The natural history of pancreatic acinar cell cystadenoma: Is resection better than surveillance? An update to a case report from 2010

David G. Darcy*, Dominique Jan
Department of Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, New York, NY, USA

A 9-year-old boy was found to have a large pancreatic mass during a routine laparoscopic appendectomy and was referred to a tertiary-care center. In a previously described report, the patient underwent a laparoscopic incisional biopsy and was diagnosed with a pancreatic acinar cell cystadenoma (PAC) [1]. The lesion was followed with serial MRIs, and the cystic portion of the pancreas was stable and asymptomatic.

Eighteen months later the patient developed symptoms of early satiety, weight loss, and epigastric pain which were interfering with his school and social activities. He visited several tertiary-care centers in multiple states, exploring the possibility of resection and pancreas transplantation. He presented to our institution with intermittent obstruction due to extrinsic duodenal compression, and was dependent on total parenteral nutrition (TPN). In March of 2010, the patient underwent evaluation for partial pancreatic resection to relieve his obstructive symptoms.

1. Clinical course

The patient was hemodynamically normal upon presentation, with a weight of 39.4 kg. He was somewhat gaunt in appearance, with a PICC line in place, a serum albumin of 4.3 g/dL, and an HgA1c of 5.6%. Our patient was evaluated by the pediatric genetics team for a possible diagnosis of von Hippel-Lindau (VHL) disease. This autosomal dominant disease is rare; however, it can manifest with simple cysts, and serous cystadenomas of the pancreas. While approximately 3 out of 4 patients with VHL will have pancreatic cysts, they have not been reported to cause extrinsic compression and gastrointestinal obstruction. Our patient did not have any genetic mutations that have been associated with VHL. The pediatric endocrinology service was consulted for perioperative management of insulin while planning for a partial pancreaticoduodenectomy.

During exploratory laparotomy in April 2010, the entire body and tail of the pancreas were grossly composed of cystic structures; however, the head and uncinate process were composed of normal-appearing tissue. The head and uncinate process derive from a distinct ventral bud during pancreatic development, and were preserved. A distal pancreatectomy was performed, and the omentum having been resected, a loop gastrojejunostomy was created to improve gastric emptying. The patient resumed enteral feeding and was discharged without need for TPN. On pathology review, the surgical specimen was consistent with his prior diagnosis of PAC (Fig. 1). In June 2010, the patient returned with bilious vomiting. Upper gastrointestinal series showed a patent duodenum with a partially-obstructed gastrojejunostomy. The gastrojejunostomy was reversed, and normal bowel continuity having been restored, the patient was discharged on regular diet.
After almost two years off TPN and tolerating diet, the patient returned in May of 2012 with weight loss, early satiety, and epigastric pain. Abdominal MRI demonstrated progressive cystic disease of the head and uncinate process of the pancreas (Fig. 2). After multidisciplinary discussion, the patient was taken back to the operating room in July 2012, where a pylorus-sparing pancreaticoduodenectomy was performed. The resected specimen contained virtually no normal pancreatic tissue, and had no evidence of malignant transformation (Fig. 3).

An insulin pump and oral pancreatic enzyme replacement were initiated. The patient has subsequently done well, followed in the last two years by our hospital. He maintains a normal diet with 3 meals a day plus snacks before exercise, with bolus insulin coverage for meals. His HgA1c is 5.9%, and his pump is managed by the patient’s parents in concert with pediatric endocrinology every three months. He takes pancreatic enzyme replacement with meals and he does not suffer from steatorrhea. He is doing well in school, and has begun playing baseball, with attention to avoid hypoglycemic episodes and with glucagon on hand at practice. His weight has steadily improved, 47 to 50 to 53 kg at his most recent clinic visits, and is in the 45th percentile.

2. Discussion

Our patient was presented previously as the youngest published case of PAC, and was initially managed conservatively with serial MRI. Our patient already had a biopsy-confirmed diagnosis, and normal HgA1c denoting functioning islet cells; the decision to intervene surgically was methodically investigated and carefully planned using a multidisciplinary approach. During his initial surgery for duodenal obstruction, the uncinate process and head of the pancreas appeared normal and they were not resected, with the hope of preserving pancreatic function. Subsequent progression of cystic disease, duodenal obstruction, TPN dependence, and weight loss ultimately necessitated a completion pancreaticoduodenectomy. A pylorus-sparing resection was performed because the indication was not malignancy, and for the possible benefits of intact gastric physiology with less dumping syndrome in the setting of diabetes. Outcomes of pylorus-sparing versus a classic pancreaticoduodenectomy are mixed in adult patients, however, in pediatric patients there is no clinical data and cases are rare. This case represents the stepwise management and considerations for PAC in an adolescent male.

Pancreatic acinar cystic lesions of the pancreas were first described as a rare cystic neoplasm by Albores-Saavedra in 2002 [2]. PAC are found mostly in middle-aged adults (mean age at diagnosis of 47-years-old), and they can be discrete or encompassing the entire gland [2–4]. Most series have an overwhelming predominance of female patients, however, our patient and occurrence in other male patients have been reported (REF Singhi 7/8, Zamboni 7/10). In a review of 10 cases, the most common indication for surgery was pain with findings of cystic neoplasm on CT scan; the other 4 had PAC found incidentally upon resection for other tumors [4]. PAC can be distinguished from branch-duct intraductal papillary mucinous neoplasms (IPMN) with high sensitivity and specificity based on four radiological criteria (CT or MRI) [5]. H&E analysis of our patient’s pathology lacked mitoses, and the acinar cells lining the cysts lacked atypia. Affected cells can be differentiated from normal acinar cells by staining positive for CK7 [6], however, this was not performed on our specimen.

The origin of PAC has not been fully elucidated. Albores-Saavedra noted cysts lined with duct-like cells representing metaplastic change [2]. Chatelain considered it to be a cystic variant of acinar cell adenomas, unrelated to normal pancreatic acini [7]. In opposition, Gumus found cysts continuous with normal pancreatic acini, without discrete lesions; therefore, they suggested the description “acinar cystic transformation” [8]. Albores-Saavedra noted fibrosis of surrounding pancreatic tissue, while Zamboni noted discrete lesions without histopathologic changes in the adjacent tissue [4].
In our patient, the original specimen was consistent with the findings of Chatelain, with a diseased pancreatic body and tail, and a normal appearing head and uncinate process. Ultimately, his disease was progressed to diffuse involvement, consistent with the description by Gumus, with almost complete replacement of normal tissue. Had we suspected it would progress, we would have done a complete resection and spared the patient two additional surgeries.

More recently genetic investigations by Khor et al. using array comparative genomic hybridization found copy number variations across 11 different chromosomes, suggesting a neoplastic process [9]. However, Singhi et al. found random chromosome X inactivation in 5 of 7 samples, denoting a polyclonal population without evidence of a neoplastic genome [10]. Genetic testing ruled out VHL syndrome in our patient, however, that diagnosis was seriously considered as it can have cystic disease of the pancreas including serous cystadenomas and neuroendocrine tumors.

3. Conclusion

While there are no published cases of PAC with malignant transformation necessitating resection, this case demonstrates a role for surgical management due to progressive cystic change and extrinsic compression. This patient was appropriately diagnosed and managed using minimally invasive techniques, and followed closely with MRI surveillance, with which we completely agree [1]. However, progression of our patient’s PAC to encompass the entire gland necessitated complete pancreaticoduodenectomy, leaving him dependent on replacement enzymes and an insulin pump. Continued development of therapeutic modalities such as pancreatic islet transplant could offer intrinsic replacement for this patient; currently he is followed closely by pediatric endocrinology, takes daily pancreatic enzyme replacement, and has a normal social life using an insulin pump. Fortunately, this rare lesion can be distinguished from VHL and IPMN through genetic testing and CT/MRI imaging. Ultimately, treatment should be based on symptoms, with serial MRI imaging for a stable lesion, and multidisciplinary planning should surgical intervention become necessary. Total pancreaticoduodenectomy was the final treatment in our patient, although whole pancreas or islet transplant are available if necessary in the future.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

References