

Do We Need to Improve Oral Chemotherapy Adherence Monitoring? A Case Report of Temozolomide Overdose

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Abstract

Accidental overdose of chemotherapy is an infrequent situation; in particular for intravenous treatments, that have guidelines that strictly address their correct prescription, preparation and administration. On the other hand, the correct use of oral antineoplastic drugs is only marginally addressed. This fact can lead to medication errors and toxicities, sometimes with fatal consequences. We describe the clinical course of a 40 years old man, affected by neuroendocrine tumor, who assumed a double dose of Temozolomide because of a wrong read hand prescription.

Keywords: Temozolomide; Oncology; Oral; Chemotherapy; Overdose; Drug

Introduction

Over the past decade, the availability of oral chemotherapy medications has largely increased. These include classic cytotoxic chemotherapy and the newest small molecule, targeting specific enzymes or receptors involved in tumor growth and progression [1]. Oral chemotherapy offers several benefits for patients like easy and needleless administration, continuous and more homogeneous exposure to chemotherapy, improvement in quality of life [2-5]. Furthermore, unlike intravenous therapy, the responsibility of correct drug administration shifts from doctors and nurses, to patients and their caregivers [6] and as a consequence of this, should be an increase in medication errors and, consequently, in toxicities [4,6].

Case Report

Here we present a report of a 40-year-old man. In October 2012, the patient underwent an abdomen ultrasonography examination for persistent abdominal pain that showed a pancreatic mass.

In November 2012, a spleen-pancreatic resection was done and revealed Neuroendocrine Tumor (NET) G2. In December

2013, an abdomen ultrasonography showed multiple liver metastasis that were subsequently excised. The histologic exam revealed high grade neuroendocrine neoplasm (G3). In March 2014, as result of liver progression, he started first line therapy with Cisplatin+Etoposide for 6 cycles, with stable disease till March 2016.

Then he experienced liver progression again and started second line treatment with Capecitabine (750 mg/mq/die from day 1 to day 14 every 28 days) and Temozolomide (200 mg/mq/die from day 10 to day 14 every 28 days); the treatment was well tolerated, with no toxicity of any grade.

According to the good clinical and instrumental response and the liver limited disease he was treated with Trans Arterial Radial Embolization (TARE). The restaging TC displayed the nearly disappearance of liver metastases, with persistence of only two nodules of 11 mm in S5 and 7 mm in S6.

In February 2017 after a multidisciplinary meeting, it was decided to restart treatment with Capecitabine plus Temozolomide (at the same dosage as before) awaiting to be able to repeat TARE.

At the beginning of cycle two his platelets were 33.000/ μ L so, considering the good tolerance in previous cycles, we asked the patients about the correct assumption of the drug. Because of a wrong read hand-written prescription, he assumed Temozolomide 200 mg/mq 2 times a day for 5 days, total dose 4000 mg. At 200 mg/mq, his total 5-day dose should have been 2000 mg; thus, he received 2 times the standard dose of the drug.

The patient was admitted to our hospital for monitoring on day 19 of treatment cycle; an hematochemical examination two times a day was planned.

On day 20 platelets were 13.000/ μ L so the patient was supported with an unit of platelet concentrate. On day 24 his white cell count (WBC) was 900/ μ L, absolute neutrophil count (ANC) 90/ μ L. Granulocyte colony stimulating factor (G-CSF) Lenograstim 33.6 MiU/die and prophylactic treatment with Ciprofloxacin was started.

On day 25 he developed fever of 40°C, associated to sore throat obtundation and confusion. The WBC was 450/ μ L, ANC

0/ μ L and platelets 13.000/ μ L. Another unit of platelet concentrate was transfused, besides *Streptococcus Pyogenes* bacteremia was identified by blood sample from central catheter and peripheral one. As indicated by infectivologist he was started on Piperaciline-Tazobactam 4.5 g every 6 h and Daptomicine 700 mg/die; besides Lenograstim was increased to two times a day.

He became afebrile on day 28, while he developed diarrhea that was successfully treated with Loperamide. On day 30 white cell count returned within normal limits and GCSF was interrupted. On day 33 platelets count was permissible (67.000/ μ L) to remove central venous catheter. The same day the patient was discharged with instructions to continue antibiotic therapy with Amoxicilline-Clavulanic acid three times a day for a week.

Two months after the overdose of Temozolomide a TC re-evaluation was performed with evidence of stable disease. A new TARE treatment has been scheduled.

Discussion

The use of oral drugs in the treatment of cancer implies the shift from doctors and nurses to patients and relatives of the medications management that means taking the right dose at the right time and under the right circumstances [6].

Non-adherence to oral chemotherapy agents, characterized by a narrow therapeutic window and generally considered by patients safer than intravenous treatments, may lead to an increased risk of toxicities, loss of treatment efficacy, increased utilization of health care resources and consequently increased healthcare costs [7-10].

Since many years various organizations like American Society of Clinical Oncology (ASCO) and Oncology Nursing Society (ONS) have offered guidelines to address prescription, preparation and administration of chemotherapy, but only from the 2013 revision indications for safe administration and management of oral chemotherapy are available [11].

The Multinational Association for Supportive Care in Cancer (MASCC) developed and evaluated a teaching tool for patients receiving oral agents for cancer treatment, the MASCC Teaching Tool for Patients Receiving Oral Agents for Cancer (MOATT). This tool, which is available in several languages, represents a help for clinicians in identifying barriers to drugs adherence and provides suggestions for patient and caregivers education about correct storing, handling and assumption of the oral anticancer agent [12].

Medication errors can occur in all the phases of the prescribing, dispensing and administration continuum [4,11,13]; but from a literature review emerged that the most common medication error is wrong dose assumption [14].

Interventions to improve oral chemotherapy adherence are essential and they can be performed in all the phases of drug administration.

The prescription should be done *via* electronic order as for IV chemotherapy [1]. The patients should be informed (including

families and caregivers in the conversation) about the importance of adherence and the risks of non-adherence to the treatment. In any case, written materials (in particular Computer written) should always be provided to patients with oral instructions [9]. A multiple checking should be performed to be sure that the correct dose, days and drugs have been dispensed to patients [14]. Finally, the follow up may continue even at patients' home, with patients being called or visited by nurses to confirm that they know what, how and why they are taking oral chemotherapy [14-17].

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