Liposomal cytarabine in leptomeningeal carcinomatosis from primary brain tumors.

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Neoplastic meningitis (NM) is diagnosed in 1%-2% of patients with primary brain tumors. All primary brain tumors may progress to leptomeningealcarcinomatosis. In particular posterior fossa tumors carry a particularly high risk for leptomeningealmetasteses (Chamberlain, 2008).Treatment of the meningeal disease is problematic because so few anticancer drugs attain therapeutic concentrations in the CSF when administered by the intravenous route. Depocyte® is an injectable, sustained-release formulation of the chemotherapeutic agent, cytarabine. In this report, we describe data on efficacy and tolerability of an intrathecalDepocyte® regimen for patients presenting with NM from primary brain tumors. All the patients were treated with repeated courses of intrathecalDepocyte® by lumbar puncture, with concomitant dexamethasone and antibiotic prophylaxis. Depocyte® 50 mg was injected once every 2 weeks for 1 month of induction therapy. Responding patients were treated with an additional 3 months consolidation therapy. Twelve patients (10 males and 2 females) who had a diagnosis of NM from a primary brain tumor and were treated at the onset of NM with intrathecalDepocyte® in the Neuro-Oncology Unit of our Institute were described in this study. In all cases, intrathecalDepocyte® by lumbar puncture was administered (in 4/12 patients this treatment was concomitant to a systemic chemotherapy). The total number of Depocyte® cycles ranged from one to nine (with a median of four). Unfortunately, in three patients only one cycle of Depocyte® was administrated due to a rapid disease progression. In six patients, a clinical improvement of symptoms was described after two or three cycles of treatment, whereas in 5/12 patients, there was a stable disease after three cycles of treatment; ss CSF is concerned, in 4/12 patients, a negativization of neoplastic cells detection was achieved after at least three cycles of treatment. In other 5/12 patients, a cells reduction was seen, as well as a protein reduction. Toxicity was moderate and transient, mainly due to the lumbar puncture procedure. The major adverse events were headache (in 11 % of cycles, 90 % were grade 1 or 2) and back pain (in 19 % of cycles). The prognosis of NM is very poor, especially in patients with a NM from systemic cancer. The majority of the patients described in the present report have a diagnosis of medulloblastoma, however, some peculiar cases are described as well, such as germinoma in two cases that responded particularly well to treatment, with CSF and MRI normalization. The small number of patients and the presence of very heterogeneous tumor types in our study is insufficient to lead a conclusion about TTP or OS; in particular 2/12 patients are alive at the moment; in this report, it is not possible to conclude that the increase in OS is related to the treatment, however, our preliminary data indicate a median OS of 180 days (range 20–300 days). These data could indicate a better prognosis of NM in patients with a primitive brain tumor in comparison with patients with NM from systemic tumors (Partap et al., 2011; Passarin et al., 2010). As side effects are concerned, in our series of patients only one experienced a probable chemical arachnoiditis, that was, however, manageable with high dose corticosteroids. In the other patients described liposomal cytarabine was easily administered and well tolerated with only a moderate and transient toxicity, mainly due to the lumbar puncture procedure. These data are comparable to results reported in literature.

Chamberlain (2008). Oncologist. 13, 967-77.

Partap et al. (2011). J Neurooncol. 103, 561–6.

Passarin et al. (2010). J Neurooncol. 97, 439–44.