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CASE REPORT

Intracranial Germ Cell Tumor Metastasis to the Peritoneal Cavity through the Ventriculoperitoneal Shunt

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Intracranial germ cell tumors (GCTs) are uncommon and may cause obstructive hydrocephalus, making adequate drainage necessary in symptomatic patients. Here, we present the case of a 36-year-old male patient with intracranial germinoma metastasis to the peritoneal cavity. He had a medical history of pineal germinoma status post ventriculoperitoneal (VP) shunt implantation and definitive radiotherapy. Two years later, the patient presented with epigastric pain, and intra-abdominal metastasis through the VP shunt with malignant transformation to a nongerminomatous GCT was noted. Chemotherapy followed by surgical resection was arranged, and he got disease free after treatment. The present report alerts clinicians to the progression of this uncommon disease and suggests that a thorough physical examination is imperative in patients with a history of intracranial GCTs who have undergone VP shunt implantation, and an alternative therapeutic plan should be considered to treat intracranial GCT-related obstructive hydrocephalus.

Key words: Intracranial germ cell tumor, germinoma, ventriculoperitoneal shunt, metastases, malignancy transformation

INTRODUCTION

Intracranial germ cell tumors (GCTs) are uncommon and have an overall annual incidence of 0.6 per million in the USA and 2.7 per million in Japan.[1] They can be classified into germinomas and nongerminomatous GCTs and are primarily located in the suprasellar or pineal region.[2] They are usually diagnosed histologically or based on elevated tumor marker levels in the presence of consistent radiological findings. Although pure germinomas are nonsecreting tumors, alpha-fetoprotein (AFP) may be secreted by nongerminomatous GCTs, including endodermal sinus tumors, mixed GCTs, and immature teratomas. Here, we present the case of a patient with intracranial germinoma metastasis to the peritoneal cavity. Diagnosis of a nongerminomatous GCT, which had metastasized from the pineal region through a ventriculoperitoneal (VP) shunt, was established based on the elevated AFP and human chorionic gonadotropin (HCG) levels along with definite pathological findings.

This case report aims to increase clinicians' awareness regarding the progression of an uncommon disease and suggests that a thorough physical examination is imperative in patients with a history of intracranial GCTs who have undergone VP shunt implantation.

CASE REPORT

A 36-year-old male presented with nausea, anorexia, epigastric and periumbilical dull pain, and weight loss for 2 months. His medical history included an unresectable pineal tumor [Figure 1a] that had caused symptomatic obstructive hydrocephalus 2 years previously. Cerebrospinal fluid (CSF) collected through emergency external ventricular drainage revealed negative beta-HCG

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(2.4 ng/mL; reference: <3.33 ng/mL) and AFP (1.3 ng/mL; reference: <10 ng/mL) levels. Based on radiological findings and tumor marker levels, germinoma was diagnosed. Subsequently, VP shunt implantation followed by definitive radiotherapy was performed. Follow-up brain magnetic resonance imaging (MRI) revealed excellent response to the treatment without recurrence, the mass at pineal gland significantly decreases in size [Figure 2a]. On the other hand, there was no elevation of tumor markers during the period until this episode.

Physical examination revealed a massive palpable mass in the right upper quadrant of the abdomen, and laboratory examination revealed normal liver and renal functions with mild anemia (hemoglobin 11.9 g/dL; reference: 13.5–18.0 g/dL), thrombocytosis (platelet 525 k/μL; reference: 150–400 k/μL), and elevated lactic dehydrogenase levels (871 U/L; reference: 140–271 U/L). During a dynamic study, abdominal computed tomography (CT) revealed multiple mass lesions (largest size: 23 cm × 12 cm) in the omentum and mesentery without contrast enhancement [Figure 1b]. Furthermore, the patient exhibited elevated total HCG (1202 mIU/mL; reference: 0–10 mIU/mL) and AFP (4507.8 ng/mL; reference: 0–20 ng/mL) levels. Ultrasound-guided biopsy of the intra-abdominal tumor confirmed the diagnosis of a mixed GCT [Figure 3a]. Scrotum sonography revealed no relevant abnormalities in both the testes. Thus, pineal germinoma transformation to a nongerminomatous GCT with metastasis to the peritoneal cavity through the VP shunt was diagnosed. The patient received treatment with bleomycin, etoposide, and cisplatin, followed by tumor resection and VP shunt removal. The pathology of the resected tumor lesion showed pictures of immature neuroectodermal components and marked necrosis, which is compatible with previous biopsy pathology report as mixed GCT [Figure 3b]. The patient is undergoing regular follow-ups and is presently disease free [Figure 2b].

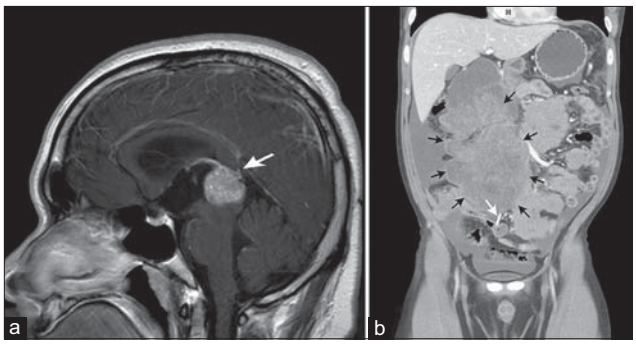

Figure 1: (a) A contrast-enhanced brain magnetic resonance imaging image shows a mass lesion (arrow) in the pineal region with compression to the third ventricle above the cerebral aqueduct. It causes obstructive hydrocephalus at bilateral and third ventricles. (b) A contrast-enhanced coronal abdominal computed tomography image shows multiple well-defined heterogeneous and homogeneous mass lesions in the omentum and mesentery (black arrows). A ventriculoperitoneal shunt (white arrow) located close to the mass lesions

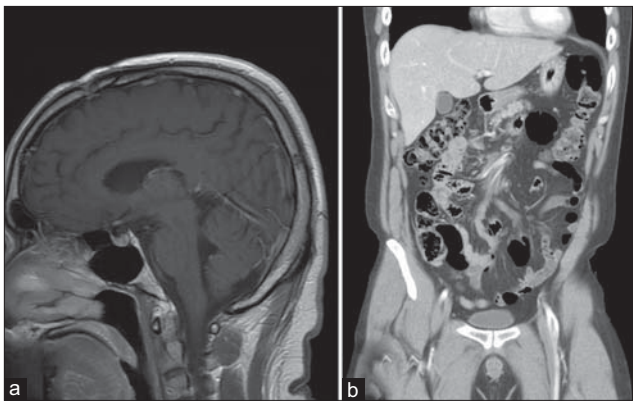

Figure 2: (a) A contrast-enhanced brain magnetic resonance imaging revealed the pineal region mass significantly decreased in size with no obstructive hydrocephalus. (b) The contrast-enhanced coronal abdominal computed tomography image shows no residual mass lesion in the abdominal cavity after radiotherapy and surgical resection

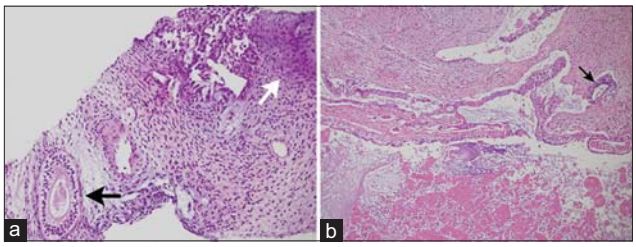

Figure 3: (a) Microscopic findings revealed immature chondroid cells (black arrow) and mature glandular cells (white arrow) (H and E, ×200). (b) Focal area showed immature neuroectodermal components (black arrow) and marked necrosis

DISCUSSION

Germinomas have high radiosensitivity and are the most curable GCTs, with a 5-year relapse-free survival rate >90% after radiotherapy. In contrast, nongerminomatous GCTs have an overall survival rate of 30%–50%, after chemotherapy combined with radiotherapy. Relapse might occur in several patients with nongerminomatous GCTs only 18 months after treatment.[2,3] In some countries, intracranial GCTs are diagnosed based on histological findings, whereas in others, it is diagnosed based on the measurement of elevated serum or CSF tumor marker (AFP and HCG) levels in addition to consistent cranial MRI characteristics.[1,2] The tumor marker threshold levels vary from country to country. In Europe, high-risk nongerminomatous GCT group is considered to have serum or CSF AFP levels >1000 kU/L. A recent study suggested the use of surgical biopsy to confirm the diagnosis if both AFP and HCG levels are lower than national protocol thresholds.[1]

Symptoms, including headache, nausea, vomiting, fatigue, and visual disturbance, are common as a pineal tumor may block CSF flow and cause hydrocephalus. Surgical intervention to drain the excess CSF should be considered for obstructive hydrocephalus. Although an endoscopic third ventriculostomy should be ideally considered, in case, it is unavailable, other alternatives, including external ventricular drain placement or permanent ventricular shunt implantation, can be considered. External ventricular drain placement, which has certain advantages over permanent ventricular shunt implantation, should be performed if feasible to avoid the inherent potential complications associated with shunting and to avoid the possibility of extracranial metastasis of the intracranial brain tumor through a VP shunt.[1] Physical examination is imperative in these patients because abdominal CT or ultrasound is not routinely arranged during follow-up. Percussion should be performed of the abdomen to determine whether there is abnormal mass with muffled sounds and the size, followed by palpation of the abdomen with pads of fingers from superficial palpation to deep palpation to evaluate whether there is internal mass. The mass is likely to be no tenderness with irregular boarder. Since the metastases that related to shunt implantation are located at the site of the shunt tip, the abdominal physical examination of the tip location should be performed very carefully. Ko *et al*. reported the case of a patient with primary CNS lymphoma that metastasized through a VP shunt. Metastasis was confirmed by the observation of enhancement along the route of the VP shunt tunnel on 18F-fluorodeoxyglucose positron emission tomography/CT and pathological findings.[4] Rickert reported an association between primary intracranial tumors with extraneural metastasis and VP shunt implantation in children. Of the 245 patients with extraneural metastasis, 67 showed an association with shunt implantation.[5] Germinomas, medulloblastomas, and endodermal sinus tumors are reportedly associated with this metastasis route.[6] Back *et al*. reported the case of a patient with intracranial germinoma metastasis through a VP shunt, with recurrence as a yolk sac tumor; however, the underlying mechanism was unclear. Seminomas and nongerminomatous GCTs have been hypothesized to have differentiation potentials.[2] Nettersheim *et al*. reported that reprogramming of seminomas into pluripotent embryonal carcinomas or direct reprogramming of them into mixed GCTs can be triggered by the microenvironment, and no genetic aberration appears to be necessary in the mechanism.[7] A subpopulation of SOX2-deficient seminomas may differentiate into cell types resembling mixed GCTs *in vivo*, which could be indicated by upregulation of the tumor marker AFP, the trophoblast stem cell/choriocarcinoma marker EOMES, and germ layer differentiation markers, such as FOXA2, PAX6, CDX1, and HAND1.[7] Our patient had symptoms of hydrocephalus. Endoscopic third ventriculostomy with biopsy was not feasible according to an expert neurosurgeon. Thus, although an external ventricular drain was placed initially, it was replaced by a VP shunt because of persistent obstructive hydrocephalus. He was discharged after VP shunt implantation, and definitive radiotherapy was performed at the outpatient department thereafter. Cranial MRI and tumor marker assessments performed every 3 months reveal that he is presently disease free. There was no enlargement of pineal gland nor typical appearance of intracranial GCTs such as hyperintense on T2 sequences or homogeneous enhancement with gadolinium. Tumor markers revealed in acceptable range until the peritoneal metastases caused elevation of the tumor markers. Abdominal metastasis through the VP shunt was diagnosed based on both tumor marker assessments, and contrast-enhanced abdominal CT performed 27 months after the definitive radiotherapy, although cranial MRI revealed no evidence of local recurrence and testis ultrasound examination findings were normal. We believe that the germinoma metastasized through the VP shunt and underwent malignant transformation to a mixed GCT, as there was no other possible origin of the mixed GCT or possible alternate malignancy transformation pathway. Otherwise, previous review has categorized the intracranial GCT with the peritoneal cavity metastases tumor located at the site of the VP shunt tip as metastases through the VP shunt.[5] Mixed GCT treatment should involve both radiotherapy and chemotherapy; however, our patient received only radiotherapy and had been disease free for 2 years. It is possible that the initial tumor was predominantly a germinoma with a small part of mixed GCT rather than a pure germinoma, resulting in neither elevation of tumor marker levels nor display of nongerminomatous GCT characteristics on cranial MRI.

CONCLUSION

The present report alerts clinicians to the progression of this uncommon disease and suggests that a thorough physical examination is imperative in patients with a history of intracranial GCTs who have undergone VP shunt implantation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that his

name and initials will not be published and due efforts will be made to conceal his identify. The study was approved by TSGH. No. C202005019 & 2020-02-17.

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Conflicts of interest

There are no conflicts of interest.

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