Severe stridor in a child with GSD type 1b

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10 y.o. boy, arab origin, unrelated parents, diagnosed as glycogen storage disease type 1b as a newborn, after TTN, prolonged jaundice, hypoglycemia, hepatomegaly and neutropenia.

- a sister died from same disease at the age of 4/12

- gastrostomy at the age of 4/12, closed at age 8/12 (infection), since then, NG tube feeding during nights

- >60 hospitalizations secondary to infections, respiratory, GI tract, oral, perianal, chronic diarrhea, skin infections, UTI.
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- **GCSF** since the age of 3 years, 55 mcg twice a week
- resprim twice a week

- IBD, Crohn’s disease, retropharyngeal abscess, esophagitis, osteoporosis, UTI with severe vesico-ureteric reflux

- October 2011: hoarseness and stridor, more nocturnal, adrenaline inhalations, susp retropharyngeal abscess, augmentin, fluconazole and nystatin, after oral candidiasis.

- still hospitalized
- flexible bronchoscopy October 30, laryngeal edema, esophageal candidiasis

- December 2011, severe stridor, bronchoscopy, operating room, laryngeal edema, intubation and ventilated for 7 days, antibiotics and steroids

- cervical CT, subglottic stenosis with thickening of tracheo-esophageal area
• abscess?
• glycogen storage?
• lymphoma? tumor?
• granuloma?
• amyloidosis?
next step?
• **trans-esophageal US-guided biopsy**: squamous cells, histiocytes (negative stains of CD1 and S100 for histiocytosis) and neutrophils, no tumor cells or evidence of glycogen storage

• **transcutaneous cervical CT-guided needle biopsy** - neutrophil and plasma cell infiltration, no tumor cells or evidence of storage disease, no granuloma.
• **Glycogen storage disease type I (GSD I)** the most common glycogen storage disease.

• **GSDIa, genetic, 80%, homozygous for G188R mutation, chromosome 17q21, deficiency of enzyme G-6-phosphatase, inability of liver to produce free glucose from G-6-P resulting in severe hypoglycemia, glycogen storage in liver and kidneys, enlargement of both**

• **GSDIb, 20%, G6P transporter mutation of gene SLC37A4 on chromosome 11q23., Most have neutropenia and impaired phagocytic functions** (Kilpatrick, Garty. J Clin Invest 1990) predisposing for severe infections

• **GSDIc (transporter of P), GSD1d (transporter of G), minority**
GSD Ib

- chronic pancreatitis, chronic IBD, Crohn's disease, oral, perianal & perirectal abscesses, severe recurrent bacterial infections, periodontal disease and recurrent mucosal ulceration, recurrent OM and externa, brain abscesses (Garty, Acta Paediatr 1992), secondary amyloidosis

- terminal kidney disease may develop, hypothyroidism (autoimmune), hepatic adenoma, splenomegaly (GCSF)

- use of GCSF to increase the number of neutrophils

- vit E supplementation improves neutropenia and reduces the frequency of infections Melis, Eur J Pediatr 2009
storage diseases and airways

- A patient with Type 2 Gaucher’s disease with respiratory disease. GER & Lysosomal storage in columnar cells of tracheal biopsy, Shebany, J Pediatr 2003
- Anesthetic considerations in the child with Gaucher disease. Hepatosplenomegaly, GER, chronic aspiration
- glycogen storage?
GSD and GER

- Treatment of GER with Nissen fundoplication and gastrostomy in infantile Pompe’s disease, 5 patients, 3 died, Hirschburger et al, Neuropediatrics 2009
Chronic laryngitis and GER

- **Medline - 176 articles**
- **2006 The Global Consensus Group in Montreal pointed out that chronic laryngitis is highly associated with gastroesophageal reflux disease (GERD).**
- Among 42 patients with chronic hoarseness, laryngopharyngeal reflux was confirmed in 35 patients (83.3%). Dymek, Otolaryngol Pol 2012
- **Chronic laryngitis-associated factors and voice assessment** The main associated factors: nicotine abuse (50 patients), GER (35 patients) and inhaled CS (25 patients). Reiter, Laryngorhinotologie 2009
- **GER disease in chronic laryngitis: prevalence ...** Prevalence of 65.6%. Qua, Aliment Pharmacol Ther 2007
GER animal models and chronic laryngitis

- **surgical rabbit model of GER:** Submucous gland hyperplasia and inflammation significantly increased in the reflux group. Hu, Eur Arch Otorhinolaryngol 2012.

- **newborn lambs, simulated reflux laryngitis caused more histological laryngitis, apnea and desaturation** Carreau, J Appl Physiol 2011
stenosing laryngitis and GER


GER and obesity (1) (n=729)

- association between gastroesophageal reflux disease and obesity. Friedenberg, Am J Gastroenterol 2008

- increased body mass index and accumulation of visceral fat are associated with a two- to threefold increased risk of developing reflux symptoms. Tutuian, Curr Gastroenterol Rep, 2011

- prevalence and risk factors for GER disease in an impoverished minority population. The highest quartile of waist circumference strong association with GERD (OR = 2.15), Smoking increased the OR by 1.72 Friedenerd, Obes Res Clin Pract 2010
GER and obesity (2)

- Obese patients have stronger peristalsis and increased acid exposure in the esophagus. Fornary, Dig Dis Sci 2011

- Obese patients show an increased number of refluxes with acid content compared to non-obese, pH-metry and impedance. Ricci et al, Obes Surg, 2011

- Abdominal visceral adipose tissue volume is associated with increased risk of erosive esophagitis in men and women. Nam, Gastroenterology 2010
GER and naso-gastric tube

- the nasogastric feeding tube as a risk factor for aspiration and aspiration pneumonia (Gomes GF, Curr Opin Clin Nutr Metab Care, 2003)

- seven patients who had preexisting GER showed significant improvement (p<0.05) of the reflux parameters after PEG placement (Jung et al, Gut Liver, 2011)

GER and naso-gastric tube (2)

- Influence of nasogastric tubes on gastroesophageal reflux in preterm infants: a multiple intraluminal impedance study. 72 reflux episodes with the esophageal placement and 122 during the gastric position (P <.01). (Peter CE, J Pediatr 2002).

- Nasogastric intubation causes gastroesophageal reflux in patients undergoing elective laparotomy. (Manning BJ et al, Surgery 2001. 15 patients, 137 episodes of GER with NGT vs. 8 without)
GER and size of NG tube (3)


- Gastroesophageal reflux with nasogastric tubes. Effect of nasogastric tube size, negative study in normal volunteers. Dotson RG, Am J Respir Crit Care Med 1994
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- glycogen storage disease type 1b, with severe hepatosplenomegaly, huge abdominal distention
- nasogastric tube for years, reinserted every week
- nocturnal severe stridor till emergency intubation
- suglottic stenosis
- neutropenia

- m/p chronic laryngitis secondary to GER
**pH metry**

- 2 weeks after cessation of NG feeding
- 259 acidic reflux episodes
- fraction time pH < 4: 13.6%
• did not respond to omeprazole
• 19 Febr 2012: gastrostomy + fundoplication + splenectomy

• ...
• slow improvement, no stridor, mild hoarseness
• gastrostomy opening inflamed
- last week, recurrence of stridor, barking cough
- ...
- next step??
- fundoplication still works!
- flexible bronchoscopy
  - subvocal cord edema
In summary,

- a 10 y.o boy with **GSD type 1b**, during the last 4 months chronic severe laryngitis with nocturnal exacerbations, GER
- responds **slowly** to gastrostomy, fundoplication and splenectomy