Case – Intra-abdominal metastases following ventriculoperitoneal shunt insertion for primary intracranial germ cell tumor

Kristen McAlpine[1], Roderick Clark[1], Maria Jiang[2], Aaron Hansen[2], Otto Hemminki[1], Robert J. Hamilton[1]

[1]Division of Urology, Department of Surgery, Princess Margaret Cancer Centre, University Health Network and the University of Toronto, Toronto, ON, Canada; [2]Division of Medical Oncology & Hematology, Department of Medicine, Princess Margaret Cancer Centre, University Health Network and the University of Toronto, Toronto, ON, Canada

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KEY MESSAGES

- Ventriculoperitoneal shunts, used to alleviate obstructive hydrocephalus, can facilitate peritoneal seeding of intracranial germ cell tumors.
- Surveillance imaging for patients with intracranial germ cell tumors should include the path of the shunt used to alleviate obstructive hydrocephalus, especially in the setting of elevated germ cell tumor markers.
- A multidisciplinary approach to treatment is necessary for patients with peritoneal seeding of primary intracranial germ cell tumors to attempt to render them disease-free.

Case report

A 20-year-old male was seen at a Canadian academic hospital for recurrence of his previously treated germ cell tumor (GCT). His past medical history was significant for a diagnosis of intracranial non-germinomatous germ cell tumor (NGGCT) at the age of 17 years old. At the time of his initial diagnosis, he had symptoms of fatigue, polydipsia, dizziness, headaches, and diplopia.

On magnetic resonance imaging (MRI), he was found to have three lesions, including one in the pituitary fossa, one in the fourth ventricle, and one in the pineal gland. The diagnosis of metastatic intracranial NGGCT was made based on characteristic MRI findings and elevated tumor markers, including a human chorionic gonadotropin (hCG) of 3425 IU/L. No biopsy, surgical resection, or imaging of the chest, abdomen, pelvis, and scrotum were performed.

He required a ventriculoperitoneal (VP) shunt insertion to alleviate symptomatic obstructive hydrocephalus. The shunt functioned well while he received six cycles of chemotherapy (carboplatin and etoposide alternating with ifosfamide) and 54 Gray radiation to treat the intracranial GCT. Upon completing chemo-radiotherapy, he was followed by the pediatric neuro-oncology and radiation oncology teams. His followup imaging showed excellent response to therapy with no evidence of disease recurrence.

Unfortunately, 17 months after completing therapy, he was found to have an elevated hCG at 44 IU/L. He underwent MRIs of the head and spine, a lumbar puncture, and a scrotal ultrasound. No evidence of recurrent GCT was detected. His hCG continued to rise and was 14 885 IU/L at his next appointment. His other tumor markers were also elevated, with an alpha fetoprotein (AFP) of 15 ug/L and lactate dehydrogenase (LDH) of 3906 U/L.

He reported an increasing abdominal girth and urgently underwent computed tomography (CT) scans of the chest, abdomen, and pelvis. These found an extensive number of soft tissue masses throughout the abdominal cavity. The masses were in atypical locations for GCTs, as they had a more peritoneal-based than nodal-based distribution. There were also multiple enlarged lymph nodes in the thorax. He was seen urgently by the adult medical oncology team that specializes in treatment of patients with testicular GCTs and started immediately on salvage chemotherapy with four cycles of paclitaxel, ifosfamide, and cisplatin (TIP).

It was felt that he had a poor prognosis, given the extent of the disease and the level of tumor marker rise; chemotherapy was provided urgently, with the understanding that surgical resection of any remaining lesions after chemotherapy would be necessary for a chance at cure. His tumor markers normalized rapidly on chemotherapy (hCG <1 IU/L, AFP 6.8 ug/L, LDH 159 U/L). Re-staging CT scans showed a dramatic

decrease in the size and number of metastatic lesions. The lymph nodes in the thorax resolved and were all <1 cm after chemotherapy. The metastatic lesions in the abdomen also drastically decreased in size (Figure 1).

He was referred to the surgical oncology team (urology, general surgery, and gynecological oncology for possible peritoneal stripping) to consider resecting the remaining lesions. The surgical teams recommended a diagnostic laparoscopy to assess the extent of the disease and to determine if complete resection with limited morbidity was possible. The patient consented and a diagnostic laparoscopy was performed. Images from the laparoscopy are shown in Figure 2.

The intraoperative opinion was that the extent of disease was resectable; however, adjuvant procedures were potentially necessary, including a bowel resection and/or partial cystectomy. The proposed operation was explained to the patient and informed consent was obtained. The patient returned to the operating room for a laparotomy three weeks later. The procedure involved a resection of all visible metastatic lesions, a retroperitoneal lymph node dissection, and a resection of the sigmoid colon, which was tethered to one of the lesions. The surgical pathology of all 16 masses and 44 lymph nodes resected was negative for malignancy, showing fibrosis/necrosis only. The patient had a prolonged postoperative recovery due to a bowel leak requiring a diverting colostomy and removal of his VP shunt leading to an intraventricular hemorrhage.

He was recently seen in clinic, 12 months postoperative, with no evidence of disease recurrence (negative CT chest/abdomen/pelvis, negative MRI head, normal tumor markers) and a good functional recovery.

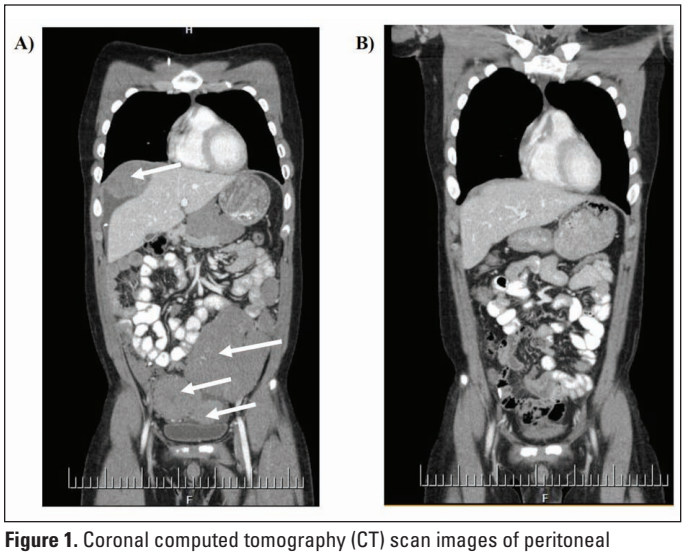

Figure 1. Coronal computed tomography (CT) scan images of peritoneal metastases along course of ventriculoperitoneal shunt **(A)** before and **(B)** after salvage chemotherapy. Arrows indicate metastatic lesions.

Discussion

Primary intracranial GCTs are a rare and heterogeneous group of malignancies.[1] Approximately 1% of pediatric primary brain tumors are GCTs, with the median age at diagnosis of 16 years old.[1] Intracranial GCTs are divided into germinomas and non-germinomas, with non-germinomas including yolk sac, embryonal, teratoma, and choriocarcinoma similar to non-seminomatous testicular GCTs. The diagnosis of intracranial GCTs can be challenging and is delayed in more than 50% of patients due to the non-specific symptoms and rare incidence of the disease.[2,3] Upon diagnosis, more than half of patients require treatment for symptomatic obstructive hydrocephalus.[4] Where appropriate based on anatomy, endoscopic third ventriculostomy is recommended to alleviate obstructive hydrocephalus in order to limit the morbidity associated with external ventricular drainage or open surgery.[5,6] When a ventriculostomy is not possible, external ventricular drainage is preferred over placement of a permanent ventricular shunt to avoid the risk of seeding to other cavities in the body.[7] Treatment of intracranial GCTs typically involves chemotherapy and radiation.[1,2]

In the case presented in this report, the patient was initially treated for metastatic primary intracranial NGGCT. A VP shunt was placed to alleviate symptomatic obstructive hydrocephalus. The patient received chemotherapy and radiotherapy with curative intent and did well with normalized tumor markers and excellent radiographic response.

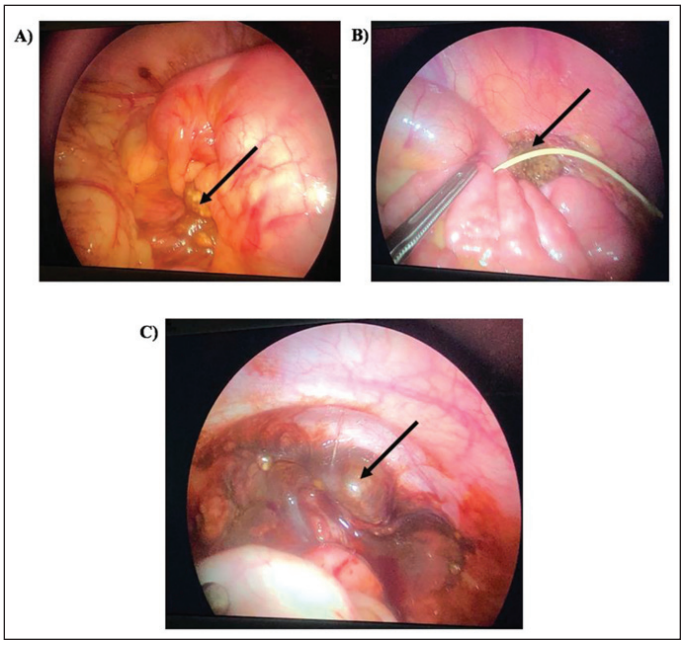

Figure 2. Images from diagnostic laparoscopy showing multiple metastatic lesions in the peritoneal cavity including **(A)** one in close proximity to the sigmoid colon, **(B)** several along the length of the ventriculoperitoneal shunt, and **(C)** in the pelvis. Metastatic lesions indicated by arrows.

The development of intraabdominal metastatic GCT lesions was unexpected.

Seeding of primary brain tumors is a known risk of shunts used to alleviate hydrocephalus and has been described in previous case reports and case series.[6] Unfortunately, intracranial GCTs are the most frequent primary pediatric intracranial malignancy associated with shunt-related metastases.[6] The average length of time from treatment of intracranial NGGCT and the development of shunt-related metastatic disease is 14 months, which was in keeping with the clinical course of our patient.[6]

Unfortunately, the prognosis of patients with shunt-related metastases from intracranial NGGCT is poor.[6] Salvage chemotherapy in the setting of elevated tumor markers is appropriate, given the presumed systemic disease. In our patient, the residual masses measuring >1 cm following an excellent response to chemotherapy were treated surgically, similar to residual tumors post-chemotherapy for non-seminomatous testicular cancer.

Peritoneal seeding of primary intracranial GCT is a known risk of VP shunt insertion for obstructive hydrocephalus. For these patients, a key point is that even though surveillance imaging of the primary tumor post-treatment would not include imaging the abdomen, it is important to monitor the path of the VP shunt with imaging and physical examinations to detect metastatic disease, especially in the setting of rising tumor markers. It is possible that alternative means to alleviate hydrocephalus may help prevent shunt-related metastases for these patients, who are often being assessed and treated by the neurosurgical and oncology teams. Treatment of residual tumor in the peritoneal cavity following normalization of tumor markers with salvage chemotherapy may be a reasonable treatment option, similar to the management of non-seminomatous testicular cancer; however, limited data is available to inform this practice. A thorough and multidisciplinary approach is necessary to ensure these patients receive the best care possible.

Conclusions

Peritoneal metastases following insertion of a VP shunt to alleviate cancer-related obstructive hydrocephalus is a known risk and followup imaging should be altered to include the shunt drainage path. Patients who are found to have extraneural spread of primary brain cancers require a multidisciplinary approach to attempt to render them disease-free. Urologists and surgical oncologists should be aware of this group of patients and the possible role for surgical resection following salvage chemotherapy; however, long-term outcomes have not been reported.

Competing interests: Dr. Jiang has been an advisory board member for EMD Serono and Pfizer; and has received payment from Amgen, Bayer, EMD Serono Canada, Ipsen, and Janssen Oncology. Dr. Hamilton has been an advisory board member for Astellas, Bayer, Janssen, TerSera; and has participated in clinical trials supported by Astellas, Bayer, Janssen. The remaining authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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Correspondence: Dr. Robert J. Hamilton, Division of Urology, Department of Surgery, Princess Margaret Cancer Centre, University Health Network and the University of Toronto, Toronto, ON, Canada; rob.hamilton@uhn.ca