STAT 1 GOF Treatment with Ruxolitinib

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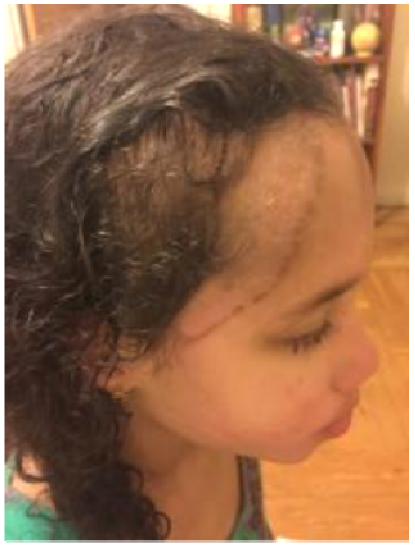
Case Presentation

11 year old girl referred to MSH for history:

- Chronic Mucocutaneous Candidiasis (age 5)
- Chronic Tinea Capitus
- Chronic apthous ulcers
- FTT (poor weight gain G-tube 4 mo-6 yrs)25th percentile age 3→<5th age 5
- Chronic diarrhea age 3 dx as Celiac due to villous atrophy
- Recurrent perianal abscess and fistula
- Autoimmune hepatitis
- HSV infection around the eyes age 6
- 2-3 sinus infections/yr since age 2
- 5 episodes of PNA (CXR) prior to age 6
- Thrombocytopenia age 7
- Alopecia (age 9)

Trt: Terbinafine and Intraconazole (poor control)

- Allergy to fluconazole
- Clotrimazole and Griseofulvan d/c



Laboratory Evaluations

CBC:
12/2011 9.6>11.2/25.4<374 74% PMN, 16 % Lymph, 9% Mono
02/2016 7.6>11.7/36.7<305 79% PMN, 12% Lymph, 9% mono
1/2013 PLT 17

Flow Cytometry:	12/1/2011	2/18/2016
ABS NK (Range:135-525 /CU MM)	18(L)	21 (L)
ABS T HELPER (Range: 412-2095 /CU MM)	402 (L)	317 (L)
ABS T SUPPR (Range:236-995 /CU MM)	401	293
ABS TOTAL B (Range: 200-1259 /CU MM)	560	368
ABS TOTAL T (Range: 876-3394 /CU MM)	892	675 (L)
HELPER/SUPPRESS 1.00-3.00	1.00	1.08

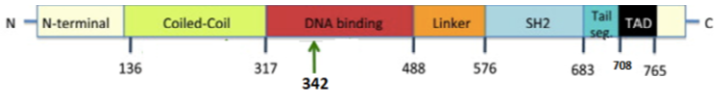
2007: IgA 68,IgE 5, IgG 866, IgM 67
2016: IgA 114, IgE <2, IgG 1217, IgM 63

2007 AST 367, ALT 688 LD 466 GGT 39 TG 164

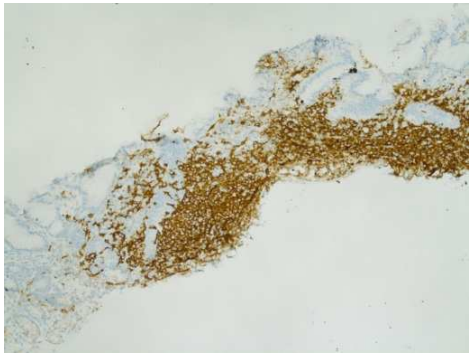
- Minimal decrease in PHA proliferation (close to lower limit of normal), nl PMW
- B cell function ok
  (+ MMR, tetanus, HIB, HSV, only 2/14 pneumococcal revaccinated)
- Anti Human TTG_IGA 5.1 wnl (ref 0-19.9)
- Outside Endocrine workup -negative
- 2012 AIRE mutation negative

Genetic Testing: STAT1 GOF

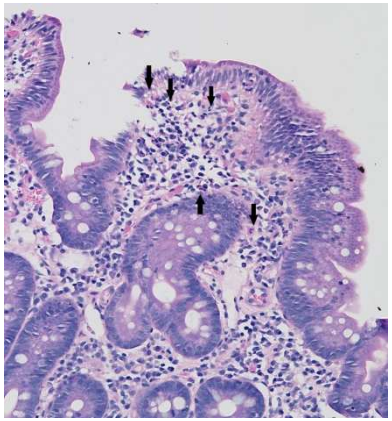
STAT1 Gene Chr 2q32
Heterozygous c971 G>A (p.C342Y)



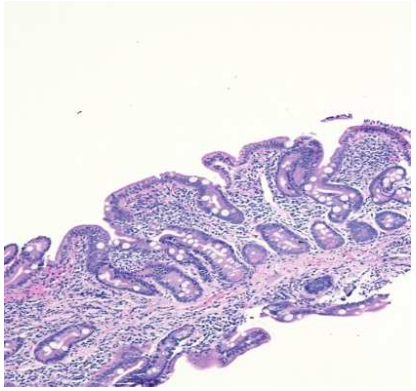
GI Biopsy Findings



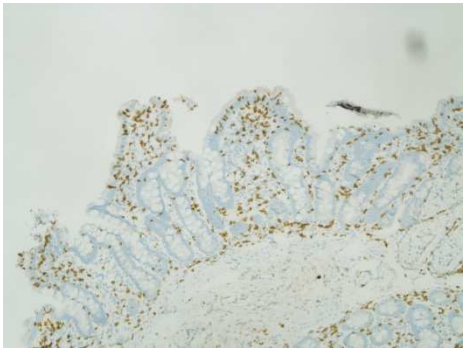
A: antrum lymphoid proliferation (B Cells)



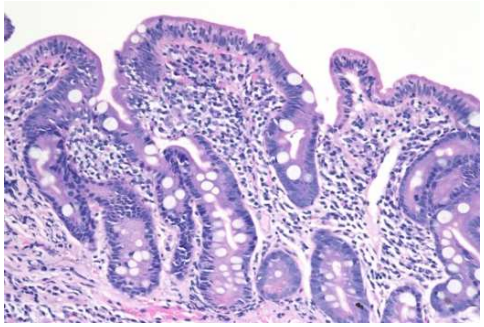
B: Duodenum with flattened villi and scattered PMN (CVID like but w/ plasma cells)



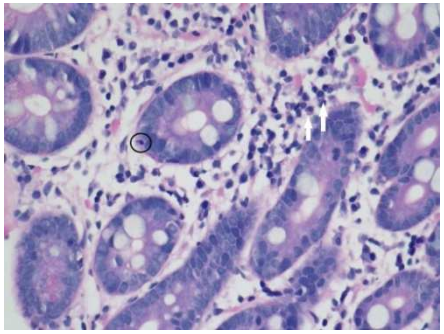
C: Duodenum IEL with villous flattening similar to Celiac



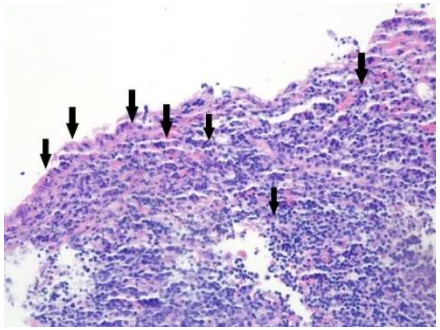
D: Duodenum IEL CD3+ mostly CD3+/CD8+ some CD3+ only



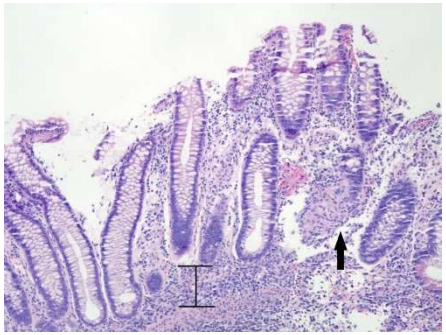
F: Duodenum with flattened villi and IEL



F: duodenum with crypt apoptosis but with abundant goblet and paneth cells

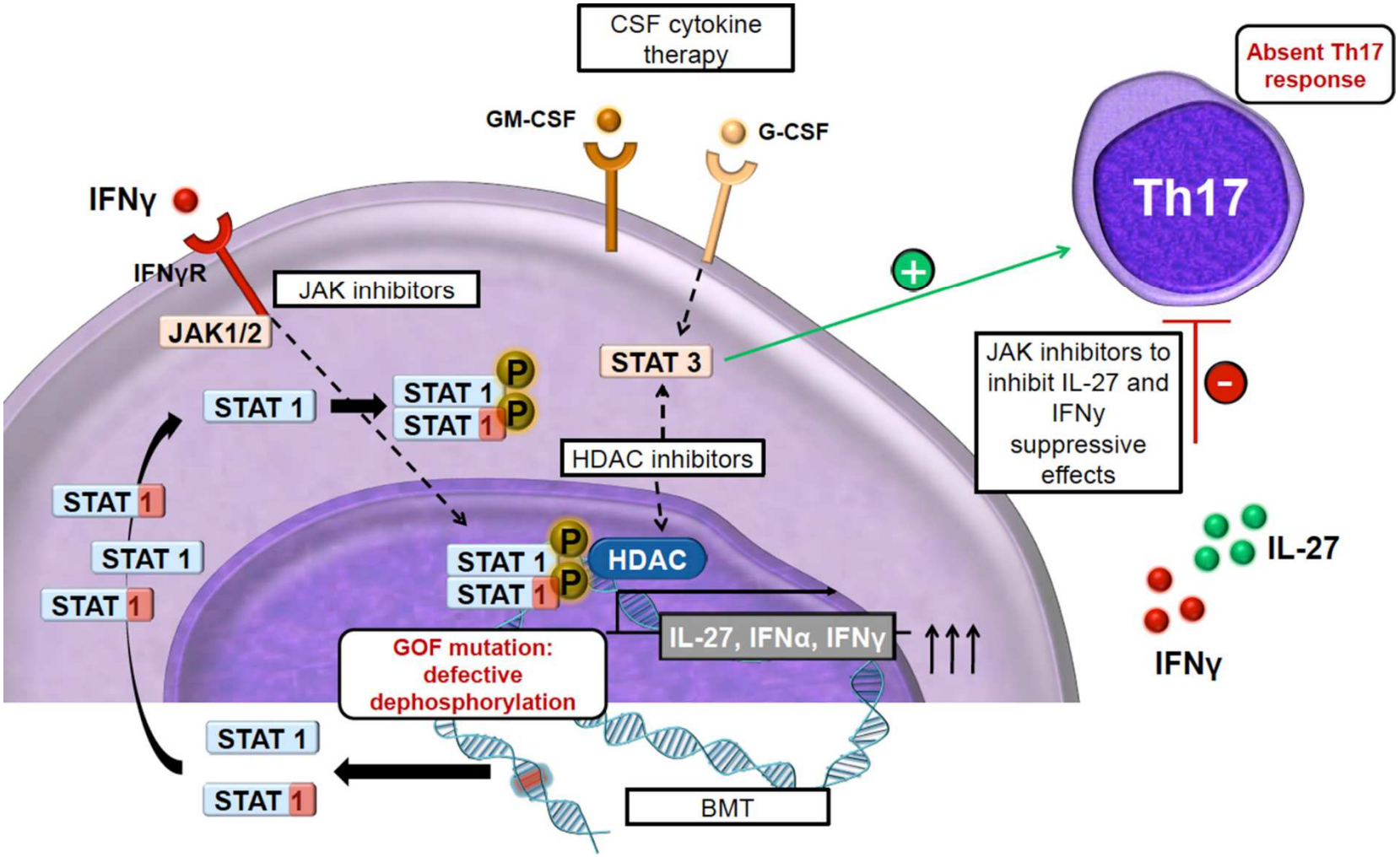


G: Cecum apthous ulcer –arrows indicating PMNs (IBD like)



H: Cecum cryptolytic granuloma with very similar to IBD, crypt shortfall indicating chronic inflammation

Treatment Considerations



van de Veerdonk, Frank L., and Mihai G. Netea. *Journal of Infection* (2016).

Treatment with JAK1/2 inhibitor Ruxolitinib