An 8-Day-Old Boy with Abdominal Distention After Oral Feeding

Robert Listernick, MD

An 8-day-old boy was transferred to the Ann & Robert H. Lurie Children’s Hospital of Chicago for evaluation of abdominal distention. He was the 3340-gram product of a 36-week gestation born to a 33-year-old G1P1 woman. He was born by Caesarian section. Apgar scores were 6 at 1 minute and 8 at 5 minutes. He had spontaneous respiratory effort, but had a large amount of upper airway secretions that were suctioned. Mild grunting was noted, he received supplemental oxygen via face mask continuous positive airway pressure, and he was transferred to the special care nursery. His first 48 hours were complicated by transient tachypnea of the newborn. Repeated attempts at oral feeding were followed by abdominal distension and discomfort. Family history was remarkable for maternal polycystic ovarian syndrome.

On physical exam, the baby was awake and active. Weight was in the 50th percentile, length in the 15th percentile, and head circumference in the 50th percentile. Physical examination was normal save for mild abdominal distention without tenderness, masses, or organomegaly.

Robert Listernick, MD, moderator: From the surgeon’s standpoint, what’s the approach to a newborn with abdominal distention and feeding intolerance?

Eric Grossman, MD, pediatric surgeon: First, we like to try to decide if there’s an anatomic obstruction (eg, Hirschsprung disease [HD], small bowel atresia, etc) versus a functional problem (eg, cystic fibrosis, hypothyroidism, etc). History is often key. I’d want to know the timing of the first passage of meconium, frequency of stools, and the feeding history. Following a complete physical exam including assessment of the patency of the anus, I’d start with an abdominal radiograph. The abdominal distention suggests the possibility of a distal intestinal obstruction.

Jack Norman, MD, pediatric radiologist: The plain film shows multiple dilated small intestinal loops suggestive of a distal obstruction. There are numerous possibilities, including ileal atresia, HD, and meconium plugs or meconium ileus.

Dr. Grossman: Agreed. I’d also add small left colon syndrome and medical causes of obstruction such as cystic fibrosis (leading to meconium ileus) or hypothyroidism. The next step would be performance of a barium enema.

Dr. Listernick: Before we see the barium enema, I was taught not to do a rectal exam or attempt to “clean out” the colon prior to barium enema if HD is suspected. Is this true?

Marleta Reynolds, MD, pediatric surgeon: This is controversial. Rectal examination gives a great deal of information such as determining the presence of a presacral mass (ie, sacrococcygeal teratoma).

Dr. Norman: I don’t think that recommendation is evidence-based. On this patient’s barium enema, the rectum has a normal caliber without a transition zone. There appears to be some redundancy in the sigmoid colon. (We tend to see short rigid colons in HD or total colonic HD.) There were some conflicting opinions, but overall the caliber of the left colon seemed somewhat small, suggesting the possibility of small left colon syndrome. This may be seen in infants of diabetic mothers, meconium plug syndrome, cystic fibrosis, or HD.

Dr. Listernick: What about false-positive and false-negative barium enemas?

Dr. Norman: The main false-negative is that often the colon in total colonic HD looks relatively normal.

Dr. Listernick: Now what?

Dr. Grossman: At a minimum, I would send for thyroid testing and
await the result of the newborn screen for cystic fibrosis. We could try to irrigate the colon, remove any functional obstruction, and see if the child starts stooling normally. Alternately, we could perform a rectal suction biopsy looking for HD.

**Dr. Listernick:** What’s the difference between a suction biopsy and a full-thickness biopsy?

**Dr. Grossman:** We can perform a rectal suction biopsy at the bedside typically until the infant is age 6 to 9 months. A suction device pulls the mucosa and submucosa into a little hole after which a blade is deployed. It’s very well tolerated and usually provides sufficient tissue in order to establish the diagnosis of HD. For older children or when the suction sample is nondiagnostic, we need to perform a full thickness biopsy in the operating room.

**Dr. Listernick:** What are the pathologic findings in HD?

**Pauline Chou, MD, pediatric pathologist:** First, we look at the adequacy of the tissue sample to ensure there is enough submucosa to establish the diagnosis. The diagnosis of HD is established if we confirm the absence of ganglion cells in the submucosal (Meissner’s) plexus and the presence of hypertrophic nerve fibers. We also need a fresh specimen for acetylcholinesterase staining. In cases of HD, we see increased acetylcholinesterase staining nerve fibers in the lamina propria and muscularis mucosae.

**Dr. Listernick:** What were the biopsy results in our patient?

**Dr. Chou:** We found multiple ganglion cells and large nerve plexuses, much more than normal, in the submucosa. These findings are abnormal but we can rule out HD because we see ganglion cells. The differential diagnosis here is hyperganglionosis, such as intestinal neuronal dysplasia. However, acetylcholinesterase staining in intestinal neuronal dysplasia should show increased nerve fibers (ie, abnormal acetylcholinesterase staining similar to those seen in HD); our child had a normal staining pattern. These findings are typical of ganglioneuromatosis.

**Dr. Reynolds:** Ultimately, we will take him to the operating room and perform multiple biopsies working from the distal end of the colon proximally. The specimens are examined in real time; we work very closely with the pathologists because we have the capability of viewing the pathology slides in the operating room. He’ll probably need a total colectomy.

**Dr. Listernick:** So, I lied a bit. I didn’t tell you the real family history.

**Donald Zimmerman, MD, pediatric endocrinologist:** I met the father when he was about age 13 years when he presented with medullary thyroid carcinoma and made the diagnosis of multiple endocrine neoplasia (MEN) type 2B. He had been diagnosed as having total colon HD as an infant, but when the biopsy specimens were re-examined, he clearly had ganglioneuromatosis. This child had been diagnosed prenatally as having a mutation in the RET proto-oncogene typical of MEN2B.

**Rachel Kadakia, MD, pediatric endocrinologist:** MEN2A and MEN2B are each caused by activating mutations in the RET proto-oncogene typical of MEN2B. Patients with MEN2A develop medullary carcinoma of the thyroid (>90%), pheochromocytomas (40% to 50%), and hyperparathyroidism due to either parathyroid adenomas or hyperplasia (10% to 20%). MEN2B is characterized by the development of medullary carcinoma of the thyroid and pheochromocytomas. These individuals also have a Marfanoid habitus and develop mucosal neuromas on the lips and tongue as well as ganglioneuromatosis.

**Dr. Listernick:** Can you predict when the patients with MEN2B will develop medullary carcinoma of the thyroid?

**Dr. Kadakia:** There’s a definite genotype-phenotype correlation between the specific mutation and the timing of the development of cancer. This family has the 918 mutation, one of the most aggressive; the recommendation is to have thyroidectomy in
the first year of life. Medullary thyroid cancer can be extremely aggressive so you want to remove the thyroid before the cancer has a chance to metastasize.

**Dr. Listernick:** What’s the role of calcitonin?

**Dr. Kadakia:** The C cells, the origin of medullary carcinoma of the thyroid, secrete calcitonin. It is an excellent marker for this cancer, particularly in following patients after surgery. Given the high likelihood of cancer in our patient, we recommended thyroidectomy regardless of the calcitonin level as soon as possible. Our patient’s calcitonin was just above the upper limit of normal.

**Dr. Listernick:** Can you remove a thyroid in an infant?

**Dr. Reynolds:** Of course! The surgery is the same but the risks are greater, those being the loss of the parathyroid glands with subsequent hypoparathyroidism and damage to the recurrent laryngeal nerve.

**Dr. Listernick:** Can you reduce these risks?

**Dr. Reynolds:** We can monitor the recurrent laryngeal nerves with a device that is placed preoperatively between the vocal cords. However, this is technically more difficult in infants.

**Dr. Listernick:** And the parathyroid glands?

**Dr. Reynolds:** They’re extremely difficult to identify at this age. I always tell the family that there’s a significant chance of hypoparathyroidism when the patient is this young. In this case, we were fairly confident that we identified two of the four glands. Fortunately, he did well without complications.

**Dr. Listernick:** The pathology demonstrated microscopic foci of medullary carcinoma.

**Dr. Kadakia:** We’ll follow calcitonin levels and hope they return to normal. Pheochromocytoma would be unlikely to arise before the teenage years.

**Dr. Listernick:** Thanks everyone.

---

**Key Learning Points**

1. There are numerous etiologies of distal intestinal obstruction in the newborn, including Hirschsprung disease, small bowel atresia, cystic fibrosis, and hypothyroidism.

2. The barium enema in patients who have total colonic involvement of Hirschsprung disease or ganglioneuromatosis may appear relatively normal.

3. The diagnosis of Hirschsprung disease relies on the absence of ganglion cells in the myenteric plexus and the presence of hypertrophic nerve fibers. Acetylcholinesterase staining demonstrates increased uptake of nerve fibers in the lamina propria and muscularis mucosae.

4. Patients with multiple endocrine neoplasia (MEN) type 2A develop medullary carcinoma of the thyroid (>90%), pheochromocytomas (40%-50%), and hyperparathyroidism due to either parathyroid adenomas or hyperplasia (10%-20%).

5. MEN2B is characterized by the development of medullary carcinoma of the thyroid and pheochromocytomas. These individuals also have a Marfanoid habitus and develop mucosal neuromas on the lips and tongue as well as ganglioneuromatosis of the colon.