The External Metastasis of The Central Nervous System Germ Cell Tumors: Case Report and Review of Literature

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Case report

Keywords: Chemotherapy, External metastasis, Germ cell tumor, Radiotherapy

Posted Date: October 23rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-94494/v1

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Abstract

**Background**: The central nervous system germ cell tumors (CNS GCTs) represent a class of rare tumors with incidences ranging from 3.6% in North America to 15.3% in some areas of Asia, and commonly occurring in children and adolescents[1]. According to the 2016 World Health Organization (WHO) classification, GCTs divided into germinomas, non-germinal germ cell tumors (NGGCT) and suprasellar with male prominent[2]. Common symptoms of GCTs include headache, dizziness, vomiting, thirst, heavy drinking, and precocious puberty[3]. Because of GCTs arising in the pineal region could compress the interventricular foramen with consequence obstructive hydrocephalus, leading to high intracranial pressure (HIP), the ventriculoperitoneal shunt is preferred to relieve severe HIP. Although CNS GCTs tend to spread through the subependymal lining and cerebrospinal fluid (CSF), the metastasis along the ventriculoperitoneal shunt is extremely rare[4]. Therefore, we reported two cases and a review of the literature.

**Case Report**

**Case 1**

A 13-year old Asian male presented with unsteady gait for four months, headache, nausea, drooping left eyelid, blurred version for 11 days and convulsions for three days. The MRI (Fig.1) scan revealed the occupation and HIP. The blood alpha-fetoprotein (AFP) was 188.2ng/ml (0-7ng/ml), blood chorionic gonadotropin β (β-HCG) was 716mIU/ml (0-2.6IU/ml). The AFP in CSF is 5.9ng/ml (0-7ng/ml), while the β-HCG is 542.9mIU/ml (0-2.6IU/ml). To relieve the HIP, the patient received ventriculoperitoneal shunt. Following the SIOP CNS GCT 96, the tumor was diagnosed as non-germinomatous germ cell tumors (NGGCTs). With establishing the diagnosis, the patient firstly received two cycles platinum-based chemotherapy followed by tumor resection and then completed left two courses of chemotherapy using the same regimen. Intraoperative pathological revealed hemorhagic degeneration and necrosis, scattered in glands and heteronuclear cells, and cellular degeneration. Immunohistochemical display CK (+), AFP (+), HCG-β (+), Ki-67 (+), Syn (+), SMA (+), CD30 (+). Radiation therapy was given after chemotherapy, with the dose of 30.6Gy/17 intensity modulated radiotherapy (IMRT) and PB 23.4Gy/13f (IMRT). However, the patient complained about cough, right costal margin and pain in the right clavicle with the blood β-HCG 742.1mIU/ml and AFP 873.3ng/ml in 8 months after the V-P shunt. The whole-body 18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) examination showed multiple intra-abdominal lesions demonstrating increased metabolic activity with a maximum standardized uptake value (Fig.4a). In combination with the imaging findings and laboratory results, we considered the extensive intraperitoneal metastasis (ENM) of CNS GCTs.

**Case 2**

A 17-year old Asian male presented with a longstanding history of generalized headache, diabetes insipidus and intermittent fever without obvious inducement. MRI examination (Fig 2) revealed hydrocephalus due to space-occupying lesions. The patient underwent VP shunt to face with the HIP. Moreover, the patient's blood β-HCG and AFP was negative. Based on the imaging feature and the patient's symptom, we believe that the patient had the GCTs with intraventricular dissemination. The patient received two circles with the regimen based on platinum. The blood tumor marker was negative and MRI revealed a 95% disappearance of the tumor after chemotherapy. Then the patient received and finished Whole Central Nerve System Irradiation with a dose of 40Gy/25f. After 32 months of chemoradiation therapy, the patient presented intermittent abdominal pain and right upper abdomen mass without obvious inducement. The blood tumor marker was negative and central nerve system MRI showed no evidence of tumor recurrence. Nevertheless, the MRI revealed the rough-edged masses in right upper abdominal (Fig.3). The patient then underwent PET-CT examination, PET-CT showed multiple site SUV elevation in the abdominal cavity, which was considered to be GCTs abdominal metastasis (Fig 4b-2). Then the patient underwent tumor resection, and the immunohistochemical results are AE1/AE3 (+), CD117 (+), Ki67(70%), OCT3/4 (+), sall-4 (+). The patient began four courses platinum-based chemotherapy followed and it is in fair condition now.

**Discussion**

Germ cell tumor is the most common tumor in the pineal region, but it is still a rare disease, accounting for less than 1% of all intracranial tumors[5]. Intracranial germ cell tumors are comparable to gonadal seminoma in histology. We reviewed the relevant data (Table.1) and found that Varan et al. ’s team completed a retrospective study of 1011 cases[6], which is the most extensive retrospective study of germinoma. Among the 1011 patients, the longest survival time reached 32 years, but only ten patients developed ENM. Among the ten patients, 2 were germ cell tumors, 6 were neural tube cell tumors, 1 was ependymoma, and 1 was an atypical rod-shaped tumor. It can be seen that only 0.98% of patients had primary intracranial tumors with ENM[7]. Recently, Schmalisch et al. reported 2 cases of the pineal tumor[8]. As with the previous cases[5], these authors demonstrated the risk of metastasis caused by endoscopic biopsy. In contrast, although no endoscopic biopsy was performed in our patient, the v-p shunt was performed to alleviate the severe hydrocephalus in the patient. Although the cause of peritoneal implant metastasis in the patient is still unclear, we highly suspect that the cause of this situation is ventriculoperitoneal shunt[9].
Consider the whole medical treatment process, and it's entirely in line with the diagnosis and treatment standard that the initial diagnosis is suspected to be GCTS. Patients treated along this clinical pathway rarely have metastases outside the nervous system. These two patients developed extensive peritoneal metastasis 8 months and 32 months after VP shunt. Furthermore, we are wondering whether it is transferred by shunt. Unfortunately, no cytological analysis was performed on the CSF of the first patient after the operation, but the second patient's pathology revealed a metastasis GCTs.

**Conclusion**

Neuroaxial dissemination of iGCTs is common but distant metastases is rare; this is why we report the index two cases of iGCTs metastasizing through the VPS into the peritoneal cavity causing widespread intra-abdominal carcinomatosis. According to Giuseppe Talamonti's report, germ cell tumors could metastasis along the endoscopic biopsy pathway[5]. Instead of the biopsy, the patient in our case had VP shunt. As ENM through a VPS is an unusual phenomenon, whether or not the placement of a VPS increases the risk of a patient with a primary intracranial tumor developing ENM remains controversial. The lack of statistical evidence means that the management and treatment of patients who require a VPS should not be changed. Alternative means of CSF drainage or diversion such as endoscopic third vetriculosfomy (ETV) merit further discussion and risk-benefit assessment. Meanwhile, clinicians should maintain a relatively high level of vigilance for patients with VPS and abdominal symptoms, upon which a low threshold for abdominopelvic imaging should be maintained.
| Author                  | Age | Sex | Histological type      | Treatment                           | Initial position                     | Metastatic area                                                                 | V-P shunt | Time to metastatic | Initial symptoms                                                                 |
|-------------------------|-----|-----|------------------------|-------------------------------------|--------------------------------------|--------------------------------------------------------------------------------|-----------|-------------------|---------------------------------------------------------------------------------|
| F.Lesoin[10]            | 4   | M   | Pineal tumor           | Radiotherapy                        | posterior part of the 3rd-ventricle   | intracranial and abdominal(mesenteric)                                       | Y         | 12mo              | bilateral,symmetrical, cerebellar syndrome, bilateral papilledema, Parinaud's syndrome |
| F.Lesoin[10]            | 3   | F   | pinealoblastoma        | Subtotal resection and radiotherapy | third ventricle                      | behind the bladder, internal mammary glands and subhepatic pulmonary         | Y         | 8mo               | character disorders, cerebellar syndrome                                         |
| F.Lesoin[10]            | 12  | M   | pinealoblastoma        | Subtotal resection and radiotherapy | pineal                               | pulmonary                                                                       | Y         | 12mo              | static,symmetrical, bilateral,cerebellar syndrome                               |
| Belongia and Jogal[7]   | 7   | M   | Mixed malignant       | Chemotherapy                        | N/A                                  | Multiple intra-abdominal masses                                               | Y         | 5mo               | Asymptomatic, incidental finding on spinal imaging                              |
| Murray et al.[11]      | 13  | F   | Pineal germinoma       | Resection of mass and chemotherapy  | pineal                               | Ascites, pelvic, mass, peritoneal, nodules                                    | Y         | 17mo              | Abdominal distension                                                            |
| Altundag et al.[12]    | 23  | M   | Pineal germinoma       | Chemotherapy                        | pineal                               | Ascites, pelvic, mass, multiple, liver nodules                                 | Y         | 24mo              | Abdominal distension                                                            |
| Back et al. [13]       | 10  | M   | Pineal germinoma       | Chemoradiotherapy and resection of mass | pineal                               | Abdominal mass                                                                 | Y         | 13mo              | Abdominal pain and distension                                                  |
| Ung et al. [14]        | 13  | M   | Pineal germinoma       | Resection of mass and chemotherapy  | pineal                               | Abdominal mass                                                                 | Y         | 37mo              | Abdominal pain                                                                 |
| Pallini et al. [15]    | 15  | M   | Pineal germinoma       | subtotal resection and radiotherapy | pineal and 3rd ventricle              | Pelvic mass, peritoneal nodules                                               | Y         | 2mo               | headache, lethargy, limitation, upward gaze, diabetes insipid                     |
| Kim et al. [16]        | 36  | M   | Pineal germinoma       | Chemotherapy                        | Pineal                               | Ascites, peritoneal nodules                                                  | Y         | 12mo              | Abdominal distension, vomiting                                                   |
| Devkota et al.[17]     | 12  | M   | Pineal germinoma       | N/A                                 | Pineal                               | Pelvic mass, peritoneal nodules                                               | Y         | 24mo              | Abdominal pain, distension, vomiting                                             |
| Haimovic et al.[18]    | 27  | M   | Pineal germinoma       | Radiotherapy                        | posterior 3rd-ventricle               | right abdominal palpable rectal                                               | Y         | 36mo              | bifrontal, headaches, diplopia, nausea, dizziness, hydrocephalus, duration       |
| Kun et al. [19]        | 14  | M   | Germinoma              | Radiotherapy                        | NA                                   | Pelvic mass                                                                    | Y         | 14mo              | Abdominal pain, constipation                                                     |
| Triolo and Schulz[20]  | 15  | M   | Pineal germinoma       | N/A                                 | Pineal                               | Pelvic abdominal mass peritoneal and omental nodules                          | Y         | N/A               | Constipation, weight loss                                                       |
| Wood et al. [21]       | 11  | M   | Pineal germinoma       | Chemoradiotherapy                   | Pineal                               | Pelvic mass                                                                    | Y         | 36mo              | Rectal discomfort                                                               |
| Wood et al. [21]       | 13  | F   | Pineal germinoma       | N/A                                 | Pineal                               | Pelvic mass                                                                    | Y         | 10mo              | N/A                                                                             |
| Wood et al. [21]       | 15  | M   | Pineal germinoma       | Chemotherapy                        | Pineal                               | Fluid collection                                                              | Y         | 36mo              | Abdominal pain distension                                                      |
Abbreviations

central nervous system germ cell tumors (CNS GCTs), World Health Organization (WHO), non germinal GCTs (NGGCTs), high intracranial pressure (HIP), cerebrospinal fluid (CSF), alpha-fetoprotein (AFP), chorionic gonadotropin β (β-HCG), ventriculoperitoneal (VP), Immunohistochemical (IHC), 18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT), extensive intraperitoneal metastasis (EIM), endoscopic third ventriculoscopy (ETV).

Declarations

Declarations of interest: None.

Ethics approval and consent to participate: Not applicable

Consent for publication: Agreed

Availability of data and material: Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests: The authors declare that they have no competing interests.

Funding: This report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions: Writing - original draft preparation: Peng Wang; Resources: Yanong Li; Writing - review and editing: Xiaoguang Qiu

Acknowledgements: The authors thank the patient for their contributions. Also thank my roommates for being quite when I was writing my manuscript, especially Bowei Xiao.

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**Figures**

![Figure 1](image-url)

**Figure 1**

MRI scan revealed a tumor arising from pineal region involving the left thalamus with hydrocephalus, the tumor has been marked with red arrow.
Figure 2

MRI examination revealed hydrocephalus due to multiple relatively space occupying lesions in the pineal region, suprasellar region, lateral ventricles, as well as in the cerebellum (Red arrow marked the lesions).
Figure 3

Contrast-enhanced MRI revealed the rough-edged masses in right upper abdominal mesentery with hyper-echo and obvious heterogeneous enhancement. Red arrow shows the abnormal enhancement in this patient’s abdominal MRI.

Figure 4

There were abnormal metabolic nodules near the inferior vena cava and the diaphragmatic apex, small nodules with slightly increased metabolism at the anterior right costal diaphragmatic Angle, and extensive nodules with increased metabolism in the peritoneum (a). (marked in red and black arrow). Multiple
site SUV elevation in the abdominal cavity, the two main metabolic enhancement foci are concentrated in the right upper quadrant (b).

Figure 5

The pathological findings of the patient showed typical characteristics of germ cell tumor. The tumor is composed of tumor cells that are similar to the original germ cells in morphology. Most of the tumor cells are large round, with abundant cytoplasm and clear boundary, and contain more polysaccharides. The nucleus is large and round with prominent nucleoli.
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