CLINICAL VIGNETTE

Carcinoid Tumor with Liver Metastases

Evangelia Kirimis, MD

A 69-year-old woman was followed for a history of breast cancer. She initially had an abnormal screening mammogram. Excisional biopsy of a left breast lesion confirmed high grade, triple negative invasive ductal carcinoma. Subsequent sentinel lymph node biopsy confirmed no nodal metastatic disease and she was staged as T1cN0. She completed six cycles of adjuvant docetaxel and cyclophosphamide followed by radiation. She was monitored expectantly with no evidence of recurrence. Two years after completion of her cancer treatment, she presented to an emergency room with new abdominal pain. Computed tomography (CT) of the chest, abdomen, and pelvis noted a 2.2 centimeter (cm) enhancing soft tissue lesion in the mesentery of the right mid-abdomen that was concerning for carcinoid or other neoplasm. There was also a 1.8cm hypodense lesion in the right lobe of the liver of indeterminate etiology. Ultrasound of the abdomen noted no abnormalities. Magnetic Resonance Imaging (MRI) of the abdomen indicated a 2.3cm segment 8 liver lesion that corresponded to the prior CT and was indeterminate. A right lower quadrant mesenteric mass with central necrosis and peripheral spiculation was also seen, consistent with carcinoid. The MRI also noted, and in retrospect was noted on prior CT, focal prominent enhancement and thickening along the terminal ileum that was suspicious for a primary tumor. Additional small arterially enhancing foci in the liver of unclear etiology were also noted. Octreotide scan was negative. Biopsy of the largest liver lesion was consistent with a well-differentiated neuroendocrine neoplasm. She proceeded with resection of the mesenteric mass and segmentectomy of the liver mass. Pathology identified well-differentiated neuroendocrine tumor cells in both cases. During surgery, she had radiofrequency ablation of ten additional small liver lesions noted in both lobes of the liver. Colonoscopy was unremarkable. She had surgical resection of the previously noted ileal lesion and pathology was consistent with the prior findings. Her post-operative course was uneventful, and monitored expectantly, free of symptoms. Labs including chromogranins over eight years have remained normal. Serial MRIs of the abdomen and pelvis have also remained stable with no new findings.

Neuroendocrine tumors (NETs) are heterogeneous indolent neoplasms.[1-3] They arise from enterochromaffin cells that are present throughout the body, but most commonly develop in the gastrointestinal or pancreatic tracts.[1-3] Carcinoid tumor incidence is reported as 2 cases per 100,000 but autopsy series note incidental carcinoid tumors in up to one percent of cases.[2,3] Incidence appears to be increasing over time, which may be related to better detection.[1] NETs are defined by well-differentiated grades and low Ki67 values and higher grade lesions are deemed neuroendocrine carcinomas.[1] Lymph nodes are the most common area of metastasis followed by the liver.[1] Concurrent liver metastases at the time of diagnosis is common with >75% in small intestine primary disease and 30-85% in pancreatic tumors.[1,3] Liver metastases are associated with worsen prognoses.[1,3] Prognoses have improved over time which may be related to use of somatostatin analogues.[2] It is not common to have a primary liver NET without evidence of other primary lesions (5-10% of cases).[1,3] Tumors can be functional, releasing vasoactive peptides.[2,3] Liver metastases correlate closely with symptoms given the liver's metabolization of the released hormones.[3] Serotonin production is the most common product especially in midgut lesions.[2] Other peptides include 5-hydroxytryptophan, bradykinins, histamine, and substance P.[2] Not all tumors secrete, but if the tumors are functional, common symptoms include diarrhea, flushing, and wheezing.[2] Complications of NETs include carcinoid heart disease, which has an unclear mechanism but is related to serotonin release.[2] Similarly, carcinoid crisis can lead to dehydration, hypotension, and arrhythmias.[2] As most primaries are related to the gut, bowel obstructions, fibrosis, abdominal pain, and intestinal ischemia may result.[2] Skin metastases are seen late in the disease and can be painful.[1]

Treatment options include surgical resection, liver transplantation, chemotherapy, somatostatin analogs, radiofrequency ablation, cryotherapy, and embolization techniques.[1] Patients with extensive liver disease may present with carcinoid syndrome. Those with limited disease have potential for cure.[1] Even with late presentation surgical treatment of the primary tumor and liver metastases improves survival.[1] Studies report extensive debulking or resection has a positive impact on patient outcomes.[1] However, a aggressive surgery may be limited by patient morbidity and organ dysfunction.[1] Combination of surgery with other local therapies are commonly used with extensive liver metastases.[1] Perioperative somatostatin analogues may be needed in functioning tumors to prevent carcinoid crises during the physiologic stress of surgery.[1] They are also used to control carcinoid symptoms.[2,3] Prophylactic cholecystectomy may be recommended due to the risk of cholelithiasis with somatostatin use.[1] Liver transplantation may be considered in select cases, however, recurrent liver disease is common.[1,3] All disease should be resected prior to transplant to minimize the risks of extensive surgeries.[1] Radiofrequency ablation uses heat via alternating electric current and is a

palliative option for carcinoid symptoms with repeat treatments feasible. It is less useful on larger tumors.[1] Chemotherapy is generally not very effective for low grade lesions, but can be considered if other options are not effective.[2,3] Newer targeted therapies such as VEGF inhibitors (bevacizumab) mTOR inhibitors (everolimus), and tyrosine kinase inhibitors (sunitinib) have shown some palliative benefits.[3]

This patient had resection of all noted intestinal lesions and radiofrequency ablation for her multiple small liver lesions. She has been monitored with labs including chromogranin and MRI imaging every six to twelve months. It is now five years from her initial surgeries, with stable laboratories and testing imaging. Given her lack of any carcinoid symptoms, she has never needed any systemic therapy. We continue to monitor her expectantly.

REFERENCES

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