Unusual presentation of adult metastatic peritoneal medulloblastoma associated with a ventriculoperitoneal shunt: A case study and review of the literature

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Received October 30, 2002; accepted March 19, 2003.

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2 Abbreviations used are as follows: CSF, cerebrospinal fluid; VP, ventriculoperitoneal.

Patients with medulloblastoma uncommonly develop extracerebral metastases. We describe an adult patient with the unusual occurrence of intraperitoneal metastases associated with a ventriculoperitoneal (VP) shunt, as well as her subsequent treatment with high-dose chemotherapy and bone marrow transplantation. We review the literature regarding this rare presentation and association of metastatic spread via VP shunt devices. A 37-year-old woman presented with a rapidly enlarging pelvic mass. She had a history of medulloblastoma and had been treated with a combination of surgery, chemotherapy, and radiation 5 years previously, at which time a VP shunt had been placed for cerebrospinal fluid leakage. At laparotomy, she had unresectable intraperitoneal metastatic medulloblastoma. After an excellent response to cyclophosphamide, etoposide, and cisplatin, she underwent a resection of residual disease, followed by high-dose chemotherapy and a bone marrow transplant. We conclude that adult onset medulloblastoma with metastasis to the peritoneal cavity is rare and may be associated with a VP shunt. Neuro-Oncology 5, 217–220, 2003 (Posted to Neuro-Oncology [serial online], Doc. 02-042, April 21, 2003. URL http://neuro-oncology.mc.duke.edu; DOI: 10.1215/S11528517-02-00042X)

Medulloblastoma is the most common primitive neuroectodermal tumor in children, and it accounts for up to 20% of all primary intracranial neoplasms in this age group (Hildebrand et al., 1997). These tumors are rare in adults and account for less than 1% of all primary brain tumors, with an annual incidence rate of 0.05 per 100,000 per year (Carrie et al., 1994). Although dissemination within the CNS is common, metastases outside the CNS are rare. In 1936, Nelson described the first well-documented case of extra-CNS metastasis in an adult patient with medulloblastoma (Nelson, 1936).

A major factor implicated in the development of extracerebral metastases is surgery, which allows neoplastic cells access to vascular and lymphatic channels. Another potential conduit for tumor dissemination is through cerebrospinal fluid (CSF) shunt devices commonly used prior to or concurrently with surgical resection (Berger et al., 1991). We discuss the case of an adult patient with medulloblastoma who presented with recurrent intraperitoneal metastases, associated with a ventriculoperitoneal (VP) shunt placed at the time of resection of the primary tumor 5 years previously.

Case Study

A 37-year-old previously healthy woman presented during her second pregnancy to her local physician with nausea and vomiting, associated with occipital headaches that increased with exertion. Initially, these symptoms were attributed to her pregnancy, but symptoms progressively worsened over the next 4 months. She then
developed blurred vision and progressive ataxia. On physical examination, she was noted to have bilateral sixth nerve palsies and left-sided ataxia. MRI scans of her head revealed a large left cerebellar mass. A subtotal resection of this lesion was performed at an outside institution. Pathological evaluation revealed medulloblastoma. Postoperatively, she required the placement of a VP shunt for the management of a CSF leak. The CSF examination at the time of surgery was positive for malignant cells.

The patient was then treated with adjuvant chemotherapy and radiation. The chemotherapy regimen used was a combination of etoposide (130 mg/m², on days 1–3) and cisplatin (30 mg/m² on days 1–3), delivered every 4 weeks. After her fourth cycle of chemotherapy, she delivered a viable 4.5-pound infant by a cesarean section at 36 weeks of gestation. This child is now 6 years old with no demonstrable developmental abnormalities. Repeat CSF examination following chemotherapy showed persistence of malignant cells. The patient was then treated with 4050 cGy to the brain and spine, with a 1440-cGy boost to the posterior fossa. She achieved a complete remission and remained disease free on prolonged follow-up. She was followed clinically and underwent serial MRI scans (which showed a minimal amount of pachymeningeal enhancement that remained stable over time) and repeated CSF cytologic examinations (which remained negative).

Five years after initial diagnosis, she developed fever, muscular aching, and increased urinary frequency. Physical examination revealed a large, firm, fixed pelvic mass, despite a reportedly normal pelvic examination performed by her gynecologist eight months previously. Ultrasound and CT scans revealed a large uterine mass and an additional mass in the right upper quadrant of the abdomen between the liver and diaphragm. An endometrial biopsy was negative, and the CA-125 level was 125 U/mL (normal range <35 U/mL). Head and spine MRI scans were negative for recurrence of medulloblastoma. The patient then presented to our institution for evaluation and treatment. Details regarding risks, complications, and alternative treatment options were discussed with the patient.

The patient was initially presumed to have a gynecologic malignancy and underwent exploratory laparotomy. Upon entry into the peritoneal cavity, we found that the VP shunt catheter was patent and that it was located in the pelvis. The pelvis was obliterated with large tumor masses displacing the bladder and rectum. The uterus was extensively replaced with tumor and was massively enlarged. An additional retroperitoneal mass was noted posterior to the uterus, firmly fixed to the sacrum and pelvic diaphragm, completely obliterating the cul de sac. In the right upper quadrant, lateral and posterior to the liver, tumor deposits were found fixed to the posterior musculature, encasing the ribs and displacing the kidney to the midline. These tumor masses were noted to be smooth surfaced and of a hard consistency. The rest of the abdomen and peritoneal surface was grossly free of disease. Intraoperative frozen section analysis confirmed the diagnosis of metastatic medulloblastoma. Histologic slides were obtained from the patient’s previous intracranial resection, and analysis confirmed intra-abdominal metastatic spread of her primary tumor. Tumor resection was not attempted given the extent of disease. The CA-125 level was presumably elevated as a result of involvement of the peritoneum with metastases.

A treatment plan was then devised in consultation with medical and radiation oncologists, gynecologic surgeons, and the bone marrow transplant team. This plan involved the use of neoadjuvant chemotherapy and debulking surgery, to be followed by an autologous stem cell transplant if a significant response was obtained. The patient was then treated with cyclophosphamide (500 mg/m² on day 1), etoposide (60 mg/m² on days 1–3), and cisplatin (20 mg/m² on days 1–5), delivered every 4 weeks. Imaging studies performed during chemotherapy demonstrated favorable shrinkage of the tumor (Fig. 1). The patient developed dose-limiting peripheral neurotoxicity after 4 cycles, and therapy had to be changed. She was treated with 1 additional cycle of ifosfamide (1.35 g/m² on days 1–3) and carboplatin (250 mg/m² on day 1), which she tolerated well. Pelvic examination after chemotherapy revealed primarily a central tumor mass, with free space between the tumor and pelvic sidewall.

Interval debulking surgery was then performed. At re-exploration, both pelvic and diaphragmatic tumor masses were found to have shrunk markedly when compared to the size noted during the previous surgery. Retroperitoneal exploration of the pelvic spaces indicated that complete resection was now possible. The patient underwent radical pelvic hysterectomy with en bloc resection of a large pararectal tumor mass and pelvic peritoneum. A decision to leave the peritoneal shunt in place was made, given the absence of any documented CNS disease.

Because the patient had an encouraging response to chemotherapy, it was decided to proceed with high-dose chemotherapy and an autologous transplant. Since attempts at harvesting stem cells from peripheral blood with hematopoietic growth factor stimulation were unsuccessful (the failed attempts probably owing to the extent of prior chemotherapy exposure), she underwent a bone marrow harvest that was adequate. There was no evidence of metastatic tumor with the bone marrow aspirate. She was then treated with a combination of thiotepa (200 mg/m² for 3 days) and carboplatin (BCNU; 100 mg/m² for 3 days), followed by an infusion of 1.66 × 10⁸ nucleated cells per kilogram. She engrafted successfully and had no major complications in the post-transplant period. She was doing well until 10 months after bone marrow transplantation, when she developed a small recurrent nodule in the intraperitoneal cavity. CT-guided biopsy confirmed recurrent disease. The patient currently is receiving chemotherapy consisting of ifosfamide and carboplatin with stabilization of her disease.

**Discussion**

Abraham and Chandy in 1963 were the first to propose the use of preoperative shunts for posterior fossa tumors.
The quoted advantages to shunting are that it reduces operative risk in patients with increased intracranial pressure and allows for prompt postoperative mobilization (Jamjoom et al., 1993). Opponents of this procedure, however, have serious reservations based on data suggesting that the CSF shunts may provide a route for systemic spread of the intracranial tumor (Hoffman et al., 1976).

Extra-CNS metastases of medulloblastoma are uncommon, and most are thought to be the result of hematogenous dissemination (Lewis et al., 1973). Rochkind et al. performed a comprehensive survey of the literature on metastases of medulloblastoma outside the CNS, revealing 119 such cases (Rochkind et al., 1991). They found that metastases to intra-abdominal organs were uncommon, the liver being the most common site (13%), followed by the pancreas (4%), kidneys (2%), ureter (1%), and ovaries (1%). In this series, recurrences in adults with VP shunts were diagnosed at a shorter interval after the primary tumor resection (mean 8 months) than those without a shunt (mean 39 months). In another study, Berger et al. reviewed 415 pediatric patients treated for a variety of primary brain tumors and found 8 patients (all with medulloblastoma) with extraneural metastases (Berger et al., 1991). The time to recurrence in patients with shunts was longer (mean 25 months) than in those without (mean 15 months). Using this data for evidence, the authors suggest that CSF shunts, regardless of type, did not predispose pediatric patients to develop extraneural metastases. However, in neither of these studies is the data conclusive, since information on the total number of patients at risk (i.e., all patients who had CSF shunts placed) is not available. The practice of routine preoperative placement of VP shunts has currently fallen out of favor, not only because of the potential for increased risk of tumor dissemination, but also because of the risk of infection and the rare but significant complication of upward transtentorial herniation (Albright, 1983).

In our case, we suspect that the VP shunt was the conduit for the spread of malignant cells to the peritoneum. At exploratory laparotomy, the tip of the shunt was found at the pelvic brim, directed toward the pelvis. Certainly, the bulk of the tumor in our patient was located in the pelvis, with the rest of the tumor being located in the right upper quadrant. The tumor likely disseminated throughout the abdomen, following the normal clockwise circulation of peritoneal fluid, thereby resulting in the greatest tumor burden in the pelvis and right diaphragm. The significant delay between shunt placement and recurrence suggests that the peritoneal cavity had been seeded initially by a very small number of cells. The long duration between the diagnosis of the primary tumor and recurrence would have been enough for a small number of cells to develop into a clinically significant lesion. This case illustrates the importance of considering metastatic disease in a patient presenting with an intraperitoneal mass and history of medulloblastoma with a VP shunt in place. In such a patient, an alternative approach to traditional laparotomy might include percutaneous tumor sampling or laparoscopic assessment of the intraperitoneal cavity.

Patients with recurrent medulloblastoma have a very poor prognosis. If treated with conventional chemother-
apy (alone, or in combination with other modalities), there are no long-term survivors (Belza et al., 1991; Torres et al., 1994). Currently, the role of bone marrow transplant in this setting remains under investigation. Data from different investigators suggests that certain subsets of patients may benefit with this treatment strategy and achieve relatively long disease-free survival (Dunkel et al., 1998). The patients who benefit the most seem to be those with chemotherapy-sensitive disease, those in whom cytoreduction could be achieved prior to therapy, and those with localized disease (as opposed to those with distant metastases). However, even after a transplant, a significant proportion of patients die of recurrent disease. These recurrences have been noted to occur over a wide range of time after the transplant. Unfortunately, disease in our patient recurred despite high-dose chemotherapy and stem-cell transplantation.

In conclusion, medulloblastoma is an uncommon tumor found in the adult patient, and metastasis to the peritoneal cavity is extremely rare. Controversy exists as to whether or not shunt devices may potentiate the risk for metastatic spread, but this risk should be considered in the patient presenting with an abdominal mass and history of medulloblastoma.

References


