

# In Depth Case Stimulation - Acne

## 2 cases

- Jonette E. Keri, M.D., Ph.D.
- Professor, Dr. Philip Frost Department of Dermatology and Cutaneous Surgery University of Miami, Miller School of Medicine
- Chief, Dermatology Service, Bruce W. Carter VAMC, Miami VA Hospital

# Disclosures:

- Galderma – Investigator and Speaker
- Almirall – Consultant
- Ortho Dermatologics – Advisory Board

# Identical Twin with Severe Acne

- 18 year old female who presents for evaluation of acne.
- She was previously on isotretinoin, with another physician, but only took it for a short period of time.
- She improved on isotretinoin, but acne has now started to come back, and she really doesn't want to take isotretinoin again.

# Identical Twin with Severe Acne

- She was not a premature baby, but...
- She is an identical twin and her twin was diagnosed with Crohn's Disease
- Her twin was recommended by another physician to get off of isotretinoin given the Crohn's Disease.
- Our patient does have a history of *C. difficile* colitis but not Crohn's Disease.

# Identical Twin with Severe Acne

- Her menstrual periods are more or less regular.
- She does have worsening of her acne around her periods.
- She is otherwise healthy.
- She reports several lesions today and reports scarring.
  
- I went to college with her mother. (☺)

# Is Isotretinoin associated with Inflammatory Bowel Disease?

Latest evidence

# Isotretinoin and Risk of Inflammatory Bowel Disease

- There is no increased risk.
  - A comprehensive search of PubMed/MEDLINE, CINAHL, the Cochrane database, and Google Scholar was performed (July 2015).
  - Looked at 6 studies
  - No increased risk of developing inflammatory bowel disease in patients exposed to isotretinoin versus those not exposed
  - Was true consistently for Crohn's Disease and Ulcerative Colitis
- Lee SY1, Jamal MM, Nguyen ET, Bechtold ML, Nguyen DL. Does exposure to isotretinoin increase the risk for the development of inflammatory bowel disease? A meta-analysis. *Eur J Gastroenterol Hepatol.* 2016 Feb;28(2):210-6.

What is the rate of concordance  
with twins with respect to  
Inflammatory Bowel Disease?



# I looked this up, and....

- Increased with monozygotic twins
- Environment does play a role
- Studies in the Gastrointestinal Literature vary, so difficult to give a number
- There is ethnic group variation

# How would you treat her acne to start?

- 1. Oral antibiotics
- 2. Only topical agents
- 3. Combined oral contraceptives
- 4. Spironolactone
- 5. Isotretinoin

# How would you treat her acne to start?

- 1. Oral antibiotics
- 2. Only topical agents
- **3. Combined oral contraceptives**
- **4. Spironolactone**
- 5. Isotretinoin

But...could you give isotretinoin

- Yes!

Any new information...

# Isotretinoin and IBD – newer information

A global population-based retrospective cohort study

- Conclusion: Isotretinoin does not confer an elevated risk of Crohn's disease, whilst it might be associated with a slight and transient increase in UC risk.

- Khalaf Kridin, Ralf J Ludwig. Isotretinoin and the risk of inflammatory bowel disease and irritable bowel syndrome: A large-scale global study. *J Am Acad Dermatol* 2022 Dec 15;S0190-9622(22)03304-7.

# Inflammatory Bowel Disease (IBD) and acne and isotretinoin and antibiotics

- Questions???
  - Is acne associated with IBD?
  - Is Isotretinoin associated with IBD?
  - Are oral tetracycline-class antibiotics associated with IBD?
- 
- Matthew T Taylor , David J Margolis , Shawn G Kwatra , John S Barbieri. A Propensity Score Matched Cohort Study Identifying an Association of Acne, But Not Oral Antibiotic or Isotretinoin Use, With Risk of Incident Inflammatory Bowel Disease. *J Am Acad Dermatol.* 2023 Jan 19;S0190-9622(23).

# IBD and acne and isotretinoin and antibiotics

There was a statistically significant association between acne and risk of incident IBD (Odds ratio 1.42; 95% CI 1.23-1.65).

There was no statistically significant association between oral tetracycline-class antibiotic or isotretinoin exposure and IBD.

- These data can provide reassurance for the use of isotretinoin in the treatment of acne.

Matthew T Taylor , David J Margolis , Shawn G Kwatra , John S Barbieri. A Propensity Score Matched Cohort Study Identifying an Association of Acne, But Not Oral Antibiotic or Isotretinoin Use, With Risk of Incident Inflammatory Bowel Disease. J Am Acad Dermatol. 2023 Jan 19;S0190-9622(23).



So, I am going to give the  
isotretinoin, but...

**Will the IBD flare?**

# Do patients with IBD flare on isotretinoin?

- Diagnosis of IBD (eg, ulcerative colitis, Crohn's disease, or both/overlap) who were treated with isotretinoin from January 2006 to January 2020 at Mass General Brigham hospitals
- 19 patients
- Looked at flares before and after isotretinoin use:
  - Mean age 35
  - Female 26.3%
  - While 94.7

9 patients flared 2 years prior to starting isotretinoin – of these 5 flared and 4 didn't flare

10 patients didn't flare in the 2 years prior to starting isotretinoin – 7 did not flare and 3 didn't flare

- There is no statistically significant association between maintenance IBD therapy use and the likelihood of flaring during isotretinoin treatment ( P = .15) (Supplementary Table I).
- Christina G. Lopez MD, Ruby Kwak MD, Lindsay McCormack MD, Guohai Zhou PhD and Alexandra Charrow MD, MBE Impact of isotretinoin on inflammatory bowel disease flare in patients with preexisting inflammatory bowel disease diagnosis: A cross-sectional study Journal of the American Academy of Dermatology, 2022-12-01, Volume 87, Issue 6, Pages 1399-1400.

# Flare of IBD on isotretinoin?

- The results suggest a limited association between isotretinoin and the worsening of a patient's baseline IBD.
- 14 years of data from large hospitals, it is limited by the small sample size and retrospective
- Christina G. Lopez MD, Ruby Kwak MD, Lindsay McCormack MD, Guohai Zhou PhD and Alexandra Charrow MD, MBE Impact of isotretinoin on inflammatory bowel disease flare in patients with preexisting inflammatory bowel disease diagnosis: A cross-sectional study *Journal of the American Academy of Dermatology*, 2022-12-01, Volume 87, Issue 6, Pages 1399-1400.

So, what do I do?

**Watch the patient and talk to the gastroenterologist.**

# CASE 2

# Patient with Minocycline Induced Lupus

- 18 year old female with minocycline induced lupus presented to my office
- Got minocycline for acne by outside physician and got severe side effects of myalgias, headaches, rash
- Acne persisted and she was tearful about the acne when seeing me
- Rheumatologist had told her possibly isotretinoin may be another trigger of drug-induced lupus and she was afraid to take any new systemic med.

# What can we do?

- Can we give isotretinoin to this patient with scarring acne and minocycline induced lupus?
- Yes, and I talked to the rheumatologist

# Success with isotretinoin

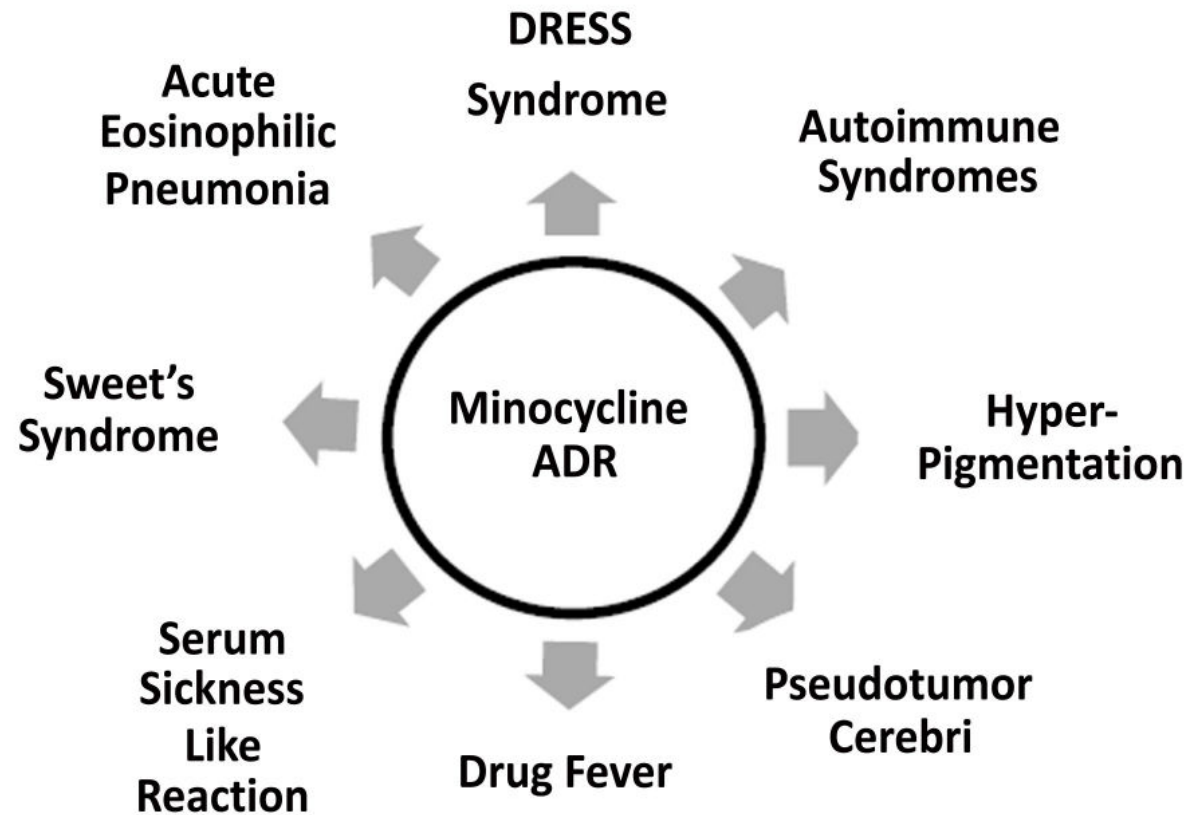
- She had long course of low dose isotretinoin reaching 150mg/kg dose
- She did at times feel a little “down” as per the patient but had a death in the family and Covid pandemic also affected her socially
- We screened repeatedly for any side effects
- Saw her 2 weeks ago and is doing well



# Drug Induced Lupus Caused by Minocycline

- Minocycline is a tetracycline antibiotic that is widely used to acne.
- Several adverse reactions, including life-threatening ones, have been reported.
- Methods: Comprehensive PubMed search of English and non-English literature for case reports of adverse reactions to minocycline was conducted.

# Minocycline Adverse Reactions



Dominic, MR.  
Adverse Reactions  
Induced by  
Minocycline: A  
Review of Literature.  
Review Curr Drug Saf.  
2021;16(3):309-321

Adverse reactions of Minocycline.

# What do you do if you suspect minocycline induced lupus?

- Stop the minocycline
- Don't ignore these calls
- Get labs
- ANA
- P-ANCA
- Refer to rheumatologist
- Continue to treat with what you feel is safe at this time
  - Topicals
  - Prednisone?

But she was a little “tearful” at times

# Isotretinoin and the risk of psychiatric disturbances

- **Methods:** A global population-based retrospective cohort study enrolled 2 groups of patients with acne managed by:
  - isotretinoin (n = 75,708)
  - oral antibiotics (n = 75,708)
- Patients were compared regarding the risk of 9 psychiatric outcomes.
- Khalaf Kridin, Ralf J Ludwig Isotretinoin and the risk of psychiatric disturbances: A global study shedding new light on a debatable story. *J Am Acad Dermatol.* 2023 Feb;88(2):388-394.

# Isotretinoin and the risk of psychiatric disturbances

- **Results: Comparing patients treated with oral antibiotics versus isotretinoin:**
- Lower risk of depression (hazard ratio [HR], 0.90; 95% CI, 0.87-0.93;  $P < .001$ )
- Comparable risk of major depressive disorder (HR, 0.97; 95% CI, 0.92-1.03;  $P = .318$ ).
- Comparable risk of suicide attempts (HR, 0.97; 95% CI, 0.85-1.11;  $P = .663$ )
  
- Elevated risk of suicidal ideation in those under isotretinoin (HR, 1.41; 95% CI, 1.32-1.50;  $P < .001$ ).
  
- **Isotretinoin confers lower risk of 6 psychiatric comorbidities and comparable risk of suicidal attempts.**
- Khalaf Kridin, Ralf J Ludwig. Isotretinoin and the risk of psychiatric disturbances: A global study shedding new light on a debatable story. *J Am Acad Dermatol.* 2023 Feb;88(2):388-394.

# Isotretinoin and the risk of psychiatric disturbances

- Patients under isotretinoin had lower risk of:
  - Depression (hazard ratio [HR], 0.90; 95% CI, 0.87-0.93; P < .001)
  - Post-traumatic stress disorder (HR, 0.75; 95% CI, 0.68-0.82; P < .001)
  - Anxiety (HR, 0.84; 95% CI, 0.82-0.87; P < .001)
  - Bipolar disorder (HR, 0.65; 95% CI, 0.59-0.72; P < .001)
  - Schizophrenia (HR, 0.60; 95% CI, 0.48-0.76; P < .001)
  - Adjustment disorder (HR, 0.82; 95% CI, 0.77-0.87; P < .001)
- **Isotretinoin confers lower risk of 6 psychiatric comorbidities and comparable risk of suicidal attempts.**
- Khalaf Kridin, Ralf J Ludwig Isotretinoin and the risk of psychiatric disturbances: A global study shedding new light on a debatable story. J Am Acad Dermatol. 2023 Feb;88(2):388-394.

Thank you!