Case report

Antiviral properties of antineoplastic drugs. From Herpes simplex-1 disappearance to a wide antiviral action: a serendipity case report

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Abstract. Herein we report the clinical case of a 46 year old female affected by lung cancer and cerebral metastases who showed, one month after the beginning of an oncologic therapy with vinorelbine and cisplatin, the complete remission of periodic (every 15 days) recurrences of herpetic mouth lesions. More than one year after the disappearance of the herpetic lesions, no further evidence of them were found. Subsequently, specific laboratory investigations, together with another case report that is presently in process, showed that vinorelbine, aside from its well known antineoplastic properties, also exerts a powerful antiviral action. (www.actabiomedica.it)

Key words: Herpes simplex, vinorelbine, cisplatin, antineoplastic, antiviral, serendipity

Introduction

The herpetic illness is a pleomorphic and multifactorial pathology which negatively engraves on the quality of life, which results particularly affected. The strategies of the treatment must take into consideration both physical and psychosocial aspects of the illness. Several molecules, with different pharmacodynamic and pharmacokinetic properties, are object of experimentation and clinical validation. A specific treatment plan must have the purpose of reaching a fast control of the illness together with its maintenance. In the reported case of HSV-1 infection, in the planning of a brief and long term control of the illness, the treatment with vinorelbine and cisplatin for antineoplastic purposes produced an unexpected complete long time resolution of the illness.

Herein we report a case of a 46 year-old female who, one month after oncologic therapy with vinorelbine and cisplatin for brain widespread of lung neoplasm, refers the complete remission of periodic (every 15 days) recurrences of herpetic mouth lesions in the past ten years. Two years after the fortuitous detection of the labial herpetic lesion disappearance, no further evidence of herpetic lesions was present.

Characteristics of used drugs

Vinorelbine

Vinorelbine is an anti-mitotic chemotherapic drug used for some types of cancer, including breast cancer and non-small cell lung cancer.

Vinorelbine is the first 5´NOR semi-synthetic vinca alkaloid. It is obtained through semi-synthesis from alkaloids extracted from the rosy periwinkle, *Catharanthus roseus*. In Europe vinorelbine is approved to

treat non-small cell lung cancer, breast cancer and, in some countries, prostate cancer. Since 2004 an oral formulation has been marketed and registered in Europe for the same settings. A similar efficacy and safety profile has been shown between both intravenous and per os formulations, avoiding local toxicity induced by the intravenous vinorelbine (1).

Cisplatin

Cisplatin is a platinum-based chemotherapic drug used to treat various types of cancers, including sarcomas, some carcinomas (e.g., small cell lung cancer and ovarian cancer), lymphomas and germ cell tumors. This class now includes carboplatin and oxaliplatin. Platinum complexes are formed in cells which bind and cause cross-linking of DNA ultimately triggering apoptosis or programmed cell death. Although cisplatin is frequently designated as an alkylating agent, it has no alkyl group and cannot carry out alkylating reactions. It is correctly classified as alkylating-like agent (2).

Case report

Here we present a clinical case of a 46 year-old female whose labial herpetic lesions were first discovered ten years before with a recurrence of every two weeks. At different times, consulted dermatologists always gave a diagnosis of Herpes simplex type A (3). During this decade she unsuccessfully underwent available antiviral therapy (4, 5). Recently she was suffering from a SCLC (small cell lung carcinoma) in a large bronchus and with metastatic cerebral solid masses; the patient therefore immediately began a first cycle of oncologic therapy, consisting in:

– CDDP (cisplatin) 50 mg/m^2/ev + VNR (vinorelbine) 30 mg/m^2/ev.

This cycle was successively repeated three times every 28 days and, successively, with oral vinorelbine 50 mg alone.

Only two weeks after the beginning of the oncologic therapy, the patient put in evidence, surprisingly, the lack of reappearance of herpetic labial lesions.

The patient continued her periodic oncologic treatment switched with radiotherapy. More than one year from the disappearance of herpetic lesions, no further clinical signs of the viral infection reappeared. Further virologic and immunologic analysis on the patient's blood revealed the complete disappearance of the several searched viruses. In fact, the PCR-RT performed for HSV-1, HSV-2, CMV, EBV, HHV-6, VZV and HHH-8 detection all gave negative results. Further immunologic investigation, made on the same patient, gave amazing results with positive values for CMV, HSV1-2, VZV, EBV relatively recent, infections.

Discussion

This complete resolution of the herpetic illness, in its singularity, represents an evaluable opportunity for clinicians to perform, in patients affected by viral infections such as HSV, CMV, HBV, EBV, VZV, clinical trials with vinorelbine (and/or cisplatin) in different dosages and formulations, in order to understand:

1. Which of the two drugs (even both) results effective in an antiviral therapy. (*A further parallel ongoing investigation on Hepatitis C resolution with vinorelbine treatment suggests vinorelbine as the drug possessing the best antiviral effects*).
2. What are the appropriate dosage levels of the presumed antiviral drugs that result effective in the antiviral treatment compared to the high doses used in the oncologic treatment.
3. What kind of drug formulation and administration way results effective and suitable for the antiviral resolutive purpose.

Although Snyder et al. (1987) firstly showed, in mice, an efficacy of platinum containing drugs in the treatment of in-vitro and in-vivo HSV2 infections, no further clinical evidences were published up to the actual clinical serendipity report on the resolution of an HSV1 infection and on the related broad antiviral spectrum surprisingly found (6).

Specific clinical studies are needed in order to give exhaustive answers to the several hypotheses raised after the complete disappearance of HSV 1 infection. Updates and hypotheses on the use of vinorelbine as an antiviral drug are suggested by another case of resolution presently under our critical evaluation, in which the treatment with vinorelbine for a chest tumour brought to the casual disappearance of the he-

patitis C virus in a 43 years old male patient who had been suffering from it for many years. Anyway, a phase II double blind randomized clinical trial is necessary to better understand the real antiviral efficacy of vinorelbine and cisplatin using them singly or in association.

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