Novel Approaches to 'Borderline Resectable' Pancreatic Tumors

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In this issue of ONCOLOGY, Shah and colleagues, through their instructive case report, draw our attention to an important area—borderline resectable pancreatic cancer—that has historically not been a major focus of the literature.[1] The authors describe the case of a 40-year-old man with an adenocarcinoma of the pancreatic head with involvement of the superior mesenteric vein–portal vein (SMV-PV) confluence resulting in limited occlusion. Preoperative systemic therapy with weekly gemcitabine (Gemzar) for four doses followed by concurrent gemcitabine-based chemoradiotherapy (54 Gy) facilitated tumor shrinkage, and the patient proceeded to undergo an R0 pancreaticoduodenectomy (PD) with a partial portal vein resection and repair using a saphenous vein patch.

‘Borderline Resectability’
This case illustrates some important considerations in the management of pancreatic cancer. In the era of multidetector computed tomography optimized for pancreatic imaging, tumors of “borderline resectability” are emerging as a distinct subset of pancreatic tumors that do not easily fit the traditional categories of resectable or locally advanced pancreatic cancers.[2] This distinction is essential because, in the absence of objective criteria for preoperative staging, some patients with borderline resectable pancreatic cancer will be treated as if they have resectable cancer (with an increased risk of margin-positive resection) while others will be treated as having locally advanced disease (and show “remarkable” downstaging)—potentially confounding the results of clinical trials in which they are enrolled.

Several years ago, the National Comprehensive Cancer Network (NCCN) described borderline resectable pancreatic adenocarcinoma as a unique category, although the criteria were not completely defined, resulting in some inconsistencies. For example, in the absence of clear characterization of abutment vs encasement of the artery, institutional definitions differ.[3]

Over the past several years, our group has attempted to develop objective radiographic criteria that define tumors of borderline resectability. These include: (1) those with tumors that exhibit encasement of a short segment of the hepatic artery (without...
evidence of tumor extension to the celiac axis, and that is amenable to resection and reconstruction); (2) tumor abutment of the superior mesenteric artery involving less than or equal to 180° of the circumference of the artery; or (3) short-segment occlusion of the superior mesenteric vein, portal vein, or the SMV-PV confluence with a suitable option available for vascular reconstruction using patent veins above and below the area of tumor involvement.[4]

This attempt to standardize the definition of borderline resectable pancreatic cancer is of course work in progress, and may be modified with time. The objective is to help establish objective radiographic criteria so that—rather than being purely a surgeon’s prerogative with a decision made at the time of laparotomy—decisions regarding tumor resection are made by a multidisciplinary group working jointly in these complicated cases.

Preoperative Therapy
As illustrated by Shah et al’s experience, with currently available surgical techniques, patients with borderline resectable pancreatic head cancer are at high risk for a margin-positive resection. The use of preoperative systemic therapy and locoregional chemoradiation can help maximize the potential for an R0 resection and to avoid R2 resections.[5] Our experience suggests that these patients are good candidates for a prolonged course of systemic therapy and chemoradiation with serial restaging scans. Patients with favorable responses to preoperative therapy supported by radiographic evidence of tumor regression and improvement in serum tumor marker levels (CA 19-9) are those who have the best chance for an R0 resection and a favorable long-lasting outcome.

A further rationale for delivering preoperative therapy to these patients is to deliver systemic therapy early, to treat micrometastases—which exist in the majority of patients—and provide a sufficient time interval to gauge the biology of the cancer. Thus, patients who will benefit most from an aggressive surgery can be selected.[6]

Further Considerations
In a recent paper published by Katz and colleagues from our institution, the authors propose two additional subsets of patients who may be considered borderline resectable based on clinical criteria.[7] Not infrequently, a patient will present with a technically resectable pancreas tumor but with unfavorable clinical features (such as indeterminate metastatic disease at presentation, a suboptimal performance status, or medical comorbidities) that make the cancer borderline resectable. This situation merits a “time-out” phase and detailed evaluation prior to a large abdominal surgery. After a prolonged program of chemotherapy and chemoradiation (lasting at least 3 to 4 months), patients who show an improvement in their performance status (eg, recovery from biliary obstruction symptoms after stent placement), and absence of metastatic disease on restaging scans are then considered for PD.

Potential barriers to the use of preoperative therapy include the need for a tissue diagnosis of pancreatic cancer and endobiliary stent placement if obstructive jaundice is present. In our experience, when the duration of preoperative therapy exceeds 6 to 8 weeks, occlusion of plastic endobiliary stents and cholangitis is of increased concern and requires vigilance. In recent years, we have made it our practice to insert coated expandable metal stents in patients who undergo more than 8 weeks of preoperative therapy, to reduce the rate of stent failure without a negative impact on subsequent PD.

Conclusions
This remains an important and evolving field, but it is becoming clear that the treatment of patients with borderline resectable tumors requires a multidisciplinary working group of surgeons, radiation and medical oncologists, gastroenterologists, radiologists, and pathologists committed to research-driven patient care. Such treatment is best suited to a high-volume center with surgical expertise in vascular resections and interposition grafting.

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References