Invited Commentary

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Carcinoids are the most common endocrine tumors of the gastroenteropancreatic axis. It is now recognized that carcinoids share a number of histologic, ultrastructural, and biochemical features with other endocrinologically-active tumors and they are considered by many authorities to be part of the APUD (amine precursor uptake and decarboxylation) system of cells [1].

Carcinoid tumors arise from a multipotential primitive stem cell and are frequently classified according to their anatomic distribution and differing patterns of secretory behavior [2]. Midgut carcinoid tumors arise from the jejunum, ileum, and right colon, are argentaffin positive, and have a high serotonin (5-HT) content. Unlike foregut carcinoids (bronchus, stomach, duodenum, and pancreas), midgut tumors generally do not secrete 5-hydroxytryptophan (5-HTP) or adrenocorticotropic hormone (ACTH) and rarely metastasize to bone. They can be easily distinguished histocytochemically from hindgut carcinoids because the latter do not contain serotonin and, therefore, stain argentaffin-negative.

Midgut carcinoids tend to be relatively slow-growing and may go undiagnosed for many years. Once the tumor has grown transmurally into the mesentery, it appears to evoke an intense desmoplastic or fibroplastic reaction causing contraction and adherence of adjacent bowel loops with resulting partial or complete intestinal obstruction. Ischemic enteritis and intestinal gangrene may also result from vascular compromise due to mesenteric fibroplasia or from periadventitial hyperelastosis leading to the development of occlusive changes in small to moderate-sized mesenteric arteries [3]. Many of these patients will present with longstanding premonitory symptoms of intermittent abdominal pain, diarrhea, and unexplained weight loss.

Prognosis appears to be determined largely by the extent of tumor involvement with reported 5-year survival rates of 94% for localized disease, 64% with regional lymph node involvement, and 18% with distant metastases [4]. Because of the indolent behavior of these tumors, surgical palliation is warranted in patients with symptomatic bowel obstruction or ischemia, even in the presence of extraintestinal disease. Five-year survival rates of 20% and 38%, respectively, have been reported for "operable" patients with hepatic and regional lymph node metastases [5]. Postoperative chemotherapy may provide substantial albeit temporary palliation.

Midgut carcinoids secrete a number of neuropeptides that have been implicated in the pathogenesis of "carcinoid syndrome." Serotonin is thought to be the primary peptide responsible for diarrhea and may be an important cause of flushing as well as extraintestinal manifestations such as arthropathy, heart disease, and retroperitoneal fibrosis [6]. Histamine and, to a lesser extent, substance P, prostaglandins, and neuropeptide K have also been implicated in the clinical manifestations of carcinoid tumors [7]

The majority of patients with midgut carcinoids develop carcinoid syndrome only in the presence of hepatic metastases and are rarely curable by surgery. Resection of hepatic metastases has been successful in carefully selected patients with severe carcinoid-induced diarrhea and flushing but should only be considered when symptoms are unresponsive to conventional chemotherapeutic agents [8]. Unfortunately, eventual relapse and tachyphylaxis to the drugs is frequently encountered. More recently, suppression with long-acting somatostatin analogue (octreotide) was evaluated in a variety of neuroendocrine tumors including carcinoid. In one recent study of octreotide in 14 patients with biochemical and clinical evidence of carcinoid syndrome, symptoms of flushing, diarrhea, and wheezing were controlled in the majority of patients, but the drug failed to suppress biochemical markers or tumor growth [7]. Despite failure to slow tumor progression, octreotide may provide excellent palliation of symptoms with relatively few adverse effects.

The authors summarize a 10-year surgical experience in 51 patients with midgut carcinoids, 26 (51%) of whom had objective evidence of carcinoid syndrome. Thirty-one patients (61%) had extensive mesenteric fibroplasia or nodal involvement that precluded radical resection and underwent surgical "debulking" or intestinal bypass procedures. Only 6 patients with hepatic involvement were suitable candidates for resection or enucleation. Although survivors were followed for a mean of 2.8 years, the authors did not describe the effects of surgery on the frequency and severity of preoperative symptoms. Since the majority of patients were given postoperative medical therapy, the usefulness of surgery per se cannot be evaluated.

Surgery has a potentially important role in patients with mid-gut carcinoids, but should be viewed as one arm of a multimodality treatment regimen. Curative resection is unusual but should be attempted in all patients with disease limited to the bowel wall and adjacent mesentery. Surgical palliation should always be considered in patients with symptoms of bowel obstruction or ischemia, even in the presence of nodal or hepatic metastases. Similarly, resection of bulky mesenteric, nodal, or hepatic metastases may be useful in carefully-selected patients with symptoms of carcinoid syndrome that prove refractory to medical management or arterial embolization [9]. Postoperative treatment with chemotherapeutic agents and hormonal suppressants may provide useful palliation, but should be withheld until the effects of surgery have been fully evaluated.

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