The External Metastasis of The Central Nerve Yystem Germ Cell Tumors: Case Report and Review of Literature

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Case report

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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.

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 vision 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 hemorrhagic 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/17f 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 cycles 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.4-b1-2). 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 ventriculostomy (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.

Table.1 Review of 18 cases of ventriculoperitoneal shunt-related intra-abdominal metastasis reported between 1979 to 2020.									
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,symmetriclea, 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 insipidus
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 ventriculostomy (ETV).

Declarations

Declarations of interest: None.

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Consent for publication: Agreed

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References

1. Thakkar JP, Chew L, Villano JL. Primary CNS germ cell tumors: current epidemiology and update on treatment. *Med Oncol*. 2013;30(2):496. doi:10.1007/s12032-013-0496-9.
2. Jennings MT, Gelman R, Hochberg F. Intracranial germ-cell tumors: natural history and pathogenesis. *J Neurosurg*. 1985;63(2):155-67. doi:10.3171/jns.1985.63.2.0155.
3. Packer RJ, Cohen BH, Cooney K. Intracranial germ cell tumors. *Oncologist*. 2000;5(4):312-20.
4. Childhood Central Nervous System Germ Cell Tumors Treatment (PDQ(R)): Patient Version. PDQ Cancer Information Summaries. Bethesda (MD)2002.
5. Talamonti G, Ligarotti GK, Bramerio M, Imbesi F. Unusual behaviour of a pineal germinoma mimicking neurosarcoidosis and metastasising along the endoscopic route. *BMJ Case Rep*. 2013;2013. doi:10.1136/bcr-2013-200278.
6. Varan A, Sari N, Akalan N, Soylemezoglu F, Akyuz C, Kutluk T, Buyukpamukcu M. Extraneural metastasis in intracranial tumors in children: the experience of a single center. *J Neurooncol*. 2006;79(2):187-90. doi:10.1007/s11060-006-9123-3.
7. Belongia M, Jogonal S. Extraneural metastasis of a nongerminomatous germ cell tumor of the central nervous system in a pediatric patient with a ventriculoperitoneal shunt: a case report and review of the literature. *J Pediatr Hematol Oncol*. 2012;34(1):e12-6. doi:10.1097/MPH.0b013e31823dd370.
8. Schmalisch K, Pantazis G, Ebner FH, Bornemann A, Honegger J, Tatagiba M. Pineal germinoma with granulomatous reaction, often a pitfall in endoscopic biopsy. Report of two cases and review of the literature. *Clin Neurol Neurosurg*. 2012;114(6):741-5. doi:10.1016/j.clineuro.2011.12.018.
9. Berger MS, Baumeister B, Geyer JR, Milstein J, Kanev PM, LeRoux PD. The risks of metastases from shunting in children with primary central nervous system tumors. *J Neurosurg*. 1991;74(6):872-7. doi:10.3171/jns.1991.74.6.0872.
10. Lesoin F, Cama A, Dhellemmes P, Nuyts JP, Andreussi L, Jomin M, Vallee L. Extraneural metastasis of a pineal tumor. Report of 3 cases and review of the literature. *Eur Neurol*. 1987;27(1):55-61. doi:10.1159/000116130.
11. Murray MJ, Metayer LE, Mallucci CL, Hale JP, Nicholson JC, Kirollos RW, Burke GA. Intra-abdominal metastasis of an intracranial germinoma via ventriculo-peritoneal shunt in a 13-year-old female. *Br J Neurosurg*. 2011;25(6):747-9. doi:10.3109/02688697.2011.566383.
12. Altundag OO, Celik I, Kars A. Pineal germ cell tumor metastasis via ventriculoperitoneal shunt. *Am J Clin Oncol*. 2002;25(1):104-5. doi:10.1097/00000421-200202000-00025.
13. Back MR, Hu B, Rutgers J, French S, Moore TC. Metastasis of an intracranial germinoma through a ventriculoperitoneal shunt: recurrence as a yolk-sac tumor. *Pediatr Surg Int*. 1997;12(1):24-7. doi:10.1007/BF01194796.
14. Ung AO, Triscott JA, Leditschke JF, Smith JA. Metastasis of pineal germinoma via ventriculoperitoneal shunt. *Aust N Z J Surg*. 1993;63(5):409-12. doi:10.1111/j.1445-2197.1993.tb00412.x.
15. Pallini R, Bozzini V, Scerrati M, Zuppi C, Zappacosta B, Rossi GF. Bone metastasis associated with shunt-related peritoneal deposits from a pineal germinoma. Case report and review of the literature. *Acta Neurochir (Wien)*. 1991;109(1-2):78-83. doi:10.1007/bf01405704.
16. Kim K, Koo BC, Delaflor RR, Shaikh BS. Pineal germinoma with widespread extracranial metastases. *Diagn Cytopathol*. 1985;1(2):118-22. doi:10.1002/dc.2840010207.
17. Devkota J, Brooks BS, el Gammal T. Ventriculoperitoneal shunt metastasis of a pineal germinoma. *Comput Radiol*. 1984;8(3):141-5. doi:10.1016/0730-4862(84)90051-9.

18. Haimovic IC, Sharer L, Hyman RA, Beresford HR. Metastasis of intracranial germinoma through a ventriculoperitoneal shunt. *Cancer*. 1981;48(4):1033-6.
doi:10.1002/1097-0142(19810815)48:4<1033::aid-cncr2820480430>3.0.co;2-r.
19. Kun LE, Tang TT, Sty JR, Camitta BM. Primary cerebral germinoma and ventriculoperitoneal shunt metastasis. *Cancer*. 1981;48(1):213-6.
doi:10.1002/1097-0142(19810701)48:1<213::aid-cncr2820480134>3.0.co;2-5.
20. Triolo PJ, Schulz EE. Metastatic germinoma (pinealoma) via a ventriculoperitoneal shunt. *AJR Am J Roentgenol*. 1980;135(4):854-5.
doi:10.2214/ajr.135.4.854.
21. Wood BP, Haller JO, Berdon WE, Lin SR. Shunt metastases of pineal tumors presenting as a pelvic mass. *Pediatr Radiol*. 1979;8(2):108-9.
doi:10.1007/bf00974001.

Figures

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.

Figure 6

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.