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A Novel Case of Carcinoid Tumor in a Pediatric Patient With Short Bowel Syndrome Secondary to Gastroschisis

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INTRODUCTION

Well-differentiated endocrine neoplasms, or carcinoid tumors, are rare gastrointestinal (GI) neoplasms (1). Neuroendocrine cell hyperplasia (NCH), a precursor to neuroendocrine tumors (NETs), has been reported with chronic mucosal inflammation (2). Microcarcinoids, or small NETs, have been reported in a few adults with diversion colitis (DC) (3,4), inflammatory bowel disease (4–6), and prolonged exposure to urine in the colon (7).

Carcinoid tumors have not been reported in gastroschisis or short-bowel syndrome (SBS). We report an asymptomatic ten-year-old male with SBS and a well-differentiated endocrine neoplasm (grade 1) of the sigmoid colon visualized during ostomy takedown. To our knowledge, this is the first report of a carcinoid tumor in a pediatric patient with gastroschisis and SBS.

CASE REPORT

At diagnosis with intestinal failure, our patient had 18 cm of small bowel terminating in a proximal jejunostomy and 10 cm of sigmoid colon without an ileocecal valve. His lack of adaptation was multifactorial and was hindered by oral aversion, lack of enteral feeding tube, dysmotility, and high output stoma in the context of gastroschisis. Dependent on parenteral nutrition support before takedown, he was asymptomatic with no symptoms to indicate DC, like rectal discharge, elevated inflammatory markers, poor growth, hematochezia, abdominal pain, or tenesmus. He never used teduglutide.

During ostomy closure, 2 cm of sigmoid colon was resected to make a jejunocolonic anastomosis. Resection pathology showed a 0.4 cm, T2, well-differentiated neuroendocrine malignancy (grade 1) with positive margins, NCH, and inflammatory changes at the anastomosis (Figs. 1 and 2). Table 1 summarizes laboratory analysis, which showed an elevated serum chromogranin A, serum neuron-specific enolase, and normal serum serotonin and 24-hour urine 5-hydroxyindoleacetic acid.

Lesion histology showed small clusters and linear nests of monotonous epithelial cells with round nuclei, stippled chromatin, and eosinophilic cytoplasm within the submucosa focally invading the muscularis propria. The neoplastic cells expressed cytokeratins (AE1/CAM5.2) and synaptophysin with Ki-67 of less than 1%. The specimen showed lymphoid hyperplasia, surface erosion, crypt distortion, submucosal fibrosis, and superficial aggregates of synaptophysin- and cytokeratin-positive neuroendocrine cells, consistent with background NCH (Figs. 1 and 2). A 68-Gallium DOTATATE positron emission tomography of the whole body/magnetic resonance imaging of the abdomen/pelvis were negative for metabolically active disease.

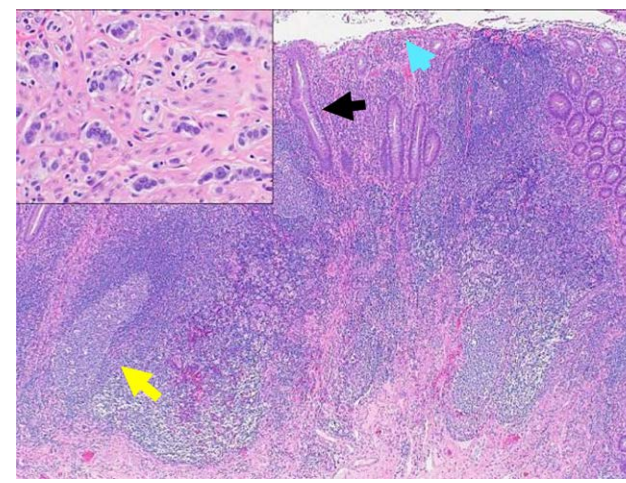

FIGURE 1. Sigmoid colon histology showing neuroendocrine cell proliferation associated with chronic inflammation. Routine hematoxylin & eosin-stained sections show lymphoid hyperplasia (yellow arrow), mild crypt distortion (black arrow), and surface erosion (cyan arrow), indicative of chronic mucosal injury. Clusters and linear nests of neuroendocrine cells (inset) are seen in the background submucosa and focally infiltrating into the muscularis propria.

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A.C.H. had participated in patient's care, drafted the initial manuscript, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. R.M.-E. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. G.S. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. B.M. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. M.B. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. M.K. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. S.N. had participated in patient's care, reviewed and revised the initial manuscript, and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable to all aspects of the work.

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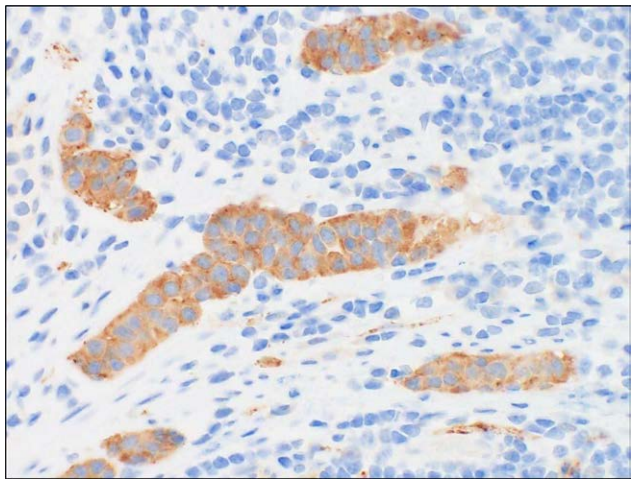

FIGURE 2. Confirmation of neuroendocrine differentiation by synaptophysin immunohistochemistry. The infiltrating cells show strong and diffuse cytoplasmic expression for synaptophysin.

Taken together, these data indicate a well-differentiated carcinoid tumor rather than reactive changes sometimes seen at anastomoses. Our team opted against resection due to low metastatic potential, lack of metastases on imaging, and potential exacerbation of his intestinal failure with additional resection. Multiple specialties agreed to monitor him with imaging, colonoscopy, and chromogranin A serum assessment every 4 months for the first year post-resection.

Follow-up surveillance magnetic resonance imaging abdomen 20 weeks after diagnosis showed mildly enhancing asymmetric thickening at the anastomosis between the jejunum and remnant colon and a mid-abdomen soft tissue lesion, concerning for tumor growth.

DISCUSSION

We are the first to report a carcinoid tumor in a child with gastroschisis and SBS. There is no data on serum analysis of chromogranin A in patients with anastomotic inflammation or those experiencing bowel adaptation. There has been a single report of an infant with gastroschisis with congenital neuroblastoma, but ours is the first report of a patient with gastroschisis or SBS to have a carcinoid tumor (7).

Originating from embryonic enterochromaffin cells, the majority of carcinoid tumors are found in the appendix and are sporadic, presenting with vague symptoms. Rarely, carcinoid NETs present with carcinoid syndrome: abdominal pain, rash, wheezing, palpitations, diaphoresis, flushing, diarrhea, and hypotension (1). Like most with NETs, our patient was asymptomatic. The evaluation of NETs includes laboratory analysis of serum chromogranin A, 24-hour 5-hydroxyindoleacetic acid urine collection, and imaging for metastases, like In-DTPA octreotide with computed tomography or 68-Ga-DOTA-tyrosine-octreotide with positron emission tomography (1).

Neuroendocrine cells in the GI tract proliferate with mucosal injury. NCH, a precursor to NETs, has been reported in celiac disease, autoimmune chronic atrophic gastritis (2,3) DC (3,4), inflammatory bowel disease (4–6), and chronic GI tract urinary exposure (7), all conditions with chronic GI tract inflammation. Our patient is the youngest case to have a NET with a background of NCH. A limitation of this study is our inability to determine if this tumor represents progression from NCH or primary development of a NET at an anastomotic site.

Due to the infiltrative nature and notable invasion of the muscularis, we do not believe this tumor represents reactive changes alone at the anastomosis. His tumor showed minimal cytologic atypia, diffuse staining for chromogranin A, synaptophysin, and neuro-specific enolase, size less than 2 cm, low proliferative indices, and lack of lymphatic and vascular involvement. This phenotype is consistent with a well-differentiated tumor with favorable prognostic features. The multidisciplinary team chose to treat the patient as a carcinoid tumor because there is insufficient evidence to accurately predict how this mass may behave and the WHO classification of digestive system tumors does not recognize any size cutoff for a "tumor" versus "microcarcinoid" in the GI tract (8).

Because the child remains asymptomatic, he has not received somatostatin analogs or chemotherapy, treatments used in symptomatic or metastatic disease (1). Given appropriate growth, and improved stool output after ostomy takedown, we chose to monitor serum neuroendocrine markers, imaging, and colonoscopy every 4 months for the first year after resection. Chromogranin A elevation, as seen in our patient, can be a reliable predictor of tumor relapse, though a limitation of our study is that these levels have not been routinely monitored in patients adapting from SBS. Our monitoring schedule aligns with recommended monitoring for carcinoid tumors in 3–6-month intervals (1).

TABLE 1. Serum Analysis After Diagnosis of Carcinoid Tumor Showed Elevated Serum Chromogranin A and Elevated Neuron Specific Enolase

Laboratory Markers	Units	Normal Range	Patient's levels
Chromogranin A (serum)	Nanograms/milliliter	<93	172–1051
Neuron-specific enolase (serum)	Microgram/liter	3.7–8.9	17.1
Serotonin (serum)	Nanograms/milliliter	<230	30
24-hour urine 5-hydroxyindoleacetic acid	Milligram/24 hours	<5.1	1.6

CONCLUSION

We present the first case of a carcinoid tumor in the setting of NCH in a pediatric patient with SBS and gastroschisis. Our case suggests that NETs may develop in the setting of chronic mucosal injury. Given indolent course, subclinical presentation, and lack of established pediatric NET guidelines, prompt expert referral is necessary to learn more about this condition. Future studies should assess mechanisms of tumor growth in a controlled setting and should assess baseline chromogranin A in bowel adaptation and injury.

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