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Pancreatic Cancer *in brief*

News from the UPMC Pancreatic Cancer Center

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Dr. Moser

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For patients with pancreatic cancer, treatment options include surgical resection, radiation therapy, or chemotherapy. Determining the ideal therapy for each patient depends on the stage of the cancer. At the UPMC Pancreatic Cancer Center, we offer state-of-the-art surgical options, comprehensive clinical services, and cutting-edge clinical trials to treat this complex disease.

In this issue of *Pancreatic Cancer in Brief*, we highlight the use of the state-of-the-art robotic Whipple procedure, or pancreaticoduodenectomy – a surgical procedure known to have a positive impact on survival. We feature a case study that follows a patient selected for this complex surgery.

Another focus is the use of stereotactic body radiation therapy (SBRT) for high-risk patients who are not candidates for surgery. This type of radiation delivery provides pinpoint accuracy, minimizing damage to healthy tissue, and allows for a shorter treatment time so patients may begin systemic chemotherapy sooner.

Finally, we would like to make you aware of the Pancreatic Cancer Specialty Care Center, which provides a multidisciplinary approach to diagnosing and treating pancreatic cancer. Experts from surgical, medical, and radiation oncology are brought together to expedite the development and implementation of a treatment plan.

Pancreatic cancer remains one of the leading causes of cancer deaths in the United States and UPMC Pancreatic Cancer Center recognizes the need for innovative approaches to enhance the diagnoses and treatment of the disease. We hope you find this information useful in your day-to-day practice and welcome the opportunity to discuss our clinical research or patient care opportunities. Please contact us at 1-888-623-PANC (7262) or visit us at UPMC.com.

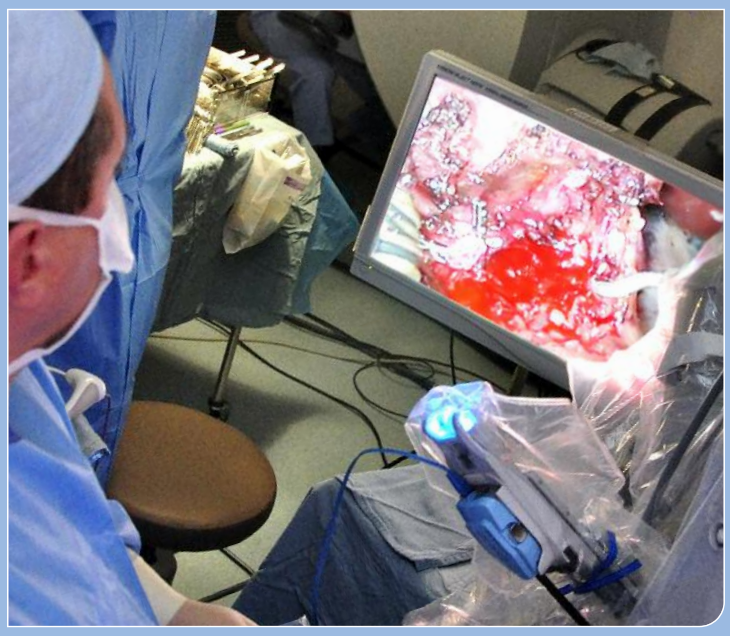
Sincerely,

A. James Moser, MD, FACS
Co-director, UPMC Pancreatic Cancer Center and Pancreatic Cancer Specialty Care Center

Herbert J. Zeh, MD
Co-director, UPMC Pancreatic Cancer Center and Pancreatic Cancer Specialty Care Center

Case report

Neoadjuvant therapy and minimally invasive pancreaticoduodenectomy in a patient with acinar cell carcinoma



A 70-year-old man, who reports a lifelong history of stomach problems, including bloating, gas, and reflux, began to experience increasing frequency of symptoms. The month prior to presentation, the pain became constant and much more severe. He was also diagnosed with type II diabetes. He presented to his local emergency room where computed tomography revealed a large pancreatic mass measuring 5.2 cm x 6.0 cm. There was no obvious evidence of metastatic disease. He was transferred to the UPMC Pancreatic Cancer Center for further evaluation and care. He underwent an ERCP as his liver functions were elevated, with a total bilirubin of 2.0. The ERCP revealed a biliary tract obstruction in the lower third of the common bile duct. A short metal stent was placed. An EUS was performed that revealed a well-circumscribed mass in the pancreatic head measuring 5 cm x 6 cm. There was sonographic evidence suggesting invasion into the portal vein and the superior mesenteric vein. There were several malignant-appearing lymph nodes in the peripancreatic region. Fine needle aspiration of this mass was performed, and cytology was positive for malignant cells. Immunostains were performed and were positive for trypsin and cytokeratin AE1/AE3. The morphological features, along with the immunohistochemical stains, favored acinar cell carcinoma of the pancreas.

Patient was staged as type A borderline resectable based on the vascular involvement and was offered neoadjuvant therapy, with intent to perform advanced pancreaticoduodenectomy with portal vein resection following successful completion of therapy. Based on anecdotal reports of increased response of acinar carcinoma to platinum-based regimens, patient was offered FOLFOX. Patient completed six cycles of FOLFOX and had repeat staging CT. CT revealed greater than 50% reduction in the size of the tumor and no evidence of metastatic disease.

Patient was taken to the operating room where he underwent a minimally invasive robot-assisted pancreaticoduodenectomy. Intraoperative findings were significant for no evidence of metastatic disease or vascular involvement. Postoperative course was uneventful. Patient resumed clear liquid diet on postoperative day 3 and regular diet day 5. His surgical drains were removed and he was discharged to home on day 7. Final pathology revealed a 2 cm acinar cell carcinoma; margins were free of tumor and no lymph nodes were involved.

Patient returned to clinic four weeks postoperatively, with near full return of ADLs and function. Adjuvant chemotherapy was resumed six weeks postoperatively. Patient remains with no evidence of disease.

This case report illustrates several important features of state-of-the-art care for patients with malignancies of the pancreas. First, early multidisciplinary involvement in the care and decision making led to prompt palliation of biliary obstruction and diagnosis. Early involvement of medical oncology allowed the benefit of the most up-to-date chemotherapeutic options for this patient with locally advanced disease. The application of effective neoadjuvant therapy obviated the need to perform portal venous reconstruction, thus allowing minimally invasive approaches to surgical extirpation of the tumor. Lastly, the innovative minimally invasive robotic approach to the pancreaticoduodenectomy led to accelerated recovery postoperatively, which ultimately facilitated resumption of adjuvant chemotherapy. ■

Robotic technology enhances a suite of surgical procedures

The Division of Surgical Oncology at UPMC Cancer Centers is expanding the scope of the Surgical Robotics Program to include the pylorus-preserving pancreaticoduodenectomy (Whipple), a highly technical procedure used to treat a number of tumors of the pancreas, duodenum, and bile duct. During the Whipple, surgeons must reattach vital organs, requiring flexibility and precision that conventional minimally invasive surgery (MIS) — performed using two-dimensional, long-shafted instruments — does not provide.

A. James Moser, MD, and Herbert J. Zeh, MD, co-directors of the UPMC Pancreatic Cancer Center, are two of only a handful of surgeons worldwide who perform the Whipple using robotic surgical technology. The Whipple joins the wide range of surgical robotic procedures now being performed at UPMC Cancer Centers. Surgeons with the Division of Surgical Oncology analyzed the first 30 robot-assisted Whipple resections performed from October 2008 to December 2009, focusing on the safety and short-term operative outcomes. The data showed that the robotic platform outcomes are consistent with the traditional open procedure. ■

Stereotactic radiotherapy: transcending the conventional

Curative treatment for adenocarcinoma of the pancreas has proved difficult to achieve and even palliation of locally-advanced and metastatic disease is challenging. While surgical resection offers the best chance of long-term control in pancreatic cancers, very few patients present with early-stage disease that is amenable to surgical resection. As a result, chemotherapy with or without radiation often is the treatment of choice for patients with unresectable disease, but with modest results and frequently with significant toxicities. Contradictory studies, however, have shown adjuvant radiotherapy to be ineffective or deleterious. Currently available forms of therapy have provided a less-than-expected survival advantage and are frequently associated with significant toxicities.

Improvements in radiological imaging and increasingly sophisticated treatment planning and delivery systems have revolutionized the field of radiation oncology. Modern techniques permit radiation oncologists at UPMC Cancer Centers to escalate the radiation dose to tumors while simultaneously minimizing the dose to normal tissues in ways previously not possible. Stereotactic body radiation therapy (SBRT), defined as treatment of an extracranial lesion with a single or very few (five or fewer) high-dose fractions, is one such application of these technologies, and has shown encouraging results with promising local control rates and very low toxicity for pancreatic cancer patients.

Conventional radiation therapy fields for pancreatic carcinoma have been large, to encompass the primary tumor and regional lymph nodes, and frequently resulted in significant treatment-related toxicities, especially when combined with concurrent chemotherapy. The stomach, small bowel, liver, and kidneys are dose-limiting organs, restricting the ability to give higher doses to the tumor. Standard radiation techniques also subject the patient to six weeks of daily treatments.

SBRT allows delivery of a potent, ablative dose of radiation to tumors of the pancreas in one to three treatments, sparing the surrounding normal tissue and significantly decreasing toxicity. The sophisticated image guidance corrects for motion of tumors with respiration and prospective studies have consistently shown promising local control.

In addition, the overall treatment time is shorter, which may minimize delays in starting systemic chemotherapy.

A study performed by the University of Pittsburgh Cancer Institute (UPCI) confirmed the feasibility, tolerability, and safety of SBRT for the treatment of pancreatic cancer. Local control rates were comparable to those with conventional radiation therapy, with the benefit of shorter treatment time and fewer toxicities. Post-SBRT chemotherapy resumed in fewer than 10 days, which is a great advance in these challenging cases. Moreover, SBRT was completed in one to three days, as compared to the typical five or more weeks required to complete external beam radiotherapy (EBRT). An additional benefit of SBRT is pain relief, which was achieved in more than 80 percent of our patients who presented with pain prior to SBRT. SBRT also was well tolerated in our patient population, with most toxicities being mild.

SBRT is an effective method of treating patients resulting in excellent local control. Current research is aimed at defining the optimal method of combining this treatment with other targeted cancer therapies. The UPCI Department of Radiation Oncology is one of the world's leading centers for stereotactic radiosurgery, and we are actively investigating strategies to convert otherwise unresectable pancreatic patients into operable patients. ■

Open clinical trials

The Pancreatic Cancer Specialty Care Center provides cancer patients with access to the latest therapies and clinical trials through our collaboration with the University of Pittsburgh Cancer Institute, western Pennsylvania's only National Cancer Institute-designated Comprehensive Cancer Center. For more information on clinical trials and eligibility criteria call 888-623-PANC (7262).

UPCI 09-086

PI: Nathan Bahary, MD, PhD

A Phase II, multi-center, double-blind, placebo-controlled, randomized trial of gemcitabine plus GDC-0449 (NSC 747691), a Hh pathway inhibitor in patients with metastatic pancreatic cancer

UPCI 06-035

PI: A. James Moser, MD

A Phase II study of the antivascular endothelial growth factor (Q-VEGF) monoclonal antibody bevacizumab in combination with fixed dose rate (FDR) gemcitabine and rapid-fractionation radiotherapy in the preoperative treatment of potentially resectable pancreatic cancer

UPCI 06-041

PI: Herbert J. Zeh, MD

A Phase I dose escalation trial of wDD-CDSR (double deleted vaccina virus plus CD/SMR) administered by intratumoral injection in patients with superficial injectable tumors

UPCI 09-011

PI: Nathan Bahary, MD, PhD

A randomized Phase III study of weekly ABI-007 plus gemcitabine versus gemcitabine alone in patients with metastatic adenocarcinoma of the pancreas

UPCI 09-122

PI: Herbert J. Zeh, MD

A Phase I/II study of preoperative gemcitabine in combination with oral hydroxychloroquine (GcHC) in subjects with high-risk stage IIb or III adenocarcinoma of the pancreas.

Our multidisciplinary approach to cancer care

Disease-specific Specialty Care Centers

For many patients, the time from diagnosis to the start of treatment can be frustrating and lengthy. To streamline the process for newly diagnosed cancer patients, UPMC Cancer Centers has created the Specialty Care Centers of UPMC Cancer Centers and University of Pittsburgh Cancer Institute — a multidisciplinary model where patients see the entire team of specialists in a concentrated period of time, expediting the development and implementation of a treatment plan. Specialty Care Centers also serve as a resource for referring physicians for second opinions or consultations on challenging cases.

Specialty Care Centers exist for 16 diseases within UPMC Cancer Centers. Newly diagnosed patients work with a nurse coordinator who serves as the point person for the treatment team – reviewing the patient's history and making appropriate appointments based on the patient's needs and the team's recommendations.

Multidisciplinary teams include medical, radiation, and surgical oncologists; disease-specific specialists (such as gastroenterologists, pulmonologists, and neurologists); pathologists and radiologists; as well as ancillary support services including:

- nutrition experts
- behavioral medicine and palliative care
- pain and rehabilitation services
- oncology social workers
- cancer education specialists
- genetic counseling

Once the patient has been evaluated, the treatment team meets to discuss the case and coordinate care with referring physicians. Patients leave with a plan of care in place. "The cornerstone of our approach is the close coordination with the referring physician," says David L. Bartlett, MD, chief, Division of Surgical Oncology, and director, Multidisciplinary Disease Site Clinical and Research Programs. "Once a treatment plan has been developed, the team provides immediate feedback to the referring physician to ensure a complete continuum of care."

An important component of the multidisciplinary model is ensuring that a patient's treatment plan combines innovative and promising clinical trial options with the best standard of care therapies for his or her specific cancer. "Integrating research into treatment plans improves care and ultimately improves outcomes," says Dr. Bartlett.

To learn more about our Specialty Care Centers, to refer a patient, or request a consultation, call **412-647-2811.**

The Pancreatic Cancer Specialty Care Center is available as a resource for second opinions or consultations on your most challenging cases. To learn more about the Pancreatic Cancer Specialty Care Center, to refer a patient, or request a consultation, call 888-623-PANC (7262).