

War and peace? The oncologic and the palliative care perspective on personalized cancer treatment in a patient with advanced cancer

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Summary Personalized cancer treatment utilizing targeted therapies in a tailored approach is based on tumor and/or patient-specific molecular profiles. Recent clinical trials continue to look for new potential targets in heavily pretreated patients or rare disease entities. Careful selection of patients who may derive benefit from such therapies constitutes a challenge. This case report presents an experimental personalized cancer treatment in an advanced cancer patient and provides a list of issues for discussion: How can we combine treatment goals and simultaneously meet the individual needs in advanced cancer reconciling both perspectives: oncology and palliative care?

Keywords Medical oncology · Molecular targeted therapy · Neoplasms · Palliative care · Terminal care

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Introduction

Personalized cancer medicine is searching for effective treatment strategies by acting on the individual tumors' immunological and/or metabolic features in an attempt to cause fewer side effects and better outcomes as compared to standard treatments [1]. By targeting an essential tumor pathway, shrinking of tumor masses can be achieved, as shown e.g., with imatinib against gastrointestinal stromal tumor (GIST). Personalized medicine might offer a chance for disease stabilization even in advanced tumor stages and pretreated patients. At some point however, patients might not derive further benefit from systemic antitumoral therapy. Identifying this time-point represents a major task for oncologists and palliative care specialists. Several questions arise when caring for patients with advanced diseases: (1) How and when should clinicians responsible for cancer treatment cooperate with those responsible for palliative care? (2) How do we advise and support patients with very limited life expectancy? (3) How do experts of different fields deal with the theme of realistic hope and death? It appears mandatory to address these questions from different perspectives early on when dealing with patients suffering from heavily advanced diseases.

Here, we report on a young patient suffering from terminal urachal cancer and discuss these questions from different perspectives.

Case report

A 28-year-old male patient with urachal carcinoma of the small pelvis with hepatic, lymph node, and pulmonary metastasis and peritoneal carcinosis was transferred from a community hospital to the Medical University of Vienna in March 2013.

He had been diagnosed with urachal carcinoma of the rectum in November 2012 and had previously undergone surgery with resection of the primary tumor, liver metastases, and subsequent colostomy. Between December 2012 and January 2013 he had received one course of gemcitabine and cisplatin without clinical benefit. Subsequent treatment consisted of two courses of cisplatin and 5-fluorouracil, which however also failed to prevent rapid disease progression.

A magnetic resonance imaging of the small pelvis done upon admission at the Medical University showed disease progression with infiltration of the coccygeal bone, the obturator muscle, and the left ureter with hydronephrosis grade two, progression of liver metastasis and peritoneal carcinosis. As the patient presented with extensive gastrointestinal discomfort and vomiting, a computerized tomography (CT) scan was performed confirming mechanical obstruction. Because of grade 4 thrombocytopenia and poor performance status, a multidisciplinary team came to the conclusion to offer a colorectal stent rather than immediate surgery. However, due to rapid clinical deterioration, an ileostomy had to be performed as an emergency procedure three days later.

After recovery from surgery, the patient received the first cycle of FOLFOX-6, based on encouraging results from published case reports [2]. However, he required antimicrobial therapy only seven days later due to neutropenic fever. After recovery and normalization of blood cell counts, the patient underwent palliative radiotherapy for pain of the small pelvis (11 fractions, 30 Gy GHD, 3 Gy single dose), which had to be discontinued early due to deep-vein thrombosis and pulmonary embolism.

While the patient reported on a short interval of pain relief after radiotherapy, the clinical situation got further complicated by increasing respiratory compromise. A patient-controlled analgesia infusion pump (PCA-pump) with hydromorphone was initiated.

Further treatment options were discussed with the patient. As no standard of care has been available, the decision was made to follow an experimental approach using molecular signatures from tumor material collected during emergency surgery. Histological and molecular pathological testing of omental tumor tissue had shown *K-RAS* mutation and *BRAF*-mutation, while *N-RAS* mutation or *Her-2/Neu* amplification were not found. In addition, immunohistochemistry had revealed high expression for *C-MET* and *ALK* translocation. Based on these findings, the oral c-MET and Alk-inhibitor crizotinib was considered a potentially promising strategy. Findings and therapeutic recommendations were discussed with the patient, who then gave informed consent to this treatment. However, therapy had to be administered via a nasogastric tube because the patient had meanwhile developed chronic subileus caused by carcinosis. Following treatment initiation, it was the wish of the patient and his relatives to be discharged with support of a mobile palliative care team.

After a short time at home, the patient had to be readmitted because of bleeding from the ileostoma and renal

failure. Transfer to the palliative care unit was discussed. However, the patient preferred to remain in the oncological ward with staff whom he was familiar with. Two days later symptoms worsened: The patient got breathless. Based on the recommendation from the palliative care team, the PCA-pump was switched to a syringe driver, crizotinib treatment was discontinued and palliative sedation was initiated after discussion with the patient. Mr. E. died in the presence of his fiancée and his mother.

Discussion

Kairos (καῖρός) is an ancient Greek word meaning the right or opportune moment. The transition from life-prolonging care to palliative care might be an area where views of different medical teams may heavily diverge. From an ethical perspective, it is the responsibility of the medical staff to express appreciation for each person. However, every medical discipline takes that into account within its own perspectives.

Novel agents have led to a paradigm shift in medical oncology. These new strategies may be even more successful in the future by using treatments based on the molecular signature of a tumor. In this context, personalized medicine is currently in a crucial phase of development. Human nature is motivated to support what is the current topic [3]. As long as treatment options exist, it may prove challenging for health care teams to switch the focus from cure to care. This is particularly true when the patient is young and when experimental treatment has just been initiated. With the rapid development of targeted agents, this issue will become increasingly important in the future.

Progression of advanced disease causes a vulnerable time in the lives of patients and their caregivers. Key signs of progressive disease, such as deterioration of performance status and increasing symptoms might stimulate involvement of the palliative care team. In contrast, optimistic patients and caregivers might encourage oncologists to pursue active treatment.

The discontinuation of inappropriate medication is a core topic of palliative care, whereas from an oncological perspective, some may argue that treatment should be continued as long as options exist. Moreover, preserving hope [4] is a common attitude of physicians involved in life-threatening diseases. “Why not stopping something if the outcome might be marginal?”, says the palliative care physician. “Why not continuing treatment, if there is nothing left to lose?”, says the oncologist.

Two prerequisites exist for starting anticancer treatment: first, treatment needs to be indicated; second, the patient needs to give informed consent. In this context, patients often—though not always—desire information on their expected survival [5]. Due to the lack of data and unpredictable outcomes, decisions to initiate treatment in the context of far advanced diseases are difficult. Advances in oncology may not always translate into improved survival. Fojo et al. [3] reported that approved

therapies for solid tumors between 2002 and 2014 gained modest effects in progression-free and overall survival of only 2.5 and 2.1 months, respectively. It has been commonly accepted that medical care is considered futile when an intervention is not expected to produce its desired physiologic effect [6]. However, this can be perceived in different ways. Some patients might consider this period as worthwhile for continuing treatment while others might expect much more survival time [7]. In the case of experimental treatments, success or failure are difficult to measure. When the clinical condition gives the impression that little can be gained, one should remember that “not to act” and to discontinue treatment is also a worthwhile option. Distress associated with serious illness emphasizes the need of communicating risks and benefits to patients and their relatives. Enabling patients to live to the maximum of physical ability, relationships, and preservation of personal choices are the goals of end-of-life care [8]. Decision making might be difficult by conflicting goals among palliative care physicians and oncologists [9].

In this patient, there were many discussions about the right time to discontinue antineoplastic treatment. The oncological approach was that the patient might still benefit from treatment, even if the disease is no longer curable. The palliative approach was to provide best supportive care and to maximize quality of life in a terminally ill patient. In this context, it is crucial to define what “palliative treatment” actually means? Palliative antineoplastic therapy at the end of life has to be distinguished from end-of-life care. It is difficult to estimate when to stop one in favor of the other. We may need new terms to distinguish potentially life-extending palliative antineoplastic treatment from palliative care and end of life care. In this context, the question arises as to whether “*end of life boards*” should be established in addition to conventional tumor boards.

Delivering information on an experimental therapy is challenging. Strasser et al. [10] defined seven practical steps for decision making in favor of invasive palliative interventions: priority, price, probability, prognosis, progression, prevention, and preference. A possible improvement of quality of life (QoL) by tumor therapy is difficult to study. The idea of QoL has become a kind of umbrella under which many different indexes are placed dealing with whatever the user wants to focus on [11]. Health care workers certainly make decisions based on reflection, an individualized and reasonable approach. Sometimes however, they might hide behind their proposed therapeutic options to procrastinate an end of life discussion [12]. A strong therapeutic cooperation was shown to be associated with improved emotional acceptance in patients with advanced cancer and terminal disease, and with decreased intensive care admission [13]. There is still the cliché that the oncologist is the fighter against death while the palliative care physician is the one accepting death. The end-of-life phase certainly is an intimate process where the inner life of physicians may play an important role [14]. A positive influence in the

course of advanced diseases requires strong cooperation among health care workers.

A common statement in palliative care is to hope for the best and prepare for the worst [15]. Thus, health care workers in oncology need to strongly communicate and cooperate rather than hiding behind the “gold standard” of their individual disciplines. Raising the bar for clinical trials by defining clinically meaningful outcomes appears essential in the comprehensive care of cancer patients [16]. Cheryn et al. [17] concluded that biologically personalized therapeutics should be combined with truly personalized medicine. Preparing for the worst does not mean giving up.

In conclusion, this case report shows the complexity of advanced oncological diseases. In general, it is difficult to say what is right and what is wrong. War and peace might stand as a symbol for fighting and letting go, both being part of the course in advanced disease. Patients can only benefit if we combine the maxims of our respective disciplines.

Conflict of interest

The authors declare that there are no actual or potential conflicts of interest in relation to this article.

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