
Dr Giunta’s letter to the editor reports on the use of an early intervention after an extravasation of a vesicant; he describes a technique whereby the placement of a subcutaneous canula in the extravasated region is flushed by a solution to decrease toxicity [1].

One of the determining factors of the extent of damage caused by extravasation is the concentration of the drug infused, and indeed by diluting the drug the damage may be decreased. However, several questions remain. First, was the wash-out procedure the only treatment given to the eight patients or did they also receive the conventional standard of care and therapy for extravasation [2]? If this is the case, it is difficult to draw firm conclusions about the technique. Secondly, the simple injection of a high volume of a solution could result in a decrease in the concentration of the extravasant, with a result similar to the wash-out procedure described by Giunta et al. [1]. An animal model might be used to test these two treatment options. However, the impact of extravasation of a vesicant on the patient is very severe, so all treatment options should be considered and the wash-out procedure might be a useful technique in the treatment of this complication.

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References

DOI: 10.1093/annonc/mdh272

Irinotecan chemotherapy associated with transient dysarthria and aphasia

Introduction
Irinotecan (CPT-11) is a semisynthetic derivative of camptothecin, an alkaloid extract from plants such as Camptotheca acuminata. It is a member of the topoisomerase I inhibitor class and exerts its activity by inhibiting DNA double-strand replication. The combination of irinotecan and 5-fluorouracil has become one of the most frequently used regimens in advanced colorectal cancer [1], and has shown to be active in several other solid tumors.

The principal toxicities of CPT-11 are a cholinergic syndrome (with acute diarrhea), delayed diarrhea, nausea and vomiting, and neutropenia. Other minor toxic effects include additional hematological toxicities (such as anemia, thrombocytopenia), alopecia, skin reactions, stomatitis and abdominal pain [2]. Dysarthria has rarely been described [3–5].

Case history
A 64-year-old man with a history of Crohn’s disease presented to our department with metastatic adenocarcinoma of the right colon. In January 2004 he received his first course of FOLFIRI chemotherapy (CPT-11 180 mg/m^2 i.v. on day 1 in a 60 min infusion, followed by 5-fluorouracil 1000 mg/m^2/day for two consecutive days) [1]. Premedication included dexamethasone, ondansetron and atropine. The patient had been receiving tramadol for pain as his only other medication. Within 30 min of initiation of the CPT-11 infusion the patient developed progressive dysarthria, which in a few minutes developed into frank aphasia. The treatment was temporarily stopped, and the dysarthria and aphasia were resolved within 15 min without the use of any medications. Complete neurological examination and a brain computed tomography scan were normal (Figure 1). The CPT-11 infusion was re-initiated and completed without any other acute toxic effects.

Figure 1. Normal brain computed tomography scan.
Discussion

An Internet-based literature search (Pubmed, Medline) revealed only three other reported cases in which irinotecan seemed to be correlated with temporary dysarthria [3–5].

The pharmacokinetics of irinotecan and its principal active metabolite, SN-38, are characterized by high plasma distribution due to its strong binding to plasma proteins and tissues [6]. In human subjects, no clear evidence of cerebrospinal fluid distribution has been demonstrated. In animal models, such as primates, the presence of this drug and its metabolites, such as other topoisomerase inhibitors (topotecan), have been found in the central nervous system (CNS) [7]. Nonetheless, the pathogenesis of irinotecan neurotoxicity has not been investigated thoroughly. Naranjo has developed criteria that estimate the probability that an adverse reaction can be due to a specific drug [8]. In this patient, as in the other three cases reported in the literature, the adverse event was most likely correlated to the irinotecan infusion.

The pharmacokinetics of irinotecan and its plasma levels should be more intensely studied because the tri-phase model of irinotecan elimination may explain a reaction in the first few minutes of infusion. In this case, however, the side-effects were observed after 30 min. The short duration and self-resolution of symptoms may be due to rapid clearance of the drug from the CNS.

Conclusions

This case history elucidates a rare, seemingly not dose-limiting and self-resolving toxic effect of irinotecan, which should be recognized by the medical oncology community given the increasing utilization worldwide of irinotecan.

References


DOI: 10.1093/annonc/mdh277