GI Manifestations in CdLS

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Gastrointestinal (GI) manifestions are very common in Cornelia de Lange Syndrome (CdLS), and include anatomic abnormalities of the GI tract, gastroesophageal reflux, constipation and feeding difficulties, as well as other diagnoses. Most children with CdLS will have some type of GI diagnostic study performed, each of which has specific indications.

Often the first diagnostic test to be performed is an **upper GI study**, in which barium is taken by mouth or instilled into the stomach, and X-rays are taken to define the anatomy of the upper GI tract. The main purpose of an upper GI study is to assess for anatomic abnormalities of the GI tract, especially intestinal malrotation. **Malrotation** is an abnormality occurring before birth, when the intestines do not turn normally during prenatal development. The upper GI study will reveal abnormal placement of the small intestine in the abdomen, which puts it at risk of twisting on itself and causing a bowel obstruction or a life-threatening condition called midgut volvulus. If this were to occur, it would usually be associated with acute abdominal pain, distension and vomiting of bilious (green/yellow) material.

Malrotation is still relatively uncommon in CdLS, but in our experience we have found that it is more common in CdLS than in the general population, so we recommend that children with CdLS have an upper GI study done to confirm normal anatomy. Other anatomic abnormalities that might be seen on an upper GI study and have been rarely reported in CdLS would be duodenal atresia (blockage) or jejunal atresia. Often an episode of gastroesophageal reflux will be visualized on an upper GI study, but since it is just one point in time it is not the best test to determine the frequency or severity of GE reflux.

Many children with CdLS are affected with gastroesophageal reflux (GE reflux), which may be severe at times. The term GE reflux simply refers to stomach contents coming up into the esophagus, and this condition is very common in infants. However, GE reflux becomes pathologic if it results in severe irritability, food refusal, poor weight gain due to excessive vomiting or respiratory complications due to aspiration of stomach contents. Children with CdLS may present with typical manifestations of GE reflux, such as spitting up, vomiting through the mouth or nose, crying with feeds or back arching. Children with CdLS may also have atypical manifestations of reflux, such as hyperactivity or behavioral issues.

Many times the diagnosis of GE reflux may be made clinically based on the history or physical examination, and treated accordingly. However, depending on the clinical presentation and response to therapy, additional testing may be necessary. For example, if a child is irritable and has feeding difficulty but is not actually vomiting, it may not be clear that the symptoms are due to reflux. In this case, a **pH probe study** (or pH/impedance study) may be useful. In this test, a small probe is placed down the nose into the esophagus. The sensors on the probe measure acid reflux (or both acid and non-acid in the case of a pH/impedance probe) for 24 hours and can determine how much of the time the child is refluxing and also correlate symptoms with reflux episodes. If respiratory symptoms are prominent, a nuclear medicine milk scan may be useful. In this study, labeled milk or formula is taken by mouth or instilled into the stomach, and then imaging is performed. Reflux episodes can be visualized on this scan, and it can also be used to determine whether the stomach empties normally and whether any of the labeled milk reaches the lungs, indicating aspiration.

Aspiration of oral feeds is fairly common in infants with CdLS, and may also be diagnosed by a **modified barium swallow**, in which different thicknesses and textures of food and drink are given and detailed images are taken to analyze the phases of the swallow. For children who have moderate to severe reflux, or who do not respond as expected to medical therapy, an upper endoscopy may be indicated. In this study, which is done under anesthesia, a small scope is inserted into the esophagus, stomach and the first part of the small intestine to take pictures and obtain biopsy specimens. Biopsies of the esophagus may reveal inflammatory changes associated with GE reflux.

In some patients with CdLS, we have found large numbers of allergic cells (eosinophils) in the esophagus, consistent with a diagnosis of eosinophilic esophagitis (EoE). This condition may require food allergy testing and treatment with dietary changes. EoE is becoming more common in the general population, so it is not clear whether it is specifically associated with CdLS. The most severe findings on upper endoscopy include Barrett's esophagus, a pre-malignant condition of the esophagus, or adenocarcinoma (esophageal cancer). With increasing awareness of GE reflux in CdLS, we hope that most patients will be treated aggressively to prevent the development of these late complications.