Pancreatic neuroendocrine tumors (pNETs), an uncommon finding, are distinct from pancreatic carcinomas. When pNETs are unresectable and progressive, visceral pain often presents and is challenging to treat. Opioids commonly used for pain control are difficult to implement in this setting because of adverse side effects such as constipation. Neurolytic celiac plexus blocks are indicated in the treatment of visceral pain related to upper abdominal malignancies when opioid analgesia does not provide adequate relief or is contraindicated because of side effects. As a result, this article presents a brief review of pNETs, celiac plexus blocks, associated side effects, and contraindications along with related literature in the context of a case study.

I.S., a 39-year-old African American woman with metastatic pancreatic neuroendocrine carcinoma, presented to the emergency department in January 2009 with abdominal pain, nausea, vomiting, and diarrhea. A computed tomography scan of the abdomen revealed a mass at the pancreatic tail and multiple hepatic lesions. In February 2009, a fine needle aspiration of the pancreatic mass revealed a neuroendocrine neoplasm. As per National Comprehensive Cancer Network ([NCCN], 2010) guidelines, an octreoscan was performed. The results showed an octreotide-avid tumor within the pancreatic tail, with multiple hepatic lesions and possible involvement in the right inguinal lymph node. Many neuroendocrine tumors have receptors with a high affinity for somatostatin. An octreoscan uses a radiolabeled somatostatin analog, octreotide, to detect tumors that are most likely to respond to somatostatin therapy ([NCCN], 2010). A liver biopsy confirmed metastatic disease. Further testing showed an elevated chromogranin A, which aids in the diagnosis of a functioning neuroendocrine tumor. I.S.’s past medical history included bipolar disorder. Her family history is noncontributory.

In March 2009, I.S. began treatment including monthly octreotide injections of 30 mg. She had been taking 4 mg dilaudid for pain as needed, with minimal symptom relief. She was converted to 20 mg oxycodone extended release with 5 mg oxycodone immediate release for breakthrough pain. In April 2009, her pain was not relieved and the oxycodone extended release was titrated to 40 mg, contributing to a significant improvement in her pain control. In October 2009, I.S. was found to have progressive disease with worsening pain. The octreotide dose was increased to 40 mg, and she was placed on oxycodone extended release 80 mg twice daily with oxycodone immediate release 5 mg every four hours as needed for abdominal pain.

I.S. again presented with increased abdominal pain in January 2010. Repeat imaging was consistent with progressive disease, and her oxycodone extended-release dosage was increased to 160 mg twice daily. Because of her worsening abdominal pain secondary to a pancreatic neuroendocrine tumor (pNET), I.S. was evaluated for a neurolytic celiac plexus block (NCPB) for pain control.

**Pancreatic Tumors**

Malignant pNETs are an uncommon finding that comprise only 1% of all malignancies diagnosed in the United States, with an incidence of 2–3 in 100,000 people per year (Grande & Haller, 2009). The tumors vary widely clinically and biologically. This heterogeneity is demonstrated in prognosis, treatment, histology (poor-to-well differentiated), and stage (I–IV) (Chadha et al., 2009). Although pNETs generally are sensitive to chemotherapy, some well-differentiated tumors produce only a 30% response rate with systemic therapy (Chadha et al., 2009). About 46%–93% of patients with pNETs develop hepatic metastasis, which often involves a large part of the liver before becoming symptomatic (Hung, Chang, Lee, & Tien, 2007).

When possible, surgical resection of the primary and metastatic lesions is preferred (Chadha et al., 2009). The first-line management of locoregional unresectable and metastatic disease is octreotide, a somatostatin analog ([NCCN], 2010). Somatostatin...
analogs help to reduce symptoms (e.g., flushing, diarrhea) and related morbidity associated with the excessive hormonal secretion in functionally active pNETs (Chadha et al., 2009). Long-term studies have shown somatostatin analogs to be safe and well tolerated while producing tumor stabilization in 30%–70% of patients for months to years at a time (Chadha et al., 2009). In contrast, adenocarcinoma of the pancreas has a bleak outcome with only 4% of patients living five years or more after diagnosis (Sauerland, Engelking, Wickham, & Pearlstone, 2009).

### Abdominal Pain

Unfortunately, when complete surgical resection is not an option, many patients experience abdominal pain despite treatment with octreotide. Severe pain may dramatically affect the quality of life of patients as well as their families. The sympathetic nerves, which innervate the pancreas, run through the celiac plexus (Kaufman et al., 2010). The celiac plexus innervates the abdominal viscera, including the pancreas, liver, gallbladder, adrenal gland, and kidney, spanning from the gastroesophageal junction to the splenic fissure of the colon (Polati, Luzzani, Schweiger, Finco, & Ischia, 2008) (see Figure 1).

Pancreatic cancer pain is likely multifactorial and often attributed to increased intrapancreatic pressure, pancreatic ischemia, fibrosis, pseudocysts, neurogenic inflammation, and invasion of cancer in the pancreatic perineural space (Kaufman et al., 2010). Patients with upper abdominal malignancies, particularly pancreatic cancer, often suffer from visceral pain. Originating from the organs, visceral pain is a poorly localized, diffuse, and deep pain that may be described as cramping or splitting (McMenamin, 2011). Visceral pain is notoriously difficult to treat with pharmacotherapy alone, and early intervention is required for optimal pain control. The Pain Relief Ladder by the World Health Organization (WHO, 2010) is a three-step guide to the treatment of cancer pain, starting with nonopioids (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], aspirin, paracetamol) and increasing to strong opioids (e.g., morphine) in a stepwise fashion. WHO (2010) stated that interventions to appropriate nerves, such as NCPB, may provide further relief when pharmacotherapy is not entirely effective.

### Neurolytic Celiac Plexus Blocks

To identify patients who will benefit from an NCPB, a diagnostic block is performed initially. In a diagnostic block, a local anesthetic is injected into the celiac plexus region to inhibit neurotransmission without ablation or permanent destruction. Several methods can be used to perform NCPB, including computed tomography, fluoroscopy, endoscopic ultrasound, percutaneous ultrasound, and direct visualization (Mauck & Rho, 2010).

This procedure provides a short duration of pain relief and is predictive of who may benefit from further neurolysis. An NCPB uses a sclerosant agent (e.g., ethanol, alcohol) to ablate the neurons at the celiac plexus, producing a longer duration of pain relief because of the permanent nature of neurolysis, proper patient selection is important.

Contraindications to NCPB include uncorrected coagulopathy, localized infections, intra-abdominal infections, and sepsis (Mauck & Rho, 2010). Unopposed parasympathetic activity after the NCPB may result in diarrhea; therefore, bowel obstruction is a contraindication (Mauck & Rho, 2010). The most common adverse events following NCPB are localized pain (96%), diarrhea (44%), and hypotension (38%), all of which are transient (Mauck & Rho, 2010). Diarrhea and hypotension usually resolve in one to two days, and the pain typically does not require intervention (Mauck & Rho, 2010). Patients who are chronically constipated by opioid use often welcome diarrhea (Mauck & Rho, 2010). Major complications (e.g., pneumothorax, pleuritic chest pain, hematuria, neurologic complications) are rare, with a reported rate of 2% (Tam & Ahrar, 2007).

### Literature Review

Limited literature is available regarding pNETs and NCPBs. However, several studies focusing on pancreatic cancer or upper abdominal malignancies have provided information related to pNETs (de Oliveira, dos Reis, & Prado, 2004; Erdek, Halpert, Fernandez, & Cohen, 2010; Jain, Shrikhande, Myatra, & Sareen, 2005; Polati et al., 2008; Wong et al., 2004). The results should be interpreted with caution because the disease trajectories of pancreatic cancer and pNETs are very different, with pancreatic cancer being more aggressive.

Controversy exists regarding the point in the disease trajectory when NCPB should be considered. Intuitively, one may hypothesize that NCPB will be less effective in advanced disease when the tumor is larger, more invasive, and infiltrating the celiac plexus or surrounding structures. In a randomized, controlled trial, de Oliveira et al. (2004) compared the effectiveness of NCPB performed in early or late phases of abdominal or pelvic cancer pain (determined by opioid consumption) versus pharmacotherapy for pain management alone. The early block group included patients who used NSAIDs or oral morphine of 90 mg per day or less, whereas the late block group included patients who used NSAIDs or oral morphine of 90 mg per day or more. A third
group maintained pharmacotherapy until pain relief was achieved. For both the early and late groups, an oral opioid was available after the procedure at an adjusted dose for pain relief as needed. The results showed that patients in both the early and late block groups experienced significant pain reduction, decreased opioid consumption, fewer opioid-related side effects, and better quality of life versus the pharmacologic group. The finding suggests that NCPBs, in combination with pharmacotherapy, may be considered throughout the disease trajectory. However, intervention during early phases of cancer pain may provide a more timely improvement in quality of life and freedom from opioid-related side effects versus intervention in later phases.

Polati et al. (2008) performed a prospective, randomized, controlled trial of 100 patients with unresectable pancreatic cancer and uncontrolled pain. Patients were either randomized to NCPB or a control group with an anaesthetic celiac plexus block (without ablation) plus analgesic drug therapy. Patients in the NCPB group had significantly higher quality of life, less analgesic drug consumption, and better pain control.

In contrast, a widely cited and well-designed controlled trial by Wong et al. (2004) analyzed 100 patients with unresectable pancreatic cancer who were randomized to receive either NCPB or systemic analgesic therapy alone with sham injection. NCPB provided improved pain relief compared to opioids alone but failed to show statistically significant improvement in quality of life or survival.

Similarly, Jain et al. (2005) evaluated the role of NCPB versus opioid analgesics and NSAIDs on pain, quality of life, performance status, and opioid consumption. The sample included 100 patients with upper abdominal malignancies and uncontrolled pain. Despite an overall improvement in quality of life in the NCPB group, the study failed to demonstrate statistical significance in quality of life, whereas pain, morphine consumption, and opioid-related side effects were significantly reduced.

Erdek et al. (2010) performed a retrospective clinical data analysis on 44 patients with terminal visceral cancer pain, mostly pancreatic, who failed conservative pain control measures. The study analyzed 50 NCPB procedures for factors associated with a positive outcome such as lower opioid use and absence of sedation. A lower opioid dose prior to the procedure was associated with a positive outcome. Variables that may have affected the results included higher tumor burden and hyperalgesia in patients who did not have improved pain control (Erdek et al., 2010).

Conclusions

NCPB is an acceptable intervention for visceral cancer pain associated with pNETs. This treatment may decrease pain, opioid consumption, and opioid-related side effects. Patients should be assessed frequently throughout their disease course for adequate pain management, opioid-related side effects, and quality of life. In the case of I.S., an evaluation for NCPB was appropriate given her progressive visceral pain. Because of the complex nature of pancreatic pain, a multidisciplinary approach to pain management may be the only way to alleviate suffering effectively. Although pNETs are not as aggressive as pancreatic cancers, pain management remains paramount, especially in unresectable, metastatic disease.

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