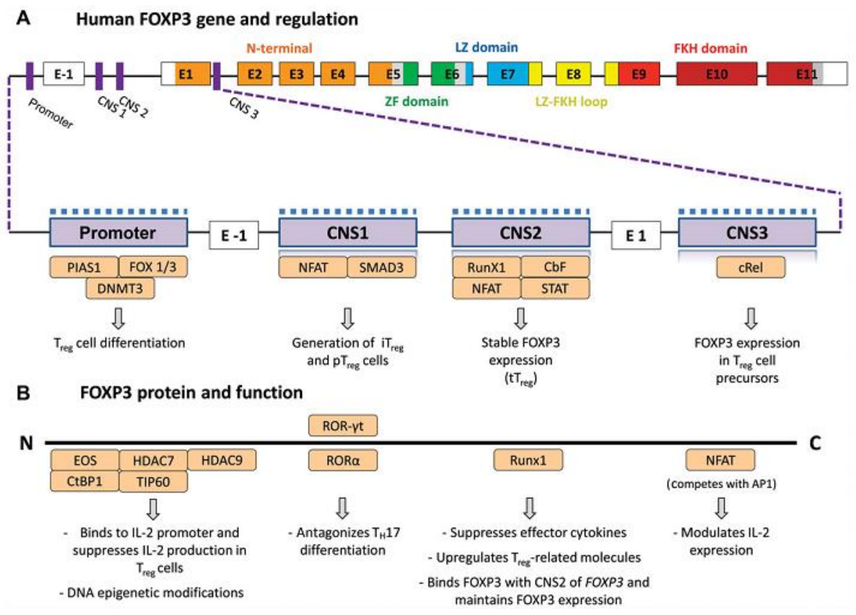
CASE REPORT: DE NOVO MUTATION OF FOXP3 CAUSING MILD PHENOTYPE OF IMMUNODYSREGULATION, POLYENDOCRINOPATHY, ENTEROPATHY, X-LINK SYNDROME

Hoang Thi Diem Thuy PhD, Nguyen Khoa Binh Minh MD
Department of endocrinology, Children's Hospital 2, HCMC, Vietnam

Poster Number: P3-P099

INTRODUCTION

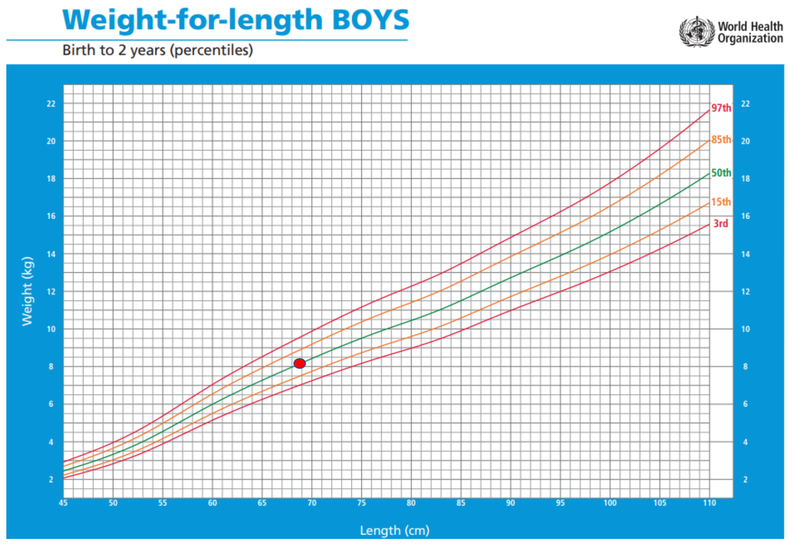
- Immune dysregulation-polyendocrinopathy-enteropathy-X-linked syndrome (IPEX) is caused by mutations in the gene for the transcription factor FOXP3. The phenotype of IPEX was first described in 1982, and the first genetic mutations in FOXP3 were identified in 2000. FOXP3 is required for the differentiation and function of CD4+CD25+ T regulatory cells.
- IPEX is rare, often fatal. However several cases present later onset, mild forms or less common clinical manifestations.

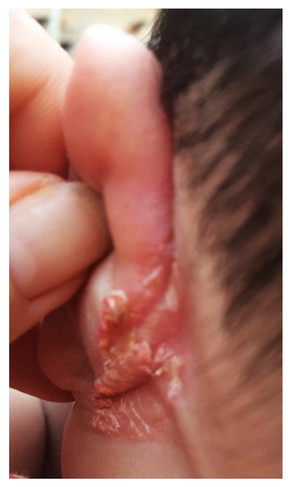


According to Bacchetta et al

CASE REPORT

- A male preterm baby was admitted at 8 day-old for diabetic ketoacidosis and sepsis. He was born at 36 weeks with a low birthweight 2200gr.
- There was no significant family medical history. TPAL 1011.
- At 4 month-old, he developed a dermatitis without recurrence. High IgE level at 700 µg/l was found. Anti-RNP was positive. Absence of other clinical manifestations in this patient.
- There wasn't any autoantibodies related to his diabetes. His diabetes has been well controlled with. The last HbA1c was 7.3% at 12 months.
- The DNA analysis found de novo missense mutation at exon 12 of FOXP3 gene c.1190G>A, p.(Arg397Gln).





DISCUSSION

- Clinical manifestations of FOXP3 mutations is variable symptoms and severity. Classically, FOXP3 mutations have been described as a severe panorama with intractable diarrhea, diabetes mellitus, eczema. However some manifestation was absent in some reports. Our patient has isolated neonatal diabetes.
- However the same genotype c.1190G>A was found by Tsuda et al with a whole manifestation decribed above.
- Some study suggested milder IPEX syndrome do not abrogate the function of forkhead domain. However in this case, we found missense mutation in FKH domain.

CONCLUSION

- FOXP3 is one of the gene mutations causing early onset insulin-dependent diabetes.
- Prognosis of FOXP3 mutations is challenging because there is no clear correlation between genotype and phenotype in patient with IPEX syndrome.

REFERENCES

1. Masanobu Tsuda, Troy R. Torgerson, Carlo Selmi, Eleonora Gambineri, Magda Carneiro-Sampaio, Sara Ciullini Mannurita, Patrick S.C. Leung, Gary L. Norman, M. Eric Gershwin. The spectrum of autoantibodies in IPEX syndrome is broad and includes anti-mitochondrial autoantibodies. Journal of Autoimmunity 2010; 35: 265-268.
2. Rosa Bacchetta, Federica Barzaghi, Maria-Grazia Roncarolo. From IPEX syndrome to FOXP3 mutation: a lesson on immune dysregulation. Ann. N.Y. Acad. Sci.2016; ISSN 0077-8923.
3. Oscar Rubio-Cabezas et al. Clinical Heterogeneity in Patients With FOXP3 Mutations Presenting With Permanent Neonatal Diabetes. Diabetes care 2009; 32: 111-116.
4. Fabrizio de Benedetti et al. Mechanistic Associations of a Mild Phenotype of Immunodysregulation, Polyendocrinopathy, Enteropathy, X-Linked Syndrome. Clinical gastroenterology and hepatology 2006;4:653–659.