Low Dose Naltrexone and Sarcoidosis Therapy

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Disclosures

- Off label use is discussed
- Information is for education
- I am not promoting prescribing LDN

Dr. Weinstock

- LDN pharmacology
- Sarcoidosis

Endorphins

- Endorphins produced in many cells
  - Examples: B-endorphin, enkephalins, endomorphin, dynorphin
  - Met-enkephalin = opioid growth factor (OGF)
  - Regulate cell growth including immune cells
  - Immune system disorders can occur with low levels of endorphins

Endogenous receptors

- CNS and PNS
- GI tract
  - Myenteric plexus
  - Mucosal plexus
  - Endocrine cells of intestinal mucosa
- Lymphocytes

LDN MOA

- LDN blocks OGF receptors for a few hrs
  - Leads to a *rebound effect*
  - Production & utilization of OGF is increased

- Endorphins now interact with more sensitive and plentiful receptors and assist in regulating cell growth and immunity

Met-Enkephalin: Immunoregulator

- MENK binds to receptors on immune cells
- Activation of CD4+ Foxp3+ Tregs suppress immune system to balance immunity

Zhao. Int Immunopharmacol .2016.
Li. Cancer Biol Ther. 2015.

LDN MOA

- Reduces/regulate T-cells, B-cells, natural killer cells, IL-2 and TH-1 improve native immune system

- Shift from TH1 to TH2 decreases autoimmune profile

Additional MOA – Toll receptors

- Endothelial receptors
  - LDN decreases permeability
- Mucosal receptors
  - LDN may stabilize receptor and decrease bacterial translocation
- Microglia – blockade reduces neuro-inflammatory pain – pain is frequent in autoimmune diseases

Li. Med Hypotheses 2012;79:754-6.
Hutchinson et al. Brain Behav Immun 2010;24:83-95.

LDN Summary

- Rebound increase in endorphins
  - Reduce T & B cell production
    - Less cytokines & antibodies
- Shift from Th1 to Th2
- Block TLR on microglia
- Block TLR on mast cells (MC)

Sarcoidosis

Granulomatous disorder with T-cells & macrophages in multiple organs

- CD3+ cells, CD4+ cells w/ HLA-DR antigen, & high CD4/CD8 ratio in bronchus
- CD4+ CD29+ memory T-cells increased

Iida K et al. Thorax 1997;52:431-7.

Sarcoidosis

- Special T-cell interactions in pulmonary and liver sarcoidosis
  - Activated memory T-cells with CD11a

Iida K et al. Thorax 1997;52:431-7.

Sarcoidosis: Pathogenesis

- Genetic susceptibility with functional polymorphisms
- Exposure to antigens leading to activation of macrophages
- Attainment of T-cell immunity against antigens mediated by antigen processing and presentation by macrophage

Zissel

Sarcoidosis vs. Crohn's disease

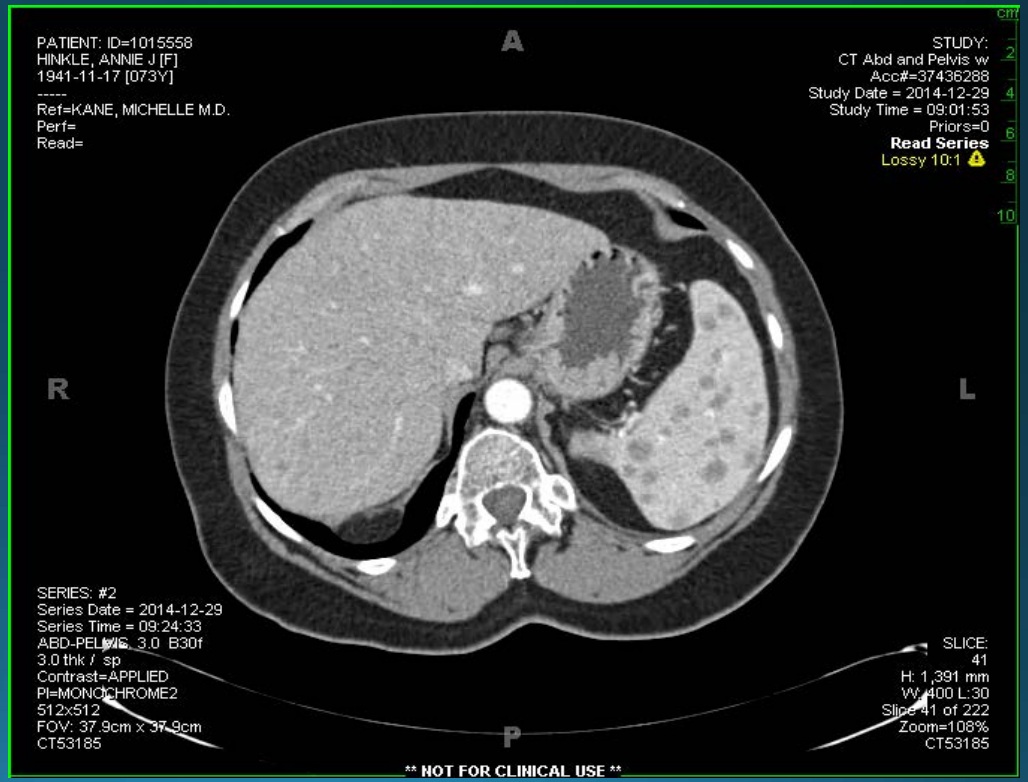
- Similar pathology
  - Unregulated T-cell activity
  - Non-caseating granulomas
- Note efficacy of LDN in Crohn's

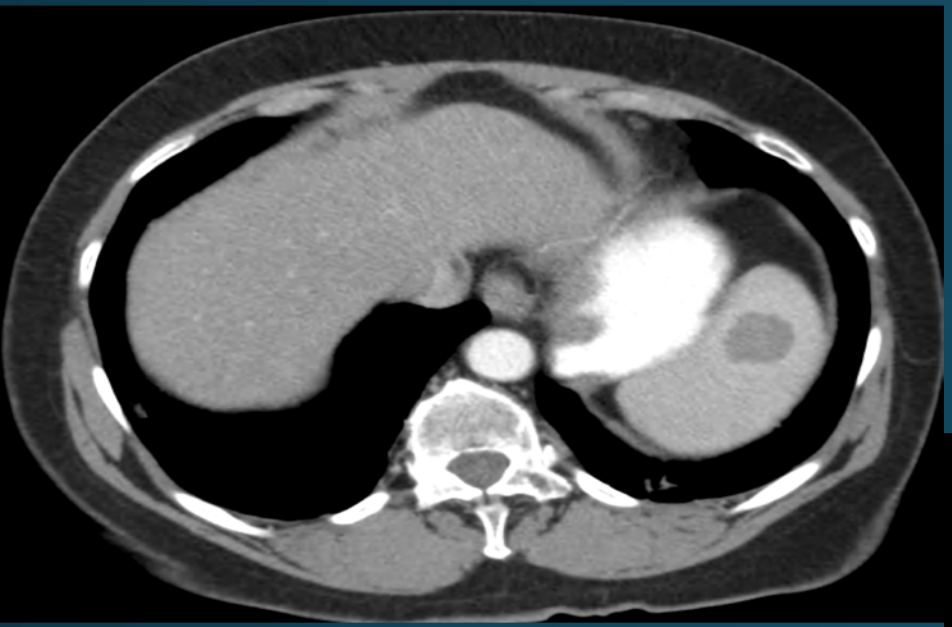
Case 1

73 y.o. AAF – supraglottic resection in 2001

- Fatigue
- Parotitis
- Painful rash
  - prevention

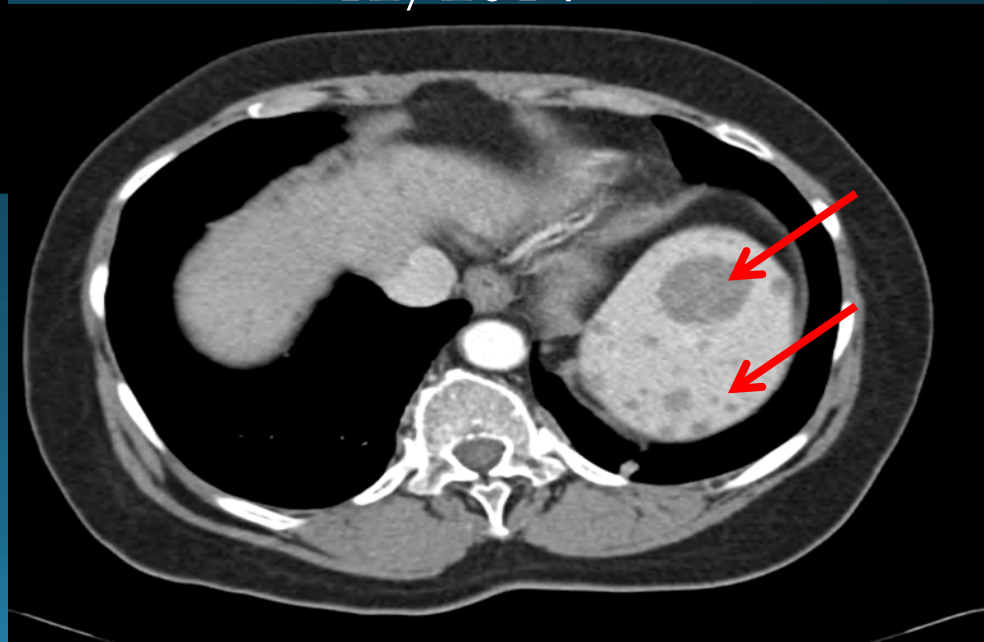
  by minocycline
- AbnI CT





11/2011

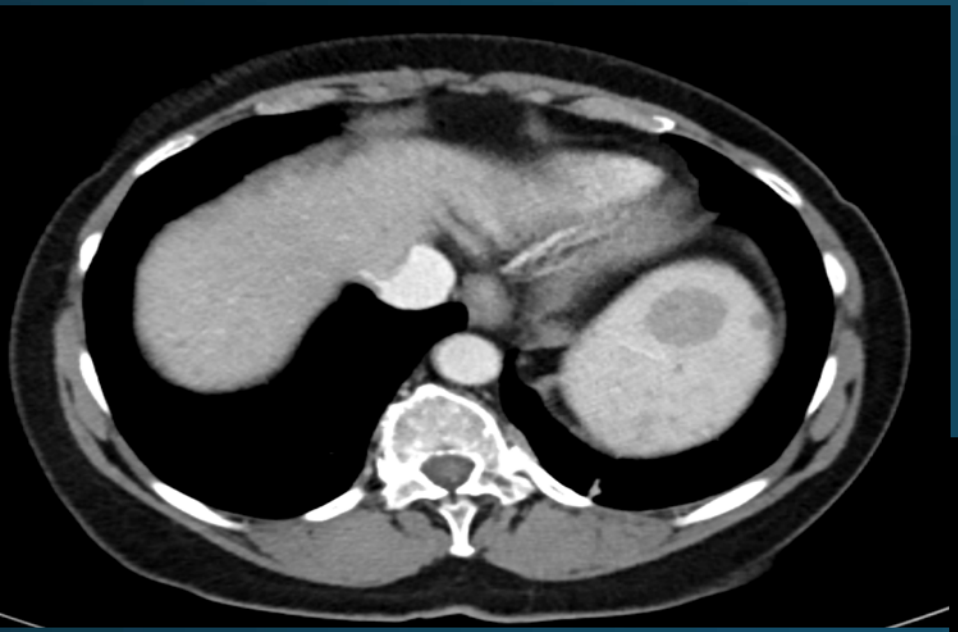
12/2014



Progression without Rx

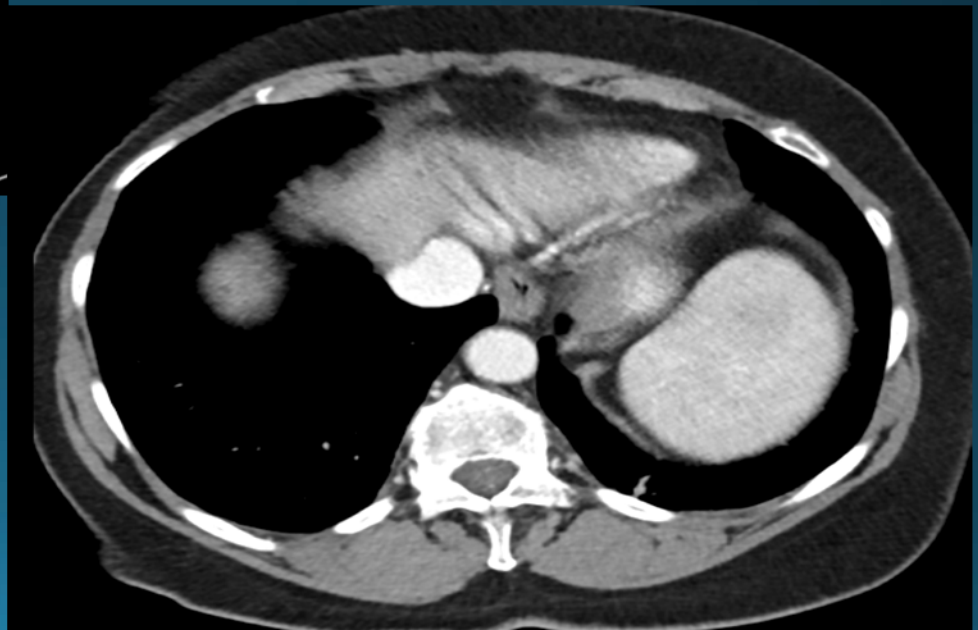
LDN Rx for Sarcoidosis

- February 2015 - LDN 1 mg/day
- March - less dyspnea, fatigue, able to stop minocycline
- March – LDN increased to 4.5 mg
- May – Dec - less DOE, more energy
- July & Dec – CT's showed reduction in the size of the splenic lesions and liver lesions



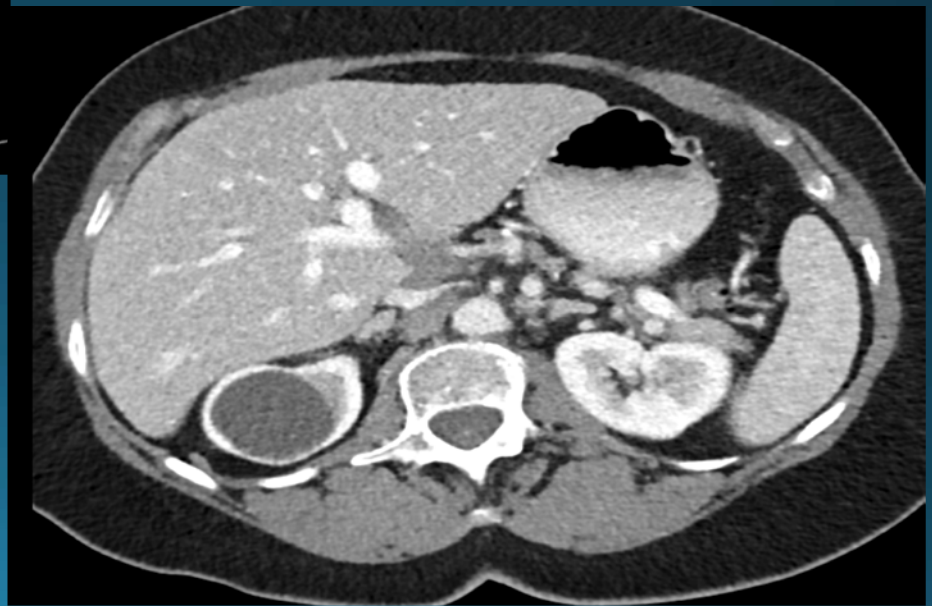
7/15 - 5 mo LDN

12/15 - 10 mo LDN



12/14

12/15 – 10 mo LDN



Case 2: 64 y.o. AAF

- 26 yr pulmonary sarcoidosis
- 2 yr home O2 (24 hr/d; 2 L)
- Dyspnea (rest/activity) and dry cough

- 7/15 - Prednisone 20 mg
  - Last used 16 yr ago
- 8/15 - LDN

Case 2: 64 y.o. AAF

- 9/15 – 1 mo LDN
  - No change
- 10/15 - 2 mo LDN
  - Less fatigue
  - Less dyspnea
  - O_2 prn for vigorous activity
  - Prednisone taper started

Case 3: 35 y.o. WM

- Ventricular tachycardia
- PET scan extensive inflammation in heart, lungs, and lymph nodes
  - Prednisone taper started 4/17 from 25 mg/d over 5 months to 10mg
  - Cannabidiol started on own
  - 10/17 – 6 mg prednisone
  - 11/17 – off prednisone
  - PVC's stabilized - 5%

Case 3: 35 y.o. WM

- Off prednisone 11/17 to 3/18
- Follow up PET scan – active in heart only
- Prednisone restarted

Case 4: 32 y.o. WF

- 5 yr pulmonary sarcoidosis
- Hx pain in joints and parotid glands
- MRI showed evidence of sarcoidosis in joints
- Severe fatigue and brain fog
- LDN started April 2018
- 1 mg rapid response in fatigue
- 2 mg joints less painful
- Increasing dose now to 4.5

LDN and Sarcoidosis

Promising therapy

- Adjunct to therapy
- Alternative to prednisone
- Alternative to immunomodulator

LDN side effects: neurologic

- Anxiety 15.7%
- Drowsiness 11.6%
- Headache 11.6%
- Insomnia 8.3%
- Muscle pain 8.3%
- Vivid dreams 5.0%
- Mood change 3.3%
- Trouble concentration 1.7%

Ploesser J, Weinstock LB, Thomas E. Internat J Pharm Compound. 2010.

LDN: additional side effects

- Nausea 12.4%
- Abd. pain 11.6%
- Diarrhea 8.3%
- Anorexia 8.3%
- Rash, hot flashes, weight gain 0.1% each

LDN: Grass-Roots Movement

LDN 2018 Conference Presentation

By Dr Leonard Weinstock

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