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Letter to the editors

Peripheral DTIC neurotoxicity: a case report

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Sir, DTIC has been available as a cytostatic agent since 1961 [10]. Nowadays, it is mainly used in the treatment of patients with melanoma [2], soft tissue sarcomas [5] and lymphomas [1].

The toxic effects of DTIC have been well described and include nausea and vomiting, myelosuppression, nephrotoxicity, phlebitis, flu-like syndrome, myalgias, and facial paraesthesias [8, 9]; neurological symptoms are less common and are mainly connected with central nervous system damage [3, 4, 7].

This report concerns one case of peripheral neurotoxicity temporarily associated with the administration of DTIC.

Case report

A male patient 70 years of age was admitted to hospital on 20 March 1982, for surgical removal of a cutaneous malignant melanoma of the left mandibular region (5th Clarke level). In June 1984, pulmonary metastases appeared and a DTIC chemotherapy treatment (300 mg/m^2 i.v. daily for 5 consecutive days) was carried out; the only side-effect recorded was grade 1 (ECOG scale) gastrointestinal toxicity. On 23 July 1984, the patient started his second course of DTIC treatment and, on 8 August 1984, developed pain in the left leg, ataxic gait and reduced muscular strength in both legs. Neurological findings related to the lower limbs were characterized by distal impairment of all kinds of sensations, with cutaneous sensory impairment of the stocking type, mild ataxia which became worse when the patient closed his eyes, weakness, muscular hypotrophy, and reduction of the deep tendon reflexes. A physical examination did not reveal any defects other than neurological impairment. The patient's history did not include chronic alcoholism, previous exposure to neurotoxic chemical agents or use of other drugs. Blood chemical analysis revealed only a slight increase in gamma glutamyltranspeptidase and alkaline phosphatase levels. Bone scan and total-body computerized tomography scan were negative (except for the previously known lung metastases).

A clinical diagnosis of polyneuropathy of unknown cause was thus made and conventional treatment was administered, resulting in a slow improvement. On 22 August 1984, a third DTIC course was started, and on the third day of this treatment the patient was found to have suffered a further loss of strength in his legs. The electrophysiological findings were characterized by signs of peripheral neuropathy in the lower limbs, i.e. by fibrillation potential and by high-frequency bizarre discharges, by a decrease in the voluntary recruitable motor unit potentials, by a slight reduction of motor and sensory velocity conduction, and by a decrease in the motor and sensory evoked potentials. These data indicated prevalent axonal damage. DTIC administration was thus discontinued and a treatment with gangliosides (20 mg daily i.m.) and vitamin B_1 (900 mg daily p.o.) and physiotherapy were given. At the end of October 1984, the patient showed a complete neurological recovery, with negative electromyogram. The patient died on 21 September 1985.

Discussion

Neurotoxicity is a well-known side-effect of many anticancer drugs [6, 11], but to our knowledge there seems to be very little evidence of this effect with DTIC. In the case described in this report it seems that the neurological symptoms were linked with DTIC administration, because of the direct connection with the infusion of the drug and with its discontinuation. Moreover, the patient showed neoplastic progression after the withdrawal of DTIC, without any evidence of neurological symptoms.

In spite of the extensive use of DTIC, no similar reports have been found in the literature; consequently, a particular individual susceptibility to DTIC or hypersensitive reaction cannot be excluded.

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