Celiac disease prevalence in Turner syndrome and association with HLA typing

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Background

- Individuals with Turner Syndrome (TS) are at higher risk for celiac disease (CD):
  - 2-5 times higher than the general population
  - Risk increases with age in childhood
  - Prevalence: 4.5%
- Limited evidence regarding CD onset, natural history, and risk factors in TS
- HLA typing previously utilized as first-line screen for CD in high-risk groups
  - Positive HLA typing does not confirm CD
- HLA-DQ2 or HLA-DQ8 negative are highly unlikely to develop CD
- Utility of HLA typing has not been studied in pediatric patients with TS in the US
- Association and predictive value of HLA typing and CD in pediatric TS is not well-established

Objectives

- To evaluate the prevalence and age of onset of CD in TS
- To identify risk factors and association between HLA typing & CD in TS

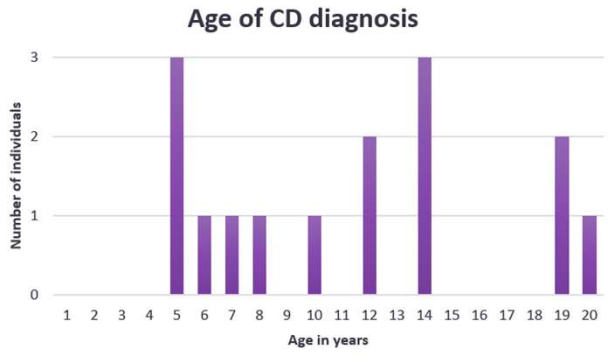
Methods

- Retrospective cross-sectional study using TS database & EMR chart review (IRB-approved)
- Data evaluated included:
  - Karyotype
  - TTG IgA levels (defined as elevated if ≥20 CU)
  - HLA allele testing (DQ2, DQ8 status)
  - Endoscopy results
  - Clinical documentation
- Diagnosis of CD defined as ICD-10 code for CD
  - Most diagnosed by a gastroenterologist with or without biopsy

Results

Celiac Disease in patients with Turner Syndrome:

The TS database included 448 individuals, including 19 with confirmed CD (prevalence 4.2%).



- Range: 5 to 55 years
- Most were diagnosed at <20 years
  - Two outliers diagnosed at 33 and 55 years

Mean	11 years old
Median	12 years old
***excluding ages 33 and 55**	

HLA genotyping in patients with TS:

Of 448 individuals in the TS database, 9 had prior HLA typing.

Participant	Celiac Disease	Highest TTG IgA	DQ Genotype	EGD Results	Karyotype	Other Autoimmune Disease
1	No	56	DQ2-,DQ8-	N/A	45,X/46,XX	-
2	No	58	DQ2-,DQ8-	N/A	45,X/46,X,i(X)q	-
3	No	13	DQ2-,DQ8-	-	45,X/46,X,i(X)q	Hashimoto's thyroiditis
4	No	<2	DQ2-,DQ8-	N/A	45,X/47,XXX	-
5	No	17	DQ2-,DQ8-	-	46,X,rX	-
6	No	4	DQ2 heterozygous	N/A	45,X/46,XX	-
7	No	51	DQ8 heterozygous	N/A	45,X/46,XX	-
8	Yes	Unavailable	DQ8 homozygous	N/A	46,XX/46,X,rX	-
9	Yes	50	DQ2/DQ8	+	45,X	Hashimoto's thyroiditis, Ankylosing spondylitis

- Two with CD diagnosis (green in table)
  - Both had GI symptoms, and one had additional autoimmune diseases
- Seven without CD (blue in table)
  - Three had elevations in TTG IgA prior to HLA typing
  - Remaining four, HLA typing obtained due to growth failure in 1 (DQ2-/DQ8-) and GI symptoms in 3 (DQ2-/DQ8- in two, DQ2 heterozygous in one)
    - Two of these three underwent EGD with normal biopsies (both DQ2-/DQ8-)

Conclusions

CD in Individuals with TS:
- Prevalence of CD is 4.2%.
- Disease onset was mostly older than 10 years with none diagnosed under the age of 5

HLA typing in individuals with TS:
- Those with CD had DQ8 homozygosity or both DQ2/DQ8 alleles
- Those without CD were either negative or heterozygous for either DQ2 or DQ8

Limitations

- HLA genotyping available for only 2 individuals with TS and CD
- Patients with TS are not routinely screened with HLA typing, leading to small sample size

Future Directions

Given the small sample size, more studies are needed to determine the utility of HLA typing in this population.

We will plan to expand this study through a prospective cohort study, where we will obtain HLA typing in TS. We will recruit participants with TS and known CD as well as those without CD.

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