# NEONATAL CHRONIC INTRACTABLE DIARRHEA A RARE CASE REPORT

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# Case History

- 15 months male child, born of NC marriage through full term vaginal delivery
- Presented with repeated episodes of intractable diarrhea since 5th day of life, with failure to thrive
- Not relieved by supportive treatment.
- Birth weight: 1.75kgs, uneventful birth history and attained normal developmental milestones.

# Case History

- Family history: Negative for any inheritable conditions.
- Immunization: Immunized till date

# Physical Examination

- On admission,
- Vitals: Within normal limits
- Systemic Examination:

  Per Abdomen Examination: Mild hepatomegaly

  Other systemic examination: Within normal limits

# Laboratory Parameters:

- Hb:12.9gm/dl
- Eosinophil Count:100 cells/microL(0-500cells/microL)
- Total Leukocyte Count: 12000/microL
- Total Serum Protein: 5.30g/dl
- Albumin:2.50 g/dl
- Urine Protein: Trace

# Laboratory Parameters:

- Stool Examination: Greenish, positive for mucus and occult blood
- Stool PCR for C. Difficile: Negative
- Fecal Calprotectin: 936.97µg/g (N= <50µg/g)
- CRP levels: 7.79 mg/L (Acute Inf >10mg/L)

# Laboratory Parameters:

- Tissue Transglutaminase IgG: 0.41U/ml
- IgG, IgA, IgM levels and Anti-TPO: WNL
- IgE levels: >2500 (20-100 I.U./ml)
- C3 level: low
- Clinical suspicion: Cystic Fibrosis
- Esophagogastroduodenoscopy:
- Reduced Duodenal Folds

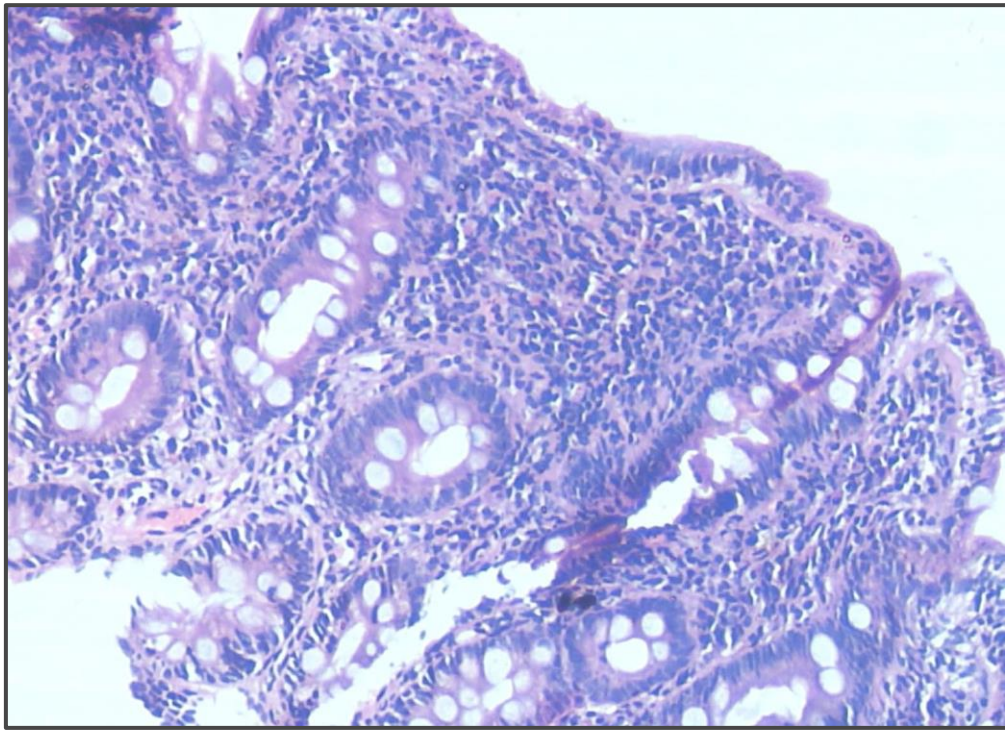
# Histpathological Examination

- Duodenal biopsy was sent for histopathological examination

- Grossly:
- Received 4 greyish white soft tissue bits ranging from 0.2 to 0.4 cms

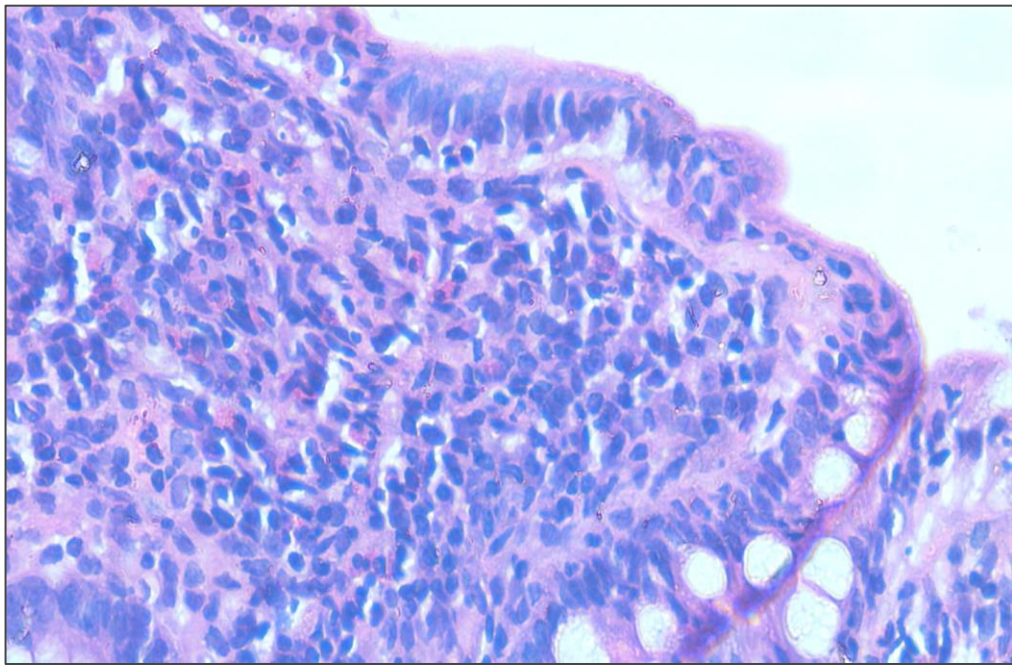
# Microscopy

- Photomicrograph showing severe villous atrophy, with maintained crypt architecture and and normal intraepithelial lymphocyte count ( H&E x100)



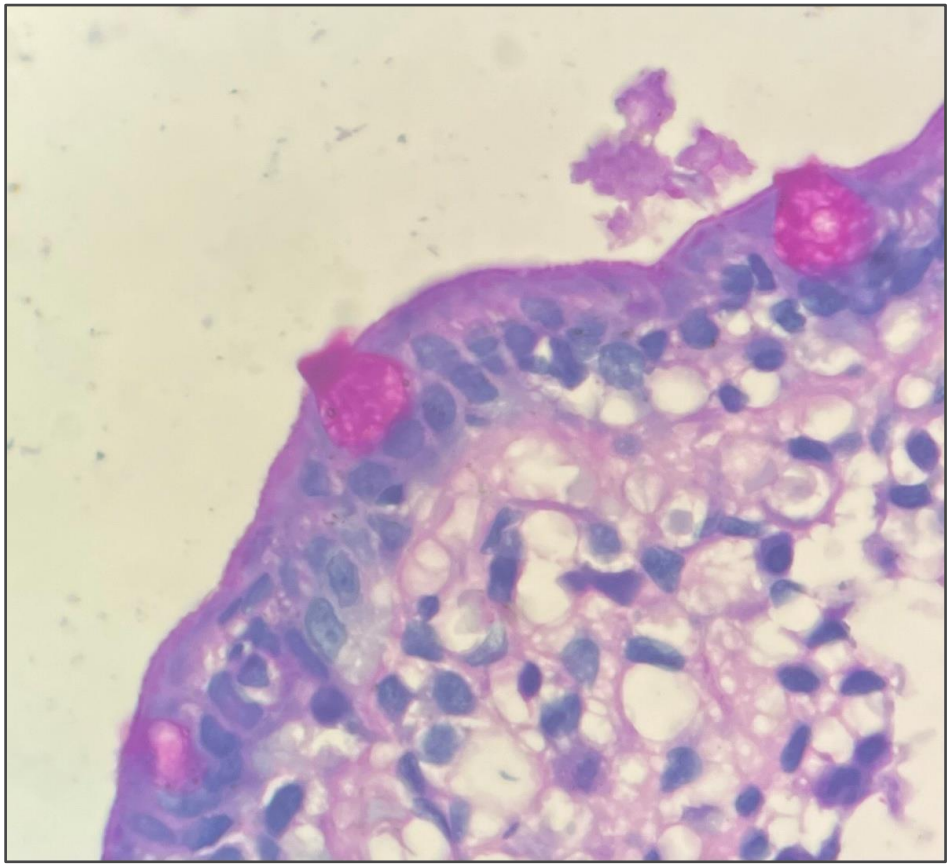
# Microscopy

- Lamina propria showed moderate inflammation consisting of lymphocytes, plasma cells, and few eosinophils ( H&E x400)



# Microscopy

- Periodic Acid Schiff stain: preserved goblet cells within crypts and the intestinal brush border appeared less apparent with small stubby microvilli (PAS X 400)



# Microscopy

- There was no evidence of enterocyte vacuolation, crypt apoptosis and tufting of villi.
- Based on above histopathological findings following differential diagnosis were considered

1) Celiac Disease

2) Tufting Enteropathy

3) Autoimmune enteropathy

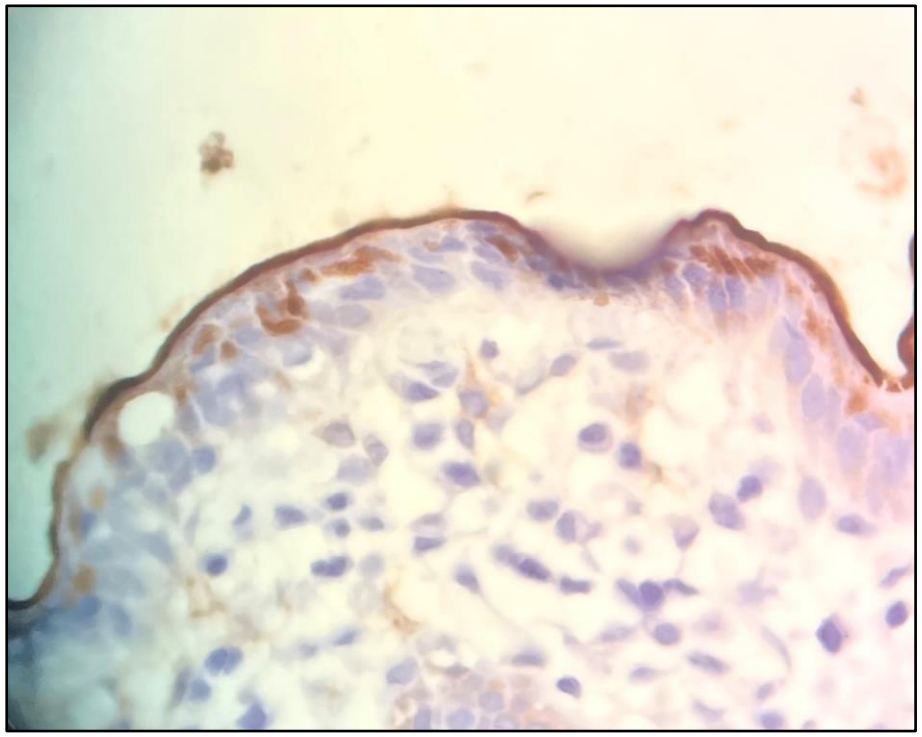
4) Mirovillus Inclusion Disease

# Histopathological Diagnosis

- After ruling out, histopathological diagnosis of **Microvillus Inclusion Disease** was made.
- To confirm the diagnosis IHC with **CD10** was done

# Immunohistochemistry

- CD10 revealing cytoplasmic luminal side staining within the enterocytes (IHC X 400)
- CD 10 positvity favoured the diagnosis of MVID



FINDINGS RELATED TO PHENOTYPE

| Gene & Transcript | Variant | Location | Zygosity | Disorder (OMIM) | Inheritance | Classification |
|---|---|---|---|---|---|---|
| *FOXP3* NM_014009.4 | c.816+1G>T | Intron 8 | Hemizygous | Immunodysregulation, polyendocrinopathy, and enteropathy, X-linked (304790) | X-linked Recessive | Likely Pathogenic |

**Final Diagnosis:**

**IPEX SYNDROME BY Whole Exome Sequencing**

**(Hemizygous FOX P3 c.816+1G>T at Intron 8 mutation)**

# Management and Follow Up

- Antibiotics, fluids and ionotropes due to dyselectrolytemia.
- Low dose steroids and immunosuppresants i.e  Sirolimus
- Presently: symptomatically improved with no diarrhea, afebrile, hemodynamically stable, gaining motor milestones and weight since 3 months.

# Discussion

**IPEX ( Immune Dysregulation, Polyendocrinopathy and Enteropathy) syndrome**:

- A rare x-linked recessive disorder, described first time in 1982.
- 300 cases reported worldwide
- Forkhead box protein 3 (FOXP3) gene mutations
- May present only with intractable diarrhea with autoimmune enteropathy as the hallmark, in the absence of any other systemic involvement: Rare presentation

# Discussion

- Only Potential Cure: Hematopoietic Stem Cell Transplant
- Prognosis: Poor and fatal if untreated

# TAKE HOME MESSAGE

- This case is unique due to clinical presentation as enteropathy without diabetes and thyroiditis , histopathology resembling MVID and a unique mutation diagnostic of IPEX Syndrome
- IPEX with this mutation can present with overlapping findings similar to MVID on HPE, hence genetic testing remains the mainstay to formulate the final diagnosis

# TAKE HOME MESSAGE

- This is the first case of IPEX syndrome with this mutation reported from Indian subcontinent as per English literature available.

# References


- 1. Barzaghi F, Passerini L, Bacchetta R. Immune Dysregulation, Polyendocrinopathy, Enteropathy, X-Linked Syndrome: A Paradigm of Immunodeficiency with Autoimmunity. Frontiers in Immunology. 2012;3.

- 2. Tan QKG, Louie RJ, Sleasman JW. IPEX Syndrome. 2004 Oct 19 [Updated 2018 Jul 19]. In: Adam MP,Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1118/

- THANKYOU