Case Report

Case Report: Chemotherapy in Conjunction With Blood–Brain Barrier Disruption for a Patient With Germ Cell Tumor With Multiple Brain Metastases

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Clinical Practice Points

- Testicular cancer with brain metastases is related to poor prognosis because the penetration of chemotherapeutic agents is decreased by the blood–brain barrier.
- The standard treatment of brain metastases—whole brain radiation therapy combined with chemotherapy—is related to a limited increase in survival and considerable deleterious cognitive effects.
- The blood–brain barrier can be transiently disrupted using hyperosmolar intra-arterial mannitol injection. When combined with intra-arterial chemotherapy, therapeutic intratumoral concentrations can be attained.
- In experienced centers, blood–brain barrier disruption therapy is relatively safe with a low incidence of catheter-related complications.
- Blood–brain barrier disruption therapy is a promising treatment modality for brain metastases as an alternative to whole brain radiation therapy.

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Introduction

Testicular cancer is a relatively rare malignancy affecting mostly young men of working age. Still, it is the most common solid tumor in men aged 20 to 34 years.[1,2] The incidence of testicular cancer in Finland is 5.8 per 100,000 men, which is comparable with that of the United States.[3,4] The incidence has been on the rise for 40 years and is estimated to further increase in the next decade.[1,2,5]

The age-adjusted 5-year relative survival rate of patients with testicular cancer in Finland is 95% because of the high sensitivity to chemotherapy.[4] Although testicular cancer, in general, has an excellent prognosis, the expected 5-year survival of patients with brain metastases (BM) at initial diagnosis is <50%.[6,7] Because surgical treatment and stereotactic radiotherapy are rarely applicable, the most frequently used therapy for BM remains multimodality treatment with chemotherapy and whole brain radiation therapy (WBRT). WBRT is possibly related to survival benefit, but also leads to cognitive decline and long-term neurotoxicity.[7,8] The most common deleterious cognitive effects are impaired memory and executive function.[9] Of patients treated with WBRT 50% to 80% show a decline in neurocognitive tests and 12% to 38% have impaired Mini-Mental State Examination scores.[10] Progressive delayed brain toxicity has also been described.[11]

Herein we report a case of a patient with BM of testicular cancer treated with chemotherapy in conjunction with blood–brain barrier disruption (BBBD). This promising treatment combines transient disruption of the blood–brain barrier with hyperosmolar intra-arterial mannitol infusion and simultaneous intra-arterial administration of chemotherapy. This is known to drastically increase the intracranial and intratumoral concentrations of chemotherapy agents.[12,13] Treating BM with BBBD therapy, we were able to avoid the deleterious cognitive effects of WBRT with a complete treatment response.

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Case

A 25-year-old man was admitted to the emergency department of Oulu University Hospital for a headache, visual field loss, and fever spanning 3 days. A week before the admission the patient was assessed for a supraclavicular mass with a diameter of 4 cm and a fine-needle aspiration was performed. A head magnetic resonance imaging (MRI) scan revealed 10 to 15 contrast-enhancing tumors in the cerebrum and cerebellum in both hemispheres (Figure 1, 1A-2C). A computed tomography scan of the chest, abdomen, and pelvis showed several contrast-enhancing nodules in the lungs and lymphadenopathy in the upper abdomen and mediastinum. Ultrasonography located a primary tumor with a diameter of 13 mm and irregular borders in the left testicle. Serum and plasma tumor markers beta-human chorionic gonadotropin (20,000 U/L) and lactate dehydrogenase (LDH) (805 U/L) were elevated indicating an advanced disease. Alpha-fetoprotein was within reference values. A radical orchiectomy from the inguinal incision was performed within 3 days. The surgical sample showed scar tissue with no viable tumor cells suggesting a regressed tumor. The fine-needle aspiration sample of the supraclavicular mass revealed the final diagnosis of advanced choriocarcinoma and metastases in the brain, lungs, abdomen, and mediastinum.

The patient was treated with 4 cycles of BEP (bleomycin, etoposide, cisplatin) as recommended by European Consensus Conference on Diagnosis and Treatment of Germ Cell Cancer report for patients with poor prognosis according to International Germ Cell Consensus Classification Group.[8,14] Trends in the tumor marker levels are shown in Figure 2. After 4 cycles of BEP, fluorodeoxyglucose (FDG) positron emission tomography scan showed accumulation of FDG in lymph nodes on the neck and para-aortic region and in the pulmonary nodules. The nuchal lymph node was surgically resected for histologic study, which revealed a necrotic tumor with no viable tumor cells. However, elevated tumor markers beta-human chorionic gonadotropin and LDH (128 U/L

Figure 1 **Magnetic Resonance Imaging Scan of the Brain Before and After Blood–Brain Barrier Disruption (BBBD) Therapy. Above Are T1-Weighted (T1 C+, 1A-C) and Susceptibility-Weighted Angiography (SWAN; 2A-C) Sequence Images Before BEP (Bleomycin, Etoposide, Cisplatin) Therapy. Several Lesions With a Low T1 Signal Are Seen in Both Hemispheres of the Cerebrum and Cerebellum (1A-C). Some Show Contrast Enhancement (1B, Arrows). Abnormalities in SWAN (2A-C) Correlate With Hemosiderin Accumulation and Bleeding. There Is a Larger Lesion With a Hematoma in the Left Occipital Lobe (1B and 2B, Arrowhead). After BBBD Therapy, the Metastatic Lesions No Longer Display Contrast Enhancement (3A-C). The Hematoma Has Reduced in Size (3B, Arrowhead). The Signal Abnormalities in SWAN Sequence Remained Unchanged (Not Shown)**