A 60-year-old Asian woman with a history of ovarian cancer presented with headaches and vomiting. She had a past medical history of pulmonary tuberculosis (TB) at age 20 years and was diagnosed with grade 2, stage IIIC serous ovarian cancer. At the time of her cancer diagnosis, her Ca125 was 1,326 IU/mL, and she underwent primary debulking surgery followed by six cycles of adjuvant carboplatin plus paclitaxel chemotherapy. Two years later, her disease relapsed with a Ca125 of 623 IU/mL, and she received six cycles of carboplatin plus liposomal doxorubicin with a complete response. Six months after completing chemotherapy, she presented with a 3-week history of headaches and vomiting and a Ca125 of 93 IU/mL. Examination demonstrated no focal neurologic deficits, and brain computed tomography (CT) and magnetic resonance imaging (MRI) showed no evidence of CNS metastases or systemic relapse on restaging. The clinical differential diagnoses were as follows: carcinomatous meningitis, tuberculous meningitis in view of her previous medical history, and/or cerebral sinus thrombosis (CST). A high opening pressure of 44 cm of H2O with lymphocytosis and increased protein (1.24 g/L) in the CSF was observed on lumbar puncture. Cytology for malignant cells was negative. Microbiology did not reveal acid-fast bacilli, and TB polymerase chain reaction was negative. In view of the markedly raised CSF pressure, a magnetic resonance venogram (MRV) and CT venogram were
performed. These showed minimal enhancement of the left transverse and left sigmoid cerebral sinus (Fig 1A, arrow) as a result of CST, and she was anticoagulated with enoxaparin.

However, 2 weeks later, the patient developed worsening headaches, swinging pyrexia, a fluctuating level of consciousness, and a right-sided third cranial nerve palsy. A repeat CT venogram and gadolinium-enhanced MRI brain studies demonstrated normal meningeval enhancement (Fig 1B, arrow; coronal T1-weighted MRI of the brain) with no convincing features of leptomeningeal disease. The patient declined spinal MRI. Given her history of previous Mycobacterium infection and immunosuppression, a presumptive diagnosis of recurrent TB was made, and she was administered high-dose steroids and empirical antituberculous treatment (isoniazid, rifampicin, pyrazinamide, and ethambutol) on the advice of the infectious diseases team. Because regular lumbar punctures were required to reduce CSF pressure, a ventriculoperitoneal shunt was inserted. Microscopic analysis of a specimen of dura mater obtained during shunt insertion was normal with no pathologic changes suggestive of TB or carcinoma. Despite shunting and anti-TB treatment, the patient developed progressive bilateral leg weakness, recurrence of vomiting, and intermittent headaches. During this period, an additional eight samples of CSF were analyzed but showed no malignant cells in the CSF and were negative for TB on culture and polymerase chain reaction. The patient finally agreed to a full craniospinal MRI. Precontrast (Fig 1C) and postcontrast (Fig 1D) sagittal T1-weighted MRI images demonstrated significant leptomeningeal enhancement around the lower spinal cord and filum terminale (Fig 1D, arrow). In view of the extensive spinal leptomeningeal carcinomatosis (LCT) with possible intracranial involvement, the patient underwent whole-brain radiotherapy (20 Gy in five fractions). Unfortunately, the patient continued to deteriorate and died 3 weeks later.

Discussion

In summary, this was a case of LCT that presented with CST. This case illustrates the importance of searching for an underlying cause for CST, the difficulties in the diagnosis of LCT, and the poor prognosis with both.

The association between cancer and an increased risk of venous thromboembolism is well established; however, data on malignancy-associated CST are limited. It is estimated that the incidence of CSTs is three to four cases per 1 million adults and seven cases per 1 million neonates and children but has a favorable prognosis in greater than 80% of cases. Only one study to date, with 20 patients from Memorial Sloan-Kettering Cancer Center, has reported specifically on CST in patients with cancer. In that series, 40% of patients presented with a headache, the thrombus involved the superior sagittal sinus in 65% of patients, and MRV was more sensitive than MRI at detection. A total of 55% of the patients had an underlying solid tumor, and 45% of patients had a hematologic malignancy. In patients with solid tumors, CST was associated with dural/calvarial metastasis in 55% of patients, antiestrogen therapy in 27%, LCT in 18%, and low prothrombin time and thrombocytosis in 9% of patients each. Overall, 27% of patients with solid tumors improved with anticoagulation.

LCT as a result of disseminated hematologic and solid tumors results in a progressive neurologic deficit, with a median survival of 8 to 16 weeks, and is most frequently associated with leukemia, lymphoma, and lung and breast cancers. However, because patients live longer with treatment, cases associated with colorectal and gynecologic malignancies are being increasingly reported. Clinically, neoplastic meningitis is detected in only 5% to 8% of patients with solid tumors and 5% to 15% of patients with lymphoproliferative malignancy but in up to 20% of patients at postmortem. Clinical signs and symptoms of neoplastic meningitis are completely absent in 25% of patients at diagnosis and, when present, are more often localized to the spinal cord and nerve roots (60%) compared with cranial nerves (35%) and cerebral hemispheres (15%). Most cases of LCT occur in patients with widely disseminated disease (>70% of patients), but it can also present in patients with no evidence of extra-axial disease (20% of patients) or as the first manifestation of malignancy (5% to 10% of patients). The gold standard for diagnosis requires a positive CSF tumor cytology, which is negative in 10% to 15% of patients. Gadolinium-enhanced MRI scanning of both the brain and spine is the usual recommendation for leptomeningeal carcinomatosis to achieve meningeval uptake of contrast medium, both focal and diffuse, in up to 40% to 60% of patients. Treatment involves either individual or combination intrathecal chemotherapy and whole-brain radiotherapy. Significant palliation, and in a few rare cases even disease remission, are possible. Despite this, overall prognosis is poor (overall survival, 18 to 16 weeks).

To our knowledge this is the first reported case of CST as a result of leptomeningeal carcinomatosis in ovarian cancer. This case illustrates the poor prognosis of patients with cancer associated CST and LCT and highlights the need to search for an underlying cause such as LCT in patients with CST. Conversely, we speculate that the potential for underdiagnosis of CST in patients with intracranial metastases/LCT may contribute to the poor prognosis of these patients. A prospective study of the utility of routine MRV assessment for CST in such patients would be informative.

Ho Kwong Li, Victoria Harding, Ruth Williamson, Sarah Blagden, Hani Gabra, and Roshan Agarwal
Hammersmith Hospital, Imperial College, London, United Kingdom

ACKNOWLEDGMENT

R.A. is funded by a Clinician Scientist Fellowship from Cancer Research United Kingdom.

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES


DOI: 10.1200/JCO.2011.38.1426; published online ahead of print at www.jco.org on December 12, 2011