May 2nd, 11:30 AM - 1:30 PM

Gastrointestinal Fibromatosis: A Case of Successful Oral Tyrosine Kinase Inhibitor Delivery to an Infant with Proximal Duodenal Obstruction

Darius Blanding
Children's Mercy Hospital

Gastrointestinal Fibromatosis: A Case of Successful Oral Tyrosine Kinase Inhibitor Delivery to an Infant with Proximal Duodenal Obstruction

Darius Blanding, MD[1]; Tracy Sandritter, Pharm.D.[2], BCPPS; Atif Ahmed[3], MD; Joel Thompson, MD[1,4]; Valentina Shakhnovich, MD[1,2,5]

1. Department of Pediatrics; 2. Division of Clinical Pharmacology, Toxicology & Therapeutic Innovation; 3. Department of Pathology; 4. Division of Hematology & Oncology; 5. Division of Gastroenterology, Hepatology & Nutrition

Children's Mercy Kansas City

Background

- Infantile myofibromatosis (IM) is a rare disorder characterized by the fibrous proliferation of the skin, bone, muscle, and viscera that usually presents at birth, or soon after.
- IM tumors are characterized as well-circumscribed masses consisting of spindle-shaped cells with characteristic features of both fibroblasts and smooth muscle cells.
- A favorable prognosis is seen in solitary and multicentric IM without visceral involvement; multicentric myofibromatosis with visceral involvement are associated with high mortality rates.
- Chemotherapy, specifically the oral tyrosine kinase inhibitor imatinib, has been used for treatment of IM with visceral involvement.[1]

Objectives

- To describe successful delivery of an oral chemotherapy agent in the setting of a partial upper gastrointestinal (GI) tract obstruction through application of clinical pharmacology principles and therapeutic drug monitoring.

References

1. Arts, F., Chad, D., Pecquet C., et al. PDGFRB mutants found in patients with familial infantile myofibromatosis or overgrowth syndrome are oncogenic and sensitive to imatinib. Oncogene 35, 3239–3248 (2016).

Case Presentation

- 6-week-old female admitted to the pediatric intensive care unit with poor feeding, electrolyte abnormalities, and subcutaneous nodules noted shortly after birth.
- A biopsy of the subcutaneous nodules was performed, showing benign spindle cell proliferation of myofibroblasts, confirming the diagnosis of IM.
- An upper and lower endoscopy confirmed visceral involvement of IM as a cause for her feeding intolerance and dependence on continuous nasogastric (NG) suctioning and total parenteral nutrition (Figure 1).
- Imatinib was initiated via NG to shrink tumor burden, but therapeutic levels could not be achieved, in part due to continuous NG suctioning.
- In order to optimize imatinib levels:
  1. She was started on IV acid suppression and octreotide to minimize gastric secretions and increase time off NG suction.
  2. Acid suppression therapy was modified to famotidine and esomeprazole to specifically target cytochrome P450 (CYP) 3A4, the pathway responsible for imatinib drug clearance.
- After instituting these pharmacologic interventions, gastric suctioning could be held for up to 60 min after imatinib administration, with less frequent emesis, and the patient's imatinib level reached therapeutic range consistently (Figure 2).
- Her tumor burden gradually shrunk, enabling for a successful small bowel resection with end jejunostomy formation, followed by subsequent reconnection and tolerance of nasogastric feeds.
- The infant was discharged home after 528 days of hospitalization.

Figures

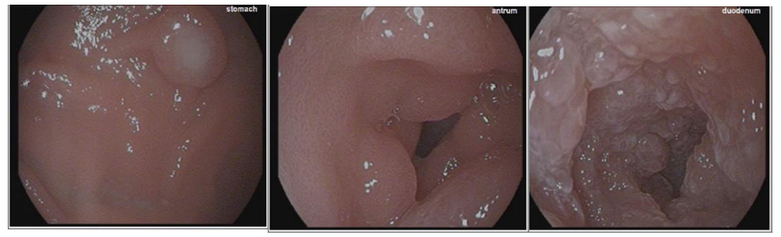
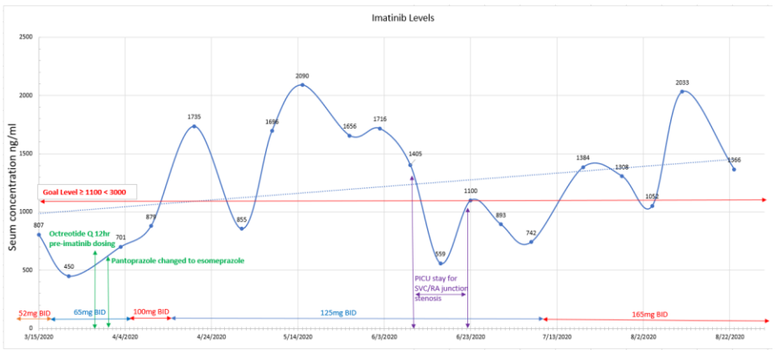


Figure 1. Endoscopic images from the patient's stomach and duodenum showing nodularity caused by visceral IM.



Conclusion

- This case highlights successful use of pharmacologic principles to increase gastric residence time and drug absorption of an oral chemotherapy agent for a critically ill infant with a partial upper GI tract obstruction from myofibromas.
- By minimizing gastric acid secretions and targeting CYP3A4, the primary drug metabolizing pathway responsible for imatinib clearance from the body, we achieved target therapeutic imatinib levels necessary for tumor shrinkage.

UMKC School of Medicine | KU School of Medicine, The University of Kansas | Children's Mercy Kansas City