Rare, Uncommon, and Unusual Complications After Pancreaticoduodenal Resection

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INTRODUCTION

The perils of pancreatic surgery, in particular pancreaticoduodenal resection (PDR), are well known to physicians, patients, and their families. Most complications are related to the operation. Vascular injuries or enterotomies usually occur during dissection. Fistulas, abscesses, and their sequelae follow anastomotic breakdown. Rarely, complications are systemic from altered immunity or changes in the cardiovascular system even when surgery was apparently uneventful for both the surgeon and the

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patient. This article reviews rare (case reports), uncommon (5%–10% incidence), and unusual (<5%) complications of PDR.

RARE COMPLICATION (CASE REPORTS)

Despite a long experience with PDR and its complications, 3 complications not technically related to PDR stand out as singularly unusual events: babesiosis, pituitary apoplexy, and transfusion-related acute lung injury (TRALI). The first 2 are discussed in detail and the case TRALI is summarized.

**Babesiosis**

Postoperative anemia is common in patients after PDR. Usually reflective of intraoperative blood loss or continued oozing from small vessels, it is usually self-limited and successfully treated with transfusion and correction of any coagulopathies. Post-PDR patients, however, in particular those who have undergone splenectomy, are a unique group of immunosuppressed patients susceptible to unusual blood-borne pathogens.

A 46-year-old healthy man from Macedonia underwent pancreaticoduodenectomy for pancreatic adenocarcinoma. He had a microscopically positive resection margin at the pancreatic tail and a completion total pancreatectomy with splenectomy. Postoperatively, the patient suffered from acute blood loss anemia and received a transfusion of 1 unit of packed red blood cells. He contracted mild *Clostridium difficile* diarrhea and was treated with vancomycin with resolution. He received all postsplenectomy vaccinations 2 weeks postoperatively. The patient was readmitted 6 weeks postoperatively and found to have new bilateral lower extremity deep vein thrombosis. While on anticoagulation, he developed anemia, altered mental status, fever, malaise, tachycardia, leukocytosis, and elevated transaminases. He again received a transfusion of 2 units of packed red blood cells without appropriate increase in hemoglobin levels. Blood smears demonstrated hemolysis, intraerythrocytic parasites and Maltese cross forms consistent with *Babesia microti* infection. This was confirmed with polymerase chain reaction (PCR) testing. The patient underwent urgent exchange transfusions and received antibiotics (quinidine and clindamycin) with decreasing parasitemia on subsequent blood smears. Testing of the index transfused unit of red blood cells showed *Babesia microti*. The donor was recalled for testing. He was clinically asymptomatic but had positive serology for the organism. The patient had a prolonged hospital course and expired 2 months postoperatively from recurrent parasitemia and vancomycin-resistant enterococcal bacteremia. This is the first report that the authors know of a patient who developed transfusion-transmitted babesiosis after pancreatectomy and splenectomy. This patient was young and previously healthy and expired within 2 months after surgery. The synergistic effects of babesiosis, asplenia, and pancreatic cancer were responsible for a fulminant process with early recurrence and death.

Babesiosis is a rare blood-borne illness caused by infection with the intraerythrocytic parasite *Babesia*. This global disease, although uncommon in the United States, is seen more frequently in parts of Europe and the developing world, where it is transmitted most commonly via tick bites. Transfusion-related babesiosis is accountable for the vast minority of cases; however, it remains an underappreciated etiology with increasing incidence. Of the 150 reported cases, 75% were reported after 2000. The parasite survives standard blood product processing and storage and there is currently no screening protocol for donor detection. Laboratory tests demonstrate hemolytic anemia; however, key to establishing the diagnosis are a blood smear with intraerythrocytic parasites and PCR testing. Although not necessarily clinically significant in all patients, the immunocompromised host is especially susceptible,
particularly patients after splenectomy. Suspicion should be increased in immunosuppressed patients with persistent anemia and signs of hemolysis. In immunocompetent patients, symptomatology may be mild with a nonspecific febrile illness. Progression to multisystem organ failure, disseminated intravascular coagulation, and death, however, have been reported in 5% to 6.5% of immunocompromised patients. Treatment consists of atovaquone and azithromycin or quinine and clindamycin for 7 days to 10 days. Severe cases may require more prolonged courses and repeat exchange transfusions. Patients who have undergone PDR are a susceptible, immunosuppressed group who are more likely to receive blood transfusions postoperatively. Additional screening measures may need to be considered in transfusing these patients.

**Pituitary Apoplexy**

A 64-year-old previously healthy woman presented for evaluation of abdominal discomfort and weight loss. Evaluation revealed a pancreatic mass suspicious for cancer, which was confirmed by biopsy. After a thorough evaluation and discussion with her and her family, she underwent a PDR for pancreatic cancer. The procedure was uneventful, with 3 hours of operative time, less than 300 mL of estimated blood loss, and no major blood pressure fluctuations. She became hypertensive in the recovery room and complained of a frontal headache. On examination, she had ophthalmoplegia with medial and lateral gaze palsies, right eye ptosis, and a right dilated nonreactive pupil. An MRI demonstrated a hypoenhancing pituitary mass with displacement of the cavernous segments of bilateral internal carotid arteries with mass effect on the optic chiasm. She underwent successful trans-sphenoidal pituitary resection the next day with complete resolution. She remains symptom-free, other than a mild proptosis 6 months later. Pathology was notable for a pituitary adenoma, gonadotroph cell–type expressing chromogranin, and leutenizing hormone. It is likely that blood pressure swing contributed to the etiology in this patient. Although there are other reports of pituitary apoplexy triggered after cardiac, orthopedic, head and neck, and laparoscopic abdominal surgeries, this is the only case report of pituitary apoplexy after pancreatic surgery.

Pituitary apoplexy was first reported by Bailey in 1898 as a cluster of symptoms, including altered mental status, headache, nausea, vomiting, and visual changes associated with hormonal dysfunction. An incidence of 0.6% to 9.1% in symptomatic patients compared with up to 25% in asymptomatic patients has been reported. The etiology remains unclear; however, it is commonly believed that tissue expansion without increase in blood flow leads to areas with tenuous blood supply. A lack of autoregulation from the transmitted systemic and intracranial pressure fluctuations during surgery can lead to ischemia with subsequent hemorrhagic necrosis. Pancreatic surgery is often associated with significant fluid shifts and hemodynamic changes. Although the surgery was uneventful, presumably these physiologic fluctuations led to a hemorrhagic infarct into a previously clinically silent pituitary adenoma. A high index of suspicion for pituitary apoplexy in patients with typical symptomatology facilitates expeditious diagnosis and prompt treatment to prevent permanent visual and neurologic deficits.

**Transfusion-Related Acute Lung Injury**

TRALI is a serious and potential fatal complication of blood product transfusion. The diagnosis is made by acute lung injury occurring within 6 hours of completed transfusion of blood or blood products, no preexisting lung injury, and no other temporarily associated risk factors for acute lung injury.
A platelet transfusion was suggested by anesthesia and given before induction of anesthesia. The PDR was uneventful, additional transfusions were not necessary, and the procedure was near completion within 3 hours when there was difficulty ventilating and oxygenating the patient. A pneumothorax was ruled out as were other airway issues. After transfer to the ICU, a diagnosis of TRALI was made and a very difficult 6 days to 7 days of ventilatory support and critical care ensued until the episode waned and then resolved. TRALI most often follows platelet transfusion but the incidence is highest after blood transfusion, where the incidence is 1/12,000 transfusions, and is usually self-limiting and resolves without steroids within 48 hours to 96 hours. Pathophysiology involves patient factors, including preexisting inflammatory conditions that cause pulmonary endothelial damage and capillary leak triggered by a transfusion containing HLAs, human neutrophil antibodies, or biologically active lipids. A major abdominal procedure like PDR can lead to an inflammatory state that predisposes patients to TRALI after platelet transfusion. Current risk-reduction approaches include screening against donors who may be alloimmunized followed by antibody testing in selected donors.

UNCOMMON COMPLICATIONS (5%–10% INCIDENCE)

Visceral Artery Pseudoaneurysms

Delayed postpancreatectomy hemorrhage is a complication in 4% to 16% of PDR, with mortality rates as high as 50%. Hemorrhage within the first 72 hours after PDR is usually due to venous bleeding from portal-mesenteric tributaries or small arteries and, if not tamponaded by surrounding viscera or clot, may require re-exploration for evacuation and hemostasis. Venous bleeding is low pressure and more apt to stop spontaneously than arterial bleeding.

Late postoperative hemorrhage (1–4 weeks) is initiated by a pancreaticojejunal fistula followed by sepsis from intestinal and biliary bacteria, a pseudoaneurysm, and then hemorrhage. It is the local sepsis that weakens the vessel wall and leads to formation of the pseudoaneurysm. The gastro-duodeno-jejunal artery stump is most often involved, followed by the hepatic, splenic, and intestinal branches of the superior mesenteric artery. An initial transient sentinel gastrointestinal or intraperitoneal bleed(s) heralds subsequent hemorrhage hours to days later. Unanticipated delayed hemorrhage should prompt a computed tomography angiogram (CTA) (diagnostic sensitivity >95%). If the amount of contrast used would limit 2 studies and suspicion and experience is high, an angiogram should be done directly. Stenting or embolization of the bleeding pseudoaneurysm is indicated and very successful. Surgical intervention should be infrequently needed because of the great success with angiography and experience that local sepsis persisting after surgery may cause rebleeding and the need for repeat angiography. The reported increased mortality with surgery reflects the critical status of at risk elderly patients with continued bleeding (47% vs 22%, P = .02). A multidisciplinary approach, particularly with experienced interventional radiologists, decreases the need for surgery and improves outcomes.

Chylous Ascites

Postoperative chyle leak occurs in 1.3% to 10.8% of patients after pancreatic resection and is due to injury of a major lymphatic channel during an extended lymphadenectomy. Often benign and self-limiting, larger leaks may need occasional oral and intravenous support with medium chain triglycerides, fluids, and electrolytes. Milky
drainage fluid with elevated drain triglycerides is diagnostic. Persistent high-volume drainage after PDR may require intravenous fluids and octreotide. Surgical ligation of the cisterna chyli or thoracic duct is infrequently needed. This is a complication best avoided because extended or radical lymphadenectomy adds nothing to survival of pancreatic cancer and is difficult to justify.

**Cholangitis**

Biliary strictures occur in 3% to 13% of patients after PDR. Although attributed to T-tube use or small ducts, the authors’ experience is they are rare, are ischemic, and present 8 to 10 or more years after PDR. Stenting and dilatation, either percutaneous or endoscopic, has been successful treatment. Surgery should rarely be needed.

**UNUSUAL COMPLICATIONS (2%–5% INCIDENCE)**

**Marginal Ulceration**

Today gastrojejunal ulceration or marginal ulcers (MUs) after PDR should be unusual. MU after duodenal ulcer surgery was a common complication until H₂-receptor antagonists were introduced. MUs after PDR were uncommon because survival was limited after PDR, and most patients were elderly with hypochlorhydria or achlorhydria, an unlikely population for duodenal ulcers. After distal gastric resection, ulceration can occur on the gastric or jejunal side of the gastrojejunostomy. Ulcerations on the gastric side are due to alkaline reflux and emesis of bile is common. Symptoms are not alleviated by antiulcer therapy. Ulcerations on the jejunal side are peptic in origin and antiulcer therapy relieves symptoms. As indications for PDR were extended to pancreatitis and cystic lesions and younger patients underwent PDR, more MUs were encountered. In 2014, the reported incidence was 2.5% after PDR and 2% after pylorus-preserving PDR. With prophylactic antisecretory medications and compliant patients, rates of ulceration are as low as 1.4%.

**Afferent Loop Syndrome**

Afferent loop syndrome (ALS) after PDR is due to a partial or complete mechanical obstruction of bile, pancreatic juices, partially digested food, and in a redundant afferent jejunal limb. ALS is usually a late and chronic complication after PDR, and the higher-pressure fluid filled distal limb untwists and rapidly empties often into the stomach and jejunum, which is relieved by emesis. Acute ALS can cause fluid distention in the afferent loop, and dehiscence of a fresh pancreatic or biliary anastomoses or disruption of the limb. Acute ALS has been recognized after gastric resection with a loop gastrojejunostomy, but an acute postoperative presentation is unusual after PDR. Five cases after PDR were cited. All required reoperation with satisfactory outcome. This is best avoided by a nonredundant limb.

**Ischemic**

The pancreatic head is perfused by the celiac axis and the superior mesenteric artery via the gastroduodenal artery and pancreaticoduodenal arcades. Ischemic complications are exceedingly rare (<2%) given the frequency of PDR and its elderly population. Significant celiac or superior mesenteric artery stenoses is seen in 11% of elderly patients and when diagnosed should be evaluated and stented if necessary preoperatively. The consequences of bowel necrosis, anastomotic dehiscence, mesenteric infarction, or hepatic failure and sepsis have a high mortality rate.
This is a situation best avoided by a thorough review of all cross-sectional imaging before surgery is considered.\textsuperscript{44–46}

SUMMARY

Complications after PDR occur in at least 30\% of patients. Nearly all early complications are a direct result of an intraoperative event, dissection, or anastomoses. By far the most common complications result from a pancreatic enteric leak or fistula. This accounts for the most serious morbidities, sepsis, pseudoaneurysms, and hemorrhage. Rarely, complications are systemic and stem from a compromised or immunosuppressed host or changes in blood flow or pressure during or after surgery. Three rare complications, which were shocking to the authors and were serious or fatal to patients are described: babesiosis, TRALI, and pituitary apoplexy, 2 of which were caused by transfusion of blood and platelets. PDR is a significant operation with serious consequences, and decisions on selection of candidates and safe operations should be thoughtful and always in surgeons’ minds.

REFERENCES

Complications After Pancreaticoduodenal Resection


