CASE REPORT

Neoadjuvant chemotherapy against newly diagnosed CNS germ-cell tumors: A case report

Mehrnosh Aeinfar[1], Mehrdad Payandeh[1], Mohammad Samadian[2], Nasrin Amiryfard[3], Mohammaderfan Zare[4], Mohammadebrahim Soltany[5], Masoud Sadeghi[6], Edris Sadeghi[6]

1. Department of Medical Oncology, Kermanshah University of Medical Science (KUMS), Kermanshah, Iran. 2. Department of neurosurgery oncology of Day hospital, Tehran University of Medical Science (TUMS), Tehran, Iran. 3. Department of radiotherapy Oncology, KUMS, Kermanshah, Iran. 4. Student research center, KUMS, Kermanshah, Iran. 5. Department of blood transfusion center, KUMS, Kermanshah, Iran. 6. Medical Biology Research Center, KUMS, Kermanshah, Iran.

Correspondence: Mehrdad Payandeh, MD, Hematologist-Medical Oncologist. Address: Kermanshah University of Medical Science (KUMS), Kermanshah, Iran. Email: md.payandeh@yahoo.com

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Abstract

Intracranial germ cell tumors (GCTs) are rare brain tumors that typically arise in the pineal or suprasellar regions. A young man (22 years old) was presented with complaint of one year of headache, and recently vomiting, and in exam papilledema, lethargy, somnolence, diabetes insipidus. A Phase II trial with carboplatin based regimen was conducted in this newly diagnosed patient histologically and was confirmed radiologically evaluable CNS germinomas before they received radiotherapy. This patient was presented with a localized hypothalamic germinoma and had a CR after two courses of carboplatin based regimen (the CEB regimen). He received 30 Gy of involved field radiotherapy and now at end of treatment after three months is well being without any sign of relapse. Neoadjuvant chemotherapy carboplatin based regimen was highly active in treating newly diagnosed CNS germinomas. Further chemotherapy studies eventually may permit additional dose reductions and/or elimination of radiotherapy for patients with CNS germinomas.

Key words

Diabetes insipidus, Germ cell, Neoadjuvant chemotherapy

1 Introduction

Germ cell tumors (GCTs) are heterogeneous groups of neoplasm with diverse variation in age, site, clinical presentation, histopathological features, and treatment modalities. Extragonadal GCTs constitute only 1%-5% of all GCTs, and are very rare [1].

Approximately 20% to 40% of patients with GCTs will need advanced medical treatment because of relapse or initial metastatic disease [2]. The GCTs represent the most common cancer in men aged 15–35 years [3], and they compromise 15%-20% of all anterior mediastinal tumors and benign mediastinal teratomas accounts for 60% of all germ cell tumors [4].

In the present study we report a patient man who was diagnosed with CNS germinomas before he received radiotherapy and neoadjuvant chemotherapy carboplatin based regimen was performed for him.

2 Case report

Young man with 22 years was presented with complaint of one year of headache, and recently vomiting, and in exam papilledema, lethargy, somnolence, diabetes insipidus (DI). On MRI, supracellar isointense mass that appear in third ventricle and hypothalamus (see Figure 1). The CT scan of chest and abdomen was normal.

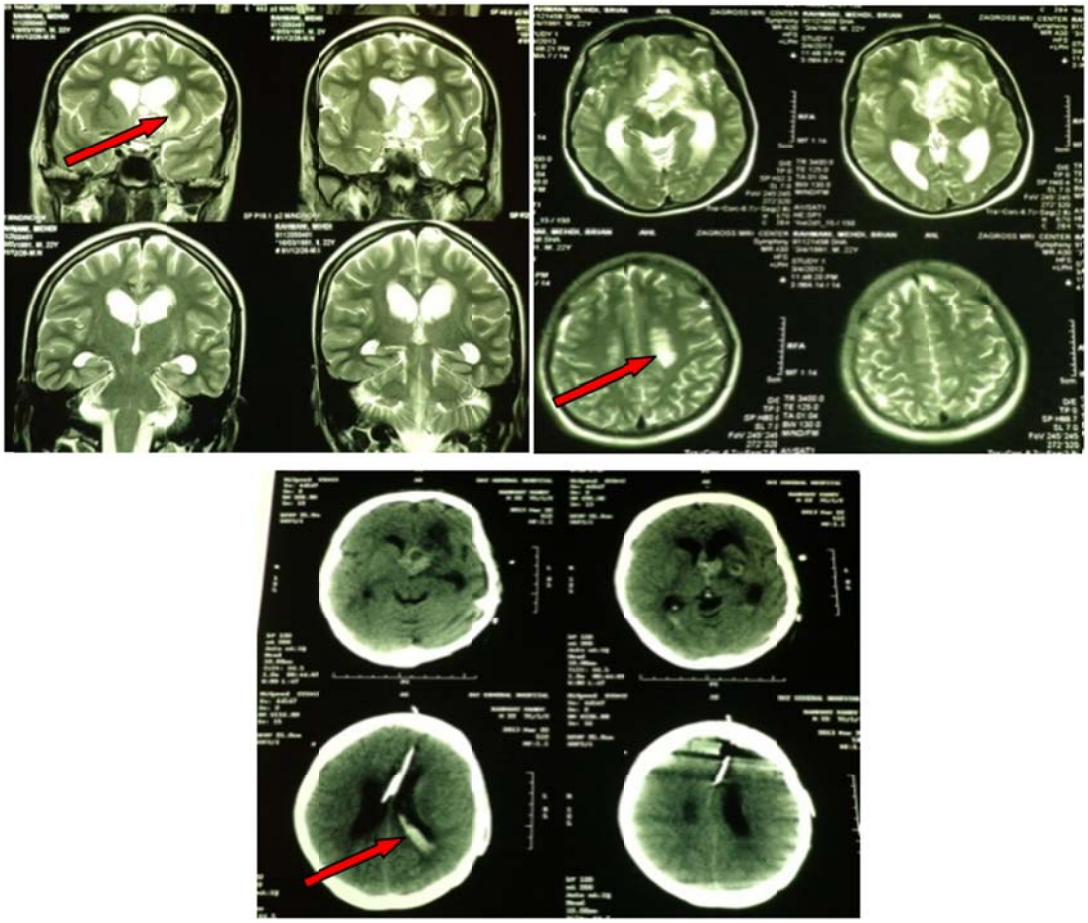

Figure 1. On Brain MRI (axial and coronal) and Brain CT SCAN, supracellar isointense mass that appear in the third ventricle and hypothalamus and shunt effect was seen.

Open surgical biopsy was done and right ventricular shunt taken, for obstructive hydrocephalus. In gross pathology, pure germinoma was recommend and established by immunostain results: PLAP and C-KIT were positive, GAFP and LCA were negative.

Patient gave written informed consent in accordance with the declaration of Helsinki. A Phase II trial with carboplatin based regimen was conducted in this newly diagnosed patient histologically and was confirmed radiologically evaluable CNS germinomas before he received radiotherapy. He had normal cerebrospinal fluid and in cytology was negative and in CSF analysis all tumor markers consist of B-HCG, LDH, AFP were in normal range. Serum tumor markers (human chorionic gonadotropin [HCG] and alpha fetoprotein [AFP] were normal) but only LDH was >1,171 IU/L. This patient had a localized tumor in the third ventricle and hypothalamus. Two courses of carboplatin based regimen (the CEB regimen) consisted of carboplatin (target AUC of 5 mg/ml × min) on first day, etoposide 100 mg/m^2 on days 1 to 5 and bleomycin 30 mg on days 1, 8 and 15. After first course of treatment vomiting, lethargy and somnolence significantly decreased and in phondoscopic examination papilledema resolved. The response was evaluated after two courses by imaging study. This patient had a complete response to this classic BEP chemotherapy regimen. After 4 months later of

beginning the patient's response was reevaluated. The radiotherapy volume was determined by the extent of disease at diagnosis (i.e., localized disease was treated with an involved field). An MRI obtained six months later, not seen any mass lesion (see Figure 2).

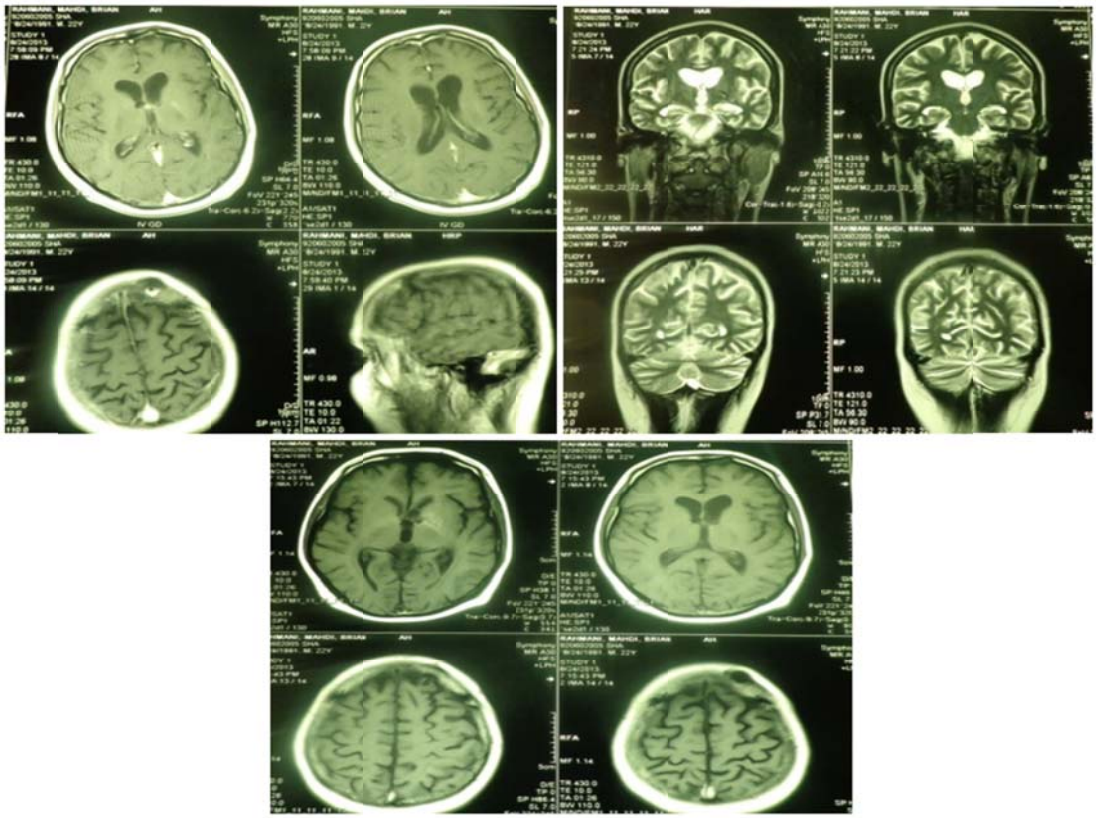

Figure 2. A MRI (axial and coronal panel) just above that obtained after ten months of first course of treatment, not seen any mass lesion or local effects that previously exist.

3 Discussion

GCTs are rare and heterogeneous with very little is known about their pathogenesis and underlying genetic abnormalities [5]. Histologic examination is needed to establish a definitive diagnosis of an intracranial GCT and to ascertain the histologic subtype. On MRI, intracranial GCTs appear isointense or hypointense on T1 sequences and hyperintense on T2 sequences [6]. The GCTs can be divided into major groups including germinomas and nongerminomatous GCTs (NGGCTs) [7], and these imaging characteristics of the histologic subtypes are similar, and MRIs cannot reliably distinguish germinomas from NGGCTs [8]. The MRI of the entire spine that was normal to this case is imperative for adequate staging of intracranial GCTs, since 10 to 15 percent of patients will have leptomeningeal spread diagnosis [6, 9]. Pure germinomas are exquisitely sensitive to radiation therapy, a gross total resection of localized germinomas is generally not recommended because of the risk of surgical complications and because pure germinomas are exquisitely sensitive to radiation therapy, intracranial germinomas are exquisitely sensitive to radiation. Most contemporary series have reported long-term progression free survival (PFS) rates >90 percent for children with localized, pure germinomas after radiation therapy (RT) alone [10-12]. Platinum-based chemotherapy regimens have a high level of activity against extracranial GCTs in children [13]. Eight of 10 recurrences occurred outside the RT field, in the periventricular area [14]. In the SIOP CNS GCT 96 study, 183 patient with localized germinomas received either chemotherapy plus 40 Gy focal RT or 24 Gy CSI with a 16 Gy tumor boost without chemotherapy [15]. The recurrence rate was higher in patients who received chemotherapy plus focal RT compared to those who received chemotherapy plus whole ventricle RT (28 versus 6 percent). The benefit of

gross total tumor resection in localized NGGCTs has not been established; several large series have not confirmed that macroscopic tumor resection improves the final outcome of patient with intracranial NGGCT [16, 17].

Although these tumors are sensitive to chemotherapy, the role of neoadjuvant chemotherapy to allow a more limited, focal RT field remains unproven, and this approach should be restricted to patients participating in formal clinical trials. The optimal chemotherapy regimen has not been defined. The available data indicate that platinum-based regimens, such as those used in other gonadal and extragonadal germ cell tumors, are effective. Available data indicate that RT is an essential component of initial treatment. Whether craniospinal irradiation is required or whether whole ventricle RT is sufficient is uncertain in patient with localized NGGCTs.

4 Conclusion

In patients with residual masses after chemotherapy and RT, second look surgery should be strongly considered. Patients with both germinomas and NGGCTs should be encouraged to participate in prospective clinical trials whenever possible. Neoadjuvant chemotherapy carboplatin based regimen was highly active in treating newly diagnosed CNS germinomas. Further chemotherapy studies eventually may permit additional dose reductions and/or elimination of radiotherapy for patients with CNS germinomas.

Conflict of interests

The authors declare no conflict of interests in this study.

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