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Letters to the editor

Friedreich's ataxia and intrathecal chemotherapy in a patient with lymphoblastic lymphoma

Friedreich's ataxia (FA) is the most common spino-cerebellar degeneration of unknown etiology, with signs and symptoms developing from 18 months to 24 years of age. Common neurological signs are limb and truncal ataxia, dysarthria, areflexia of the lower extremities; pyramidal signs, loss of position and vibratory sense evolve gradually. Distal amyotrophy, horizontal nystagmus and optic atrophy are less common. Non-neurological features include kyphoscoliosis, pes cavus and cardiomyopathy. Pathological features of FA are narrowed spinal cord with cell loss and gliosis in the spinocerebellar and corticospinal tracts and in the posterior column, Clarke's column and depleted dorsal root ganglia, such as cranial nerve nuclei VIII, X and XII. Large myelinated peripheral nerves are lost, and myocardial fibers degenerated.

We treated a 16-year-old male affected by FA, who suffers from a stage IIA bulky lymphoblastic T-cell non-Hodgkin's lymphoma with mediastinal presentation. FA-related signs were kyphoscoliosis, hypertrophical cardiomyopathy and cerebellar mild ataxia. A cerebral magnetic resonance showed a moderate spino-bulbar atrophy.

At the time of diagnosis, because of rapidly worsening dyspnea, mediastinal radiotherapy was performed in another hospital and, after partial recovery, the patient was admitted to our Department to start systemic chemotherapy.

Although lumbar puncture did not find malignant cells, we performed a prophylactic intrathecal administration with Methotrexate 10 mg, ara-C 70 mg and hydrocortisone 30 mg. Concomitant systemic chemotherapy with a five-drug regimen (adriamycin 25 mg/m^2 dd 1–8, vincristine 1 mg dd 1–8, cyclophosphamide 600 mg dd 1–8, prednisone 50 mg dd 1–> 8 and methotrexate 1.5 g/m^2 d 15) was also started. Six cycles of intrathecal and systemic chemotherapy were administered.

No acute side effects appeared during or after the intrathecal treatments, nor any neurological complications after over two years' follow-up; neurological manifestations related to FA are unchanged and the patient is still in complete remission.

We think it is very important to report this single experience, considering that no data are available about the feasibility and toxicity of intrathecal chemotherapy in patients affected by central nervous system degenerations, probably because of the extreme rarity of this combined health problem.

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Cisplatin-refractory, HER2/neu-expressing germ-cell cancer: Induction of remission by the monoclonal antibody Trastuzumab

Patients with cisplatin-refractory germ-cell cancer or relapse following cisplatin-based first-line therapy exhibit a very poor prognosis. Only 15%–20% of patients are long-term survivors after standard- or high-dose salvage chemotherapy [1].

The HER2/neu receptor has been shown to be expressed in a variety of tumors, including breast, prostate and ovarian cancer. A recently published report indicates that about 30% of all refractory germ-cell cancers may overexpress HER2/neu [2]. Trastuzumab (Herceptin®), a mouse/human IgG1 chimeric antibody not only binds to the HER2/neu receptor and subsequently inhibits cell proliferation, but is also able to mediate an antibody-dependent, cell-mediated cytotoxicity *in vitro* [3]. To date, trastuzumab has shown a marked clinical activity in patients with HER2/neu positive breast cancer.

We report a 51-year-old male with heavily pretreated, cisplatin-refractory and HER2/neu overexpressing germ-cell cancer in whom a partial remission was achieved with Trastumab therapy.

The patient had undergone a right-sided inguinal orchiectomy, as well as a retroperitoneal lymph node dissection for embryonal carcinoma in 1982. In April 1993 he was found to have paraaortal lymph node metastases. During the following six years, the patient suffered four additional relapses, all located in the retroperitoneum and in the lungs. Treatment consisted of various chemotherapy regimens, including four cisplatin-based regimens. In addition, retroperitoneal and lung metastases were repeatedly resected.

In May 1998, the patient was referred to our department for further therapy. Staging procedures revealed lung metastases and a retroperitoneal mass, as well as an elevated AFP-level. The patient received several additional salvage chemotherapy regimens, including paclitaxel and gemcitabine, both of which are known to be potentially active in metastatic GCT [1].

However, remission could not be induced and the AFP-level rose constantly. At this time, the lung metastases specimen, resected in 1998 was examined for HER2/neu expression.

Immunohistochemical staining (ABC-test; Novocasta Inc.) showed a significant HER2/neu overexpression with 90%–100% of all tumor cells being HER2/neu positive (Figure 1).

After obtaining informed consent, the patient was started on experimental treatment with trastuzumab. A loading dose of 4 mg/kg body weight was administered in week 1, followed by 2 mg/kg body weight once weekly. AFP-level at the start of trastuzumab was 6000 KU/l. The AFP-level began to decline after the first administration of trastuzumab and declined to 700 KU/l after seven weeks of therapy.

Trastuzumab therapy was very well tolerated with no side effects. Repeat echocardiograms showed no signs of cardiac toxicity. Overall, the patient received eight weeks of therapy. Unfortunately, the AFP-level started to rise following two weeks rest and the patients was started on an alternative palliative chemotherapy regimen.

Despite the high cure rate achievable in testicular cancer