A neonate with abdominal distension

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A little learning is a dangerous thing; Drink deep, or taste not the Pierian spring

Alexander Pope
An essay on criticism
Case:

- Baby girl born at 35 weeks to a 31 year old G2P0→1 mother via NSVD; IVF pregnancy, paternal Ashkenazi heritage
- Prenatal labs normal including IVF genetic testing
- Prenatal imaging:
  - Fetal ultrasound and fetal MRI demonstrating dilated bowel, intrauterine growth restriction and polyhydramnios
- Amniocentesis:
  - Normal AFP and 46XX karyotype, negative TORCH titers
- Normal fetal echocardiogram
- Abdominal distension noted at birth- imaging- intestinal obstruction-? atresia
Immunology workup

- Low ALC (1320) and TRECs (537)
- T cell subsets (Day 7, 17 of life)

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<thead>
<tr>
<th></th>
<th>Count 1</th>
<th>Count 2</th>
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<tbody>
<tr>
<td>T cell % (count)</td>
<td>67 (353)</td>
<td>66 (747)</td>
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<tr>
<td>CD4 % (count)</td>
<td>60 (314)</td>
<td>58 (666)</td>
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<tr>
<td>CD8 % (count)</td>
<td>3 (18)</td>
<td>3 (30)</td>
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<tr>
<td>B cell % (count)</td>
<td>7 (89)</td>
<td>14 (164)</td>
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<tr>
<td>NK % (count)</td>
<td>13 (69)</td>
<td>20 (224)</td>
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Immunology workup

• Decreased immunoglobulins (IgA < 6, IgG 523, IgM < 6.5)
• Decreased mitogen responses (30% response to PHA, 16% response to ConA, normal response to Pokeweed Mitogen)
• T lymphocyte subset analysis - normal CD45RA (56%) and CD45RO (15%)
• NK function decreased though NK count remained normal in subsequent testing
Surgical management

- Laparotomy on DOL #7 with small bowel resection and gastrostomy/multiple enterostomies/colostomy creation
- Pathology - occlusion of bowel lumen with fibrous and granulation tissue, areas of multinucleated foreign body giant cell reaction/calcification, along with areas of crypt dropout/absence (similar changes to GVHD) and apoptotic bodies
- Hypocellular lamina propria- CD3, CD20, and CD138 staining showing decreased lymphocytes and plasma cells along with increased numbers of eosinophils, neutrophils, and macrophages
- Pathology notable for EBER positive cells (though serum EBV PCR negative)
DIFFERENTIALS?
Genetic testing

- Genetic testing (whole exome sequencing) identified a compound heterozygous mutation in TTC7A (tetratricopeptide repeat domain 7A gene)
  - p. Ala551Asp (c.1652C >A) missense variant (exon 15)
  - p. Glut828* (c.2482C >T) nonsense variant (exon 20)

- Both variants documented to be of parental inheritance—maternal copy of c.2482C >T variant and paternal copy of c.1652C >A identified in the proband
FINAL DIAGNOSIS – HEREDITARY MULTIPLE INTESTINAL ATRESIA WITH COMBINED IMMUNODEFICIENCY SECONDARY TO TTC7A MUTATION
Clinical course

• Started IVIG therapy along with fluconazole, pentamidine and acyclovir prophylaxis

• Infectious disease history notable for multiple episodes of bacteremia (CVL related versus mucosal translocation) – Enterococcus *fecalis*, Enterobacter *cloacae*, Klebsiella *pneumoniae*, Staph *aureus* and GBS)

• Noted to have some evidence of immune recovery with increased CD4 counts (Range: 205-801), production of IgM (Range: <6.5 -19.5), IgA (Range: <6 - 42.6) and improved mitogen responses (PHA -49.8%)

• CD8 counts (Range: 18-63) have shown less variability and remain low

• Concern for development of intestinal failure associated liver disease
Questions

• Role for antibiotic prophylaxis to prevent her recurrent bacteremia with GI flora

• What is the role of TTC7A in immunologic development/maturation? Currently described as influencing intestinal epithelial cell polarity/early IBD.

• Timing, order and utility of bone marrow/HSCT and small bowel transplantation?

• How to minimize risk of GVHD post small bowel transplantation?

• Relevance of positive EBER in resected pathology?
THANK YOU