment events.

R = Robotic-assisted Colon resection; M = mFOLFOX; Y = Yttrium radio embolization; F = FOLFIRI; C = CT-guided radiofrequency ablation; S = Metastasectomy of Liver segment 2; A1 = ATV started; A2 = ATV ended; H = hepatectomy of right lobe of liver; V = Vectibix; I = Irinotecan; K = Keytruda.

Discussion

The patient, treating physician, original cancer treatment team, tertiary cancer center, and the immunology team all agree the ATV played a role in improving the patient's prognosis. For evidence, the authors reiterate the extensive number of therapies which failed to remit the cancerous lesions including; 1 colectomy, 2 exploratory laparotomies, 9 total months of chemotherapy, 2 Y90 and 1 radiofrequency ablation. Despite over a year of therapy, the tumor markers had started to increase and the patient was clinically worsening. The patient was informed there were no further treatment options that the original care team could provide, and he was referred to a tertiary cancer care center at the Cleveland Clinic. The patient started to improve during the five months of ATV administration. After 5 weeks of ATV treatment, there was a significant reduction in the tumor markers. The authors were unable to conclude that the tumor marker reduction was solely from the ATV, because there was a Y90 procedure performed 1 week prior to ATV start, which may have confounded the evidence of an ATV response. Y90 is seen as a confounder because the graph shows coincidental dips in tumor markers after each Y90. Imaging was supportive of tumor response to ATV, because an MRI with and without contrast at the end of the vaccine course showed no discrete mass or abdominal lymphadenopathy. However, monitor tumor lesions on further imaging was indeterminate with infectious/reactive etiology. The hepatic lobe resection and multiple abdominal complications such as chronic biloma, biliary leak, bilateral hernia repair, and thoracotomy, likely resulted to some extent of infectious/reactive changes within the abdomen. Nevertheless, the indeterminate imaging may prove inconsequential because the indeterminate lesions are resolving, regardless of etiology, as shown in the most recent MRI from summer 2021 reduction of prior lesions.

The Rutgers-NJMS Immunology team as trialed ATVs with other diseases such as HIV/AIDS, Laryngeal papilloma, and osteosarcoma. The use of ATVs in metastatic colon cancer shows similarities in natural history when compared with other diseases studied with ATVs. For instance, a previously published case report by authors demonstrated the efficacy of ATV in Laryngeal Papilloma.[4] Authors went on to use ATVs in an open trial with 80 children.[5] 90% of laryngeal papilloma patients treated with ATVs did not have disease recurrence (unpublished data). In laryngeal papilloma, it has been the immunology team's observation that the body takes about 5 doses (5 weeks) to start showing a therapeutic benefit - as occurred in this patient's clinical course, based on tumor markers.

The authors are hopeful that the indeterminate findings on imaging after the ATV period are a result of infectious/reactive changes. However, the possibility should be considered that findings on imaging are from a re-emergence of neoplastic growth after a clear MRI on 05/2019. A neoplastic consideration offers a chance to discuss a nascent theory that has emerged from the study of ATVs on disease processes - that is, the sustained effectiveness of the vaccine is inversely proportional to the rate of pathologic replication. For instance, the laryngeal papilloma is a slow growing tumor, and after 15 doses, the treatment is 90% effective at treatment and preventing relapse. However, colon cancer and HIV replicate quickly. In studying HIV and ATVs, the authors saw that ATVs offered a survival benefit to AIDS patients (in the period before effective antiretroviral therapies (ARTs)).[6] However, the ATV cohort was subsequently put on ARTs, and in tracking the cohort over 25 years, those that had responded now required ARTs just as someone with HIV who never received the ATV. Therefore, if neoplastic growth is assumed on imaging, then ATV's effect on colon cancer may be similar to its effect on HIV in that an initial improvement is seen, but not sustained without continued ATVs. However, the most recent imaging from 08/2021 showed resolving lesions without the use of continued ATVs, a finding which would need to be rectified with further study.

There were no side effects of this treatment beside injection site tenderness. The patient remains in remission and has shown significant improvement in overall quality of life, inclusive of being able to return to prior occupation. Four years have passed since the patient's initial diagnosis, far surpassing the expected outcome for this condition (3 year-survival rate =20.7%). The authors are hopeful that the patient will continue to remain an outlier for the 5-year survival rate of 10.5%.[2]

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