Should a biopsy be obtained prior to surgery in children with pancreatic masses? A case report describing the difficult journey of an adolescent undergoing treatments for a rhabdomyosarcoma of the head of the pancreas following primary pancreaticoduodenectomy for a suspected solid pseudopapillary tumor

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Abstract

Pancreaticoduodenectomy, a procedure rarely performed in children, can lead to significant morbidity. Rhabdomyosarcoma is the most frequent soft tissue sarcoma in pediatrics. Treatment consists of chemotherapy, while local control can be achieved through either surgery, radiotherapy or both. In this brief report, we describe the case of a 15-year-old adolescent who underwent a pancreaticoduodenectomy for a presumed solid pseudopapillary tumor of the head of the pancreas, ultimately diagnosed as a fusion-positive rhabdomyosarcoma. We review the ensuing severe side effects of the treatments, and discuss the role of biopsies for pancreatic tumors in pediatrics.

Introduction

Pancreaticoduodenectomy (PD), infrequently performed in children due to the rarity of pancreatic tumors in this age group, can lead to significant morbidity in 30 to 40 % of patients, including exocrine and endocrine pancreatic deficiency, dumping syndrome, delayed gastric emptying, diarrhea, growth retardation, pancreatic leaks and strictures[1,2]. Pancreatoblastoma and solid pseudopapillary tumors (SPN) are the most frequent pancreatic tumors in the first and second decades of life, respectively[2]; numerous other malignant tumors have been reported, however.[1–5]

Rhabdomyosarcoma (RMS), the most common soft tissue sarcoma in children and adolescents, rarely presents primarily in the gastrointestinal tract. RMS has been described involving the biliary tract, the liver or the duodenum[1,3,6–11]. Two cases of a primary pancreatic RMS have been reported, one of pleomorphic histology and one of unspecified subtype[12,13].

This article describes the first case of fusion-positive RMS arising in the pancreas of an adolescent patient, details the severe side effects she had to overcome after PD and during treatments, and explores the role of biopsy for pancreatic tumors in pediatrics.

Case report

A 15-year-old female had been investigated for a three-week history of fatigue, epigastric and right upper quadrant pain, non-bilious vomiting, progressive jaundice and weight loss of 15 pounds. As liver enzymes and lipase were elevated, a presumptive diagnosis of viral hepatitis was made. After worsening of her symptoms, an ultrasound was obtained, showing a pancreatic mass, leading to her transfer to our institution.

Initial investigations demonstrated elevated ALT (360 mmol/L; normal 1–40), AST (464 mmol/L; normal 8–32), GGT (637 U/L; normal 8–35), total (104 ?mol/L; normal 0–24) and direct (72 ?mol/L; normal 0–7) bilirubin and lipase (1329 U/L; normal 0–60); CBC, albumin, INR and PTT were normal. An MRI showed a well circumscribed 3.3 × 2.3 × 2.5 cm mass, most consistent with SPN (Figure 1), leading to mass effect on adjacent structures, with dilation of the bile duct, cystic duct, intrahepatic biliary radicles and pancreatic duct. There were no lymph node or other metastases noted.

A stent was inserted in her common biliary duct through an ERCP, temporarily resolving her symptoms. She subsequently underwent a PD with retroperitoneal lymph node dissection. Pathology was consistent with a FOXO1 fusion-positive RMS. The tumor arose from the pancreatic parenchyma and invaded the duodenum, with no involvement of the biliary tract (Figure 2). One of three lymph nodes was positive for disease. She was ultimately diagnosed with a stage III, group II fusion-positive RMS. Treatment consisted of cycles of vincristine, dactinomycin and cyclophosphamide (VAC) alternating with vincristine and irinotecan (VI)[14]. Radiation therapy completed local control.

Early in her treatment, she developed debilitating upper and lower gastrointestinal symptoms. Initially, they presented as abdominal discomfort, early satiety, nausea and vomiting. Use of antiemetic agents, acid suppression therapy, gastroprokinetic agents and antibiotic therapy did not alleviate these symptoms. Upper gastrointestinal imaging showed no strictures or stenosis. She was diagnosed as having delayed gastric emptying secondary to the PD.

She later developed diarrhea, which did not improve with loperamide. Investigations showed exocrine pancreatic insufficiency. Despite pancreatic enzyme replacement, she had long-standing grade 3 diarrhea, with bowel movements exceeding seven per day. This was thought to be multifactorial, including exocrine pancreatic insufficiency, irinotecan toxicity, post-radiation enteritis and C. difficile infection. We discontinued VI cycles, and she thereafter received only VAC chemotherapy. The symptoms resolved over a period of months.

At diagnosis, her BMI was 20.7 (50^{th} percentile). Through her treatment, her BMI declined rapidly, secondary to insufficient caloric intake and malabsorption due to ongoing nausea, vomiting and diarrhea. Once her BMI dropped to 15.7 ($<3^{\text{rd}}$ percentile), a nasojejunal (NJ) feeding tube was inserted, which helped increase her BMI to 16.3 (3^{rd} percentile). After a few weeks, she discontinued her NJ feeds and went on a regular diet with supplements. Her BMI again declined to 15.2, leading to a prolonged hospitalization. Her weight stabilized with NJ feeding and total parenteral nutrition (TPN). An increase in her symptoms led to discontinuation of feeds and prolonged TPN requirements. Her BMI ultimately reached a low of 13.7, and she refused any further investigations and hospitalizations.

Following completion of therapy, her abdominal symptoms improved, and her BMI increased to 18. Eighteen months later, she developed metastatic recurrence in both breasts, the mediastinum and right axilla. She declined further systemic therapy, and died five months later from progressive disease.

Discussion

This is the first case report describing a primary pancreatic fusion-positive RMS. The treatment of our patient lead to severe side effects that considerably affected the patient's health and quality of life.

In retrospect, while a diagnosis of SPN was strongly suspected, we wonder if obtaining a biopsy to confirm the diagnosis at presentation could have changed our treatment approach and decreased morbidity. Limited evidence can be found regarding initial diagnostic approaches for pediatric pancreatic tumors. An Italian national cooperative initiative created diagnostic and therapeutic recommendations for malignant pancreatic lesions in children. These guidelines state that primary excision should be attempted if complete and non-mutilating resection is feasible. If not, a biopsy should be attempted to direct chemotherapy, hoping for

tumor shrinkage prior to subsequent resection, including PD[15]. Recently, Law et al. showed that combining imaging (CT and/or endoscopic ultrasound [EUS]) with an EUS-fine needle biopsy (EUS-FNA) increased the diagnostic yield for SPN to 82% from 24% for CT alone[16], while another study showed a diagnostic yield of 100% with FNA for SPN when using the appropriate molecular markers[17]. Increased accuracy in determination of the malignant nature of pancreatic cyst was also achieved when using EUS-FNA compared to CT or MRI alone[18]. Interestingly, although pancreatic biopsies can lead to adverse events, the percentage of events with EUS-FNA is only 0 to 5%[19]. Taken together, these data support obtaining a biopsy by EUS-FNA or other minimally invasive methods during the initial evaluation of a pancreatic mass, especially when primary excision would involve potentially significant anatomical and functional perturbations.

Local control for intermediate-risk RMS can be achieved through surgery, radiotherapy or both. Although local failure in alveolar RMS is higher in group III tumors (19%), historically treated with radiation therapy alone, vs. group II tumors (10%), in which surgery and radiation therapy were used, the 5-year even free survival (EFS) between the two groups is similar[20]. Delayed primary excision (DPE) with reduced doses of radiation has yielded results similar to radiation alone[21]. Considering the expected morbidity associated with PD, but despite our impression that our patient had an SPN, a biopsy at the time of presentation of our patient could have led to reconsideration of surgery, potentially decreasing her long-term complications.

This case report illustrates the limitation of imaging for determination of the nature of a pancreatic mass. The evidence regarding long-term tumor outcomes of pediatric and adolescent patients undergoing PD for benign or malignant tumors is limited, but show similar deficits in endocrine and exocrine pancreatic function and gastrointestinal morbidity when compared to adults[2,3,5,22,23]. We argue that a biopsy should be obtained at initial presentation of a pancreatic mass, especially if primary excision involves a procedure with risk of significant morbidity. There is a need as well to better understand the long-term outcomes of PD in the context of pediatric benign and malignant tumors.

Conflict of interest:

We have no conflict of interest.

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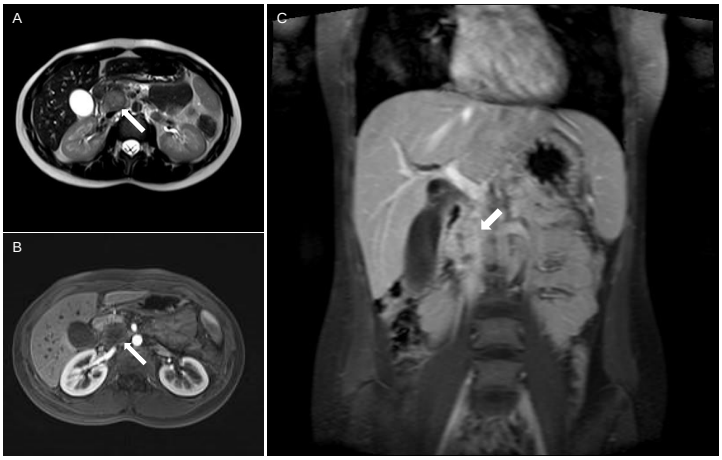
Legends

FIGURE 1 A. Axial unenhanced T2 weighted image shows a well-defined heterogeneous hyperintense mass with hypointense rim. B. Contrast enhanced arterial phase fat saturated T1 weighted image demonstrates

the lesion as hypointense. C. On a contrast-enhanced portal phase fat saturated T1 weighted image, the lesion demonstrates heterogeneous enhancement.

FIGURE 2 Pancreatic alveolar rhabdomyosarcoma. Sheets of small round blue cells with a small amount of eosinophilic cytoplasm infiltrate between pancreatic acini (*) (HE x20, original magnification. Tumor cells are positive for myogenin (inset).



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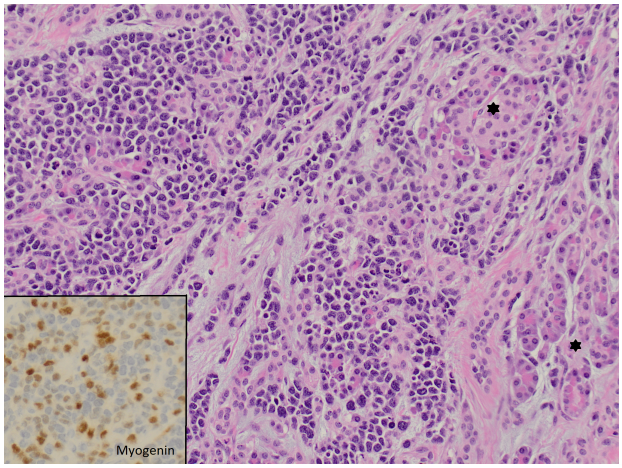

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