

Case Report

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Multilineage Cytotoxic Treatment for Advanced Colorectal Cancer in Nonagenarians

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Abstract

Decision making in older cancer patients is challenging. We present the case of a fit 90-year old patient with advanced colorectal cancer, focusing on the dilemmas we faced during multilineage systemic treatment. Although chemotherapy can be effective and tolerable in nonagenarians, current evidence on how to identify patients who will benefit from treatment is limited.

Keywords: Chemotherapy; Dilemmas; Lymph node

Introduction

Approximately 50% of patients with colorectal cancer (CRC) are \geq 70 years old and close to 35% is even older than 85 [1,2]. Although fit elderly patients benefit from systemic cytotoxic treatment, they are less likely to be offered standard treatment [3]. We present the case of a 90-year old patient with advanced CRC, focusing on the dilemmas we faced.

Case Presentation

A 90-year old male with a history of atrial fibrillation and angina pectoris was diagnosed with metastatic CRC (mCRC). There were diffuse liver metastases and a pathologically enlarged paracaval lymph node. Carcinoembryonic antigen (CEA) was 16 ug/L (reference \leq 5 ug/L). He had a Karnofsky performance score (KPS) 4 of 80%. Besides mild anemia the blood count and kidney function were normal and the liver enzymes slightly elevated. The patient lived alone, was independent in Activities of Daily Living (ADL) and only needed help from his support system for shopping and meal preparation.

Dilemma

Will this patient benefit from systemic therapy? If so: should he receive combination chemotherapy in standard dosage?

Systemic therapy in nonagenarians with advanced CRC: Data on nonagenarians treated with chemotherapy are scarce. Elderly patients are underrepresented in most clinical trials and populations are highly selected [4]. There is evidence that selected nonagenarians can receive the full array of oncological treatments [5]. However, frail elderly patients may suffer from increased toxicity of cytotoxic treatment, due to a progressive reduction of organ function reserves associated with ageing [6]. While no data are available that combination chemotherapy in the elderly should be withheld, elderly patients are less likely to

receive initial doublet chemotherapy, and a sequential treatment approach is more often used [7,8]. Overall, they are less likely to receive oxaliplatin and irinotecan during the entire treatment course [9]. A recent population based study in elderly patients with mCRC showed that only 28% received first line chemotherapy. Of these patients 74% received single-agent fluoropyrimidines [1].

Continuation of case presentation

After multidisciplinary evaluation and deliberation with the patient and his support system, we started treatment with dose escalating capecitabine. He was successfully treated with capecitabine at a dose of 1250 mg/m² twice daily on day 1-14 every three weeks. At follow-up there was regression of liver metastases and CEA below 5 ug/L. After 6 months he unfortunately developed grade 3 palmarplantar erythrodysesthesia (hand-foot syndrome). Capecitabine was discontinued and his symptoms resolved. Five months later there was progressive disease (PD) of liver metastases, paracaval lymph nodes and a new lung nodule. CEA had risen to 10 g/dL. Capecitabine was re-introduced at a lower dose (75% of original dose) without any toxicity. Evaluation after 3 months showed disease regression. Seven months after reintroduction of capecitabine he felt more fatigued and experienced some weight loss. CEA had risen to 36 g/dL and a CT scan again showed PD. He was motivated for further treatment and had a KPS of 80%. He did experience worsening of short time memory, while no other abnormalities were found.

Dilemma

Should we switch to second line chemotherapy or supportive care?

Decision making in geriatric oncology: In medical oncology, treatment decisions are based on clinical judgment and performance scales. In older patients, these scales are not as sensitive as in the adult population, because comorbidity is not thoroughly taken into account [10-12]. Multidisciplinary discussion and submission to a comprehensive geriatric assessment (CGA) can help because of their

ability to detect disabilities and comorbidity. Although there is no consensus on a standard CGA, chemotherapy regimens are modified based on CGA in 21-48% [13]. With increasing survival, more patients with advanced CRC will receive second and third line treatment, but elderly patients in general receive less second and third line chemotherapy compared to younger patients with cancer [4,7]. The South Australian Clinical Registry for mCRC documented that only 35% of patients aged ≥ 80 years went on to receive second line treatment versus 53% of younger patients [1].

Continuation of case presentation

Our patient underwent a CGA. It showed some short memory difficulties, but other cognitive domains were undisturbed (Mini Mental State Examination 25/30). There were no new comorbidities. He was ADL-independent (Katz Activities of Daily Living Scale 6/6), but dependent for taking medication, meal preparation and grocery shopping (Lawton Instrumental Activities of Daily Living Scale 5/8). Despite a good appetite he had lost 5 kg in the previous months (Mini Nutritional Assessment – Short Form 9/14). We discussed the results with our patient and his support system and decided to start second line treatment with irinotecan after arranging home care. 50% of the indicated 3-weekly dose was administered the first cycle, with intention to increase if well tolerated. Although the first treatment cycle was well tolerated and no overt irinotecan toxicities occurred, he became ADL dependent. Most likely this was caused by disease progression (further increasing CEA to 38 g/dL) and temporary absence of his most devoted family caregiver. Because of this deterioration and the indication of disease progression at a 50% dose of irinotecan, we proposed to stop further treatment, which was accepted by the patient and his support system. Our patient died two months later, 24 months after initial diagnosis with advanced CRC.

Discussion

Chemotherapy is the treatment of choice in advanced CRC. Although it is often hampered in the oldest old, chemotherapy can be effective and tolerable in nonagenarians. We can treat the oldest old with chemotherapy, but the question remains: Should we? Age cannot be a reason to exclude patients from the possible benefit of cytotoxic agents. However, older patients are less willing to accept toxicity and although median survival of a 90-year-old is still over 4 years, the population of nonagenarians with cancer is frail and median survival of nonagenarians with cancer is reduced to 1.7 years [5,14]. The small amount of evidence available for this group of patients makes you wonder whether we are ready to treat cancer in nonagenarians. When treatment is given it is important to prevent toxicity. CGA can be insightful and a good basis for discussion between medical oncologist and patient concerning systemic treatment, but there is no clear evidence that it can predict toxicity. Therefore, prospective studies on biology-based diagnostic tests and their predictive value of toxicity are needed.

What was Known on this Topic?

Nonagenarians with advanced CRC are not often treated with chemotherapy, and although there is only a small amount of evidence available, it can be effective and tolerable in this patient group.

What does this Add?

Treating selected nonagenarians with colorectal cancer with multilineage chemotherapy and acceptable treatment toxicity is possible. In selecting patients, CGA can be insightful and a good basis for discussion between medical oncologist and patient.

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