PGCR 2007 (Abstract 205)

Novel Use of Focal High-Dose IMRT for Borderline Resectable Pancreatic Cancer

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Background: Localized pancreatic adenocarcinoma involving the superior mesenteric (SMA) or celiac arteries is considered unresectable (American Joint Committee on Cancer [AJCC] staging, 2002, T4). However, this heterogeneous group of patients includes some with borderline resectable disease who may benefit from pancreatic resection after preoperative chemoradiation. Focal high-dose intensity-modulated radiation therapy (IMRT) directed to the site of arterial involvement may increase margin-negative resectability.

Methods: We treated 11 patients with locally advanced unresectable pancreatic cancer (AJCC 2002, T4) with gemcitabine-based chemotherapy (one patient did not receive chemotherapy prior to chemoradiation, median weeks of chemotherapy = 13) followed by IMRT with concurrent gemcitabine or capecitabine. Radiographic imaging using a dual phase contrast helical thin slice pancreas protocol computed tomography (CT) scan was performed on all patients. Those with tumor involving less than 180 degrees of the SMA

(n=4) or tumor involving arteries within 1 cm of the celiac axis (n=7) were treated with IMRT to a dose of 50.4 Gy to the gross tumor volume (GTV) with a clinical target volume (CTV) expansion of 5 mm and a planning target volume (PTV) expansion of 10 mm cranial-caudally and 5 mm radially. The region of arterial involvement (GTV2) was treated with a 5 mm PTV expansion to a median of 63 Gy (range, 57.5-63.6 Gy) in 28 fractions (range, 25-30). Patients were then restaged for consideration of surgical resection.

Results: The location of the lesions included pancreatic head (n=7), neck (n=2), and body (n=2). Tumor size ranged from 2.2 cm to 5.0 cm (median 2.8 cm). There was abutment of the SMA in four patients and of the splenic or common hepatic arteries < 1 cm from the celiac axis in seven patients. All patients had a patent SMV portal venous confluence. No patients developed grade 3 and only one patient developed grade 2 gastrointestinal toxicity during chemoradiation (National Cancer Institute Common Toxicity Criteria, version 3.0). Only one patient was hospitalized (stent-related cholangitis). All patients completed the planned radiotherapy without significant treatment breaks (1 and 2 day breaks in two patients). On restaging, one patient had a partial response of a treated lymph node abutting the hepatic artery (the only one with regression from an artery), three patients had minor responses, and five had stable disease. Of nine evaluable patients, four underwent margin-negative pancreatic resection. The other five were not resected due to distant metastasis. There were no perioperative complications. Three of the four resected patients are alive (19, 20, and 24 months).

Conclusions: Despite a lack of radiographic response, margin-negative pancreatic resection was safely performed in patients with borderline resectable pancreatic cancer following preoperative treatment with chemoradiation using IMRT to deliver a higher dose to the area of arterial involvement. IMRT was well tolerated with minimal acute and no late radiation toxicity. The selective use of focal high-dose IMRT in appropriately selected patients with borderline resectable pancreatic cancer should be further studied.