Introduction

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Growth Hormone Deficiency in Fungal Exposure: Primary Environmental Fungal Control Essential for Recovery

Dennis-Robertson Syndrome

Fungal exposure causes systemic inflammation that requires ENVIRONMENTAL intervention

- Small amounts of fungal superantigen activate 3000X normal T-cell inflammatory response with each T cell secreting 3 interleukins, so 9000X normal systemic inflammation occurs therefore:
  - Antigen(Fungus) removal in the patient and environment is essential for success
  - Environmental air mold plate counts of 0-2 colonies (0 in some) is required for recovery
  - All other treatments are not effective long term unless mold control is accomplished

Fungal Effects on Pituitary Axis is Multifactorial:
Hypothesis: Fungi cause HGH Deficiency

- The incidence of GH deficiency in chronic rhinosinusitis (CRS), fatigue, and significant mold exposure is 63 times higher than in population known to be GH deficient: children with short stature, patients with head trauma, pituitary tumors or infiltrating disease (approximately 60 thousand vs. 4.8 million).
- CRS patients have an immune reaction to fungus.
- It is known that fungal cell wall Glucans bind to Anterior Pituitary Folliculostellate (FS) cells & activate Innate Immune system.
- Mycotoxins are neurotoxic especially Aflatoxins and Trichothecenes.
- APECED (autoimmune polyendocrinopathy-Candidiasis-ectodermal dystrophy) chromosome 21q22.3 gene called AIRE (autoimmune regulator) characterized by 2 or more of Hypothyroid, Hypoparathyroid, Candidiasis, adrenal insufficiency.

Major Symptoms of HGH Deficiency in CRS Patients

- Fatigue
- N-Terminal Insomnia
- Exercise Intolerance
- Abdominal Fat
- Poor Short Term Memory

If these are present & resting IGF1 is normal, patient has a 30% chance of needing HGH.
Add CRS & Hx Fungal exposure & incidence is 35%.

Differential for HGH Deficiency

- Head Trauma
- Pituitary Tumor, infiltrating disease
- Isolated GHD
- Fungal Exposure: Hx fungal exposure, persistent fatigue after clearing fungus from environmental air and detoxification.

Probability of GHD Increases with Each Tropic Hormone Deficiency

- e.g. ACTH-cortisol, TSH-thyroid, LH FSH-estrogen
- 80% GHD if one hormone deficient
- 90% GHD if two hormone deficient
- 100% GHD if three hormone deficient
Incidence of Adult GH Deficiency

- Now 2 in 10,000 or 60,000 cases in US, finding 6000 per yr., looking @ pts wi/ Head injury, Tumors, & isolated cases represents 0.02% of population*
- GH deficiency incidence in Pts. with Fungal Exposure, Fatigue, CRS = > approx. 4.8 million or 10.5% of CRS patients or 63 times more patients.
- 53% of CRS with significant mold exposure Hx & Fatigue

* Mathioudakis 2008

Incidence of Anterior Pituitary Deficiency in CRS with Fungal Exposure & Fatigue: Possible Mechanism

Anterior Lobe

- Folliculostellate (FS) cells
- Anterior Lobe in CRS due to fungal exposure
- Fungal exposure activates TLR4 and CD14 gene expression, pattern recognition stimulates cytokines & macrophages
- Macrophage input destroys FS cells

Incidence of Adult Pituitary Deficiency in CRS with Fungal Exposure & Fatigue: Possible Mechanism

Anterior Lobe is destroyed by activation of TLR4 and CD14 gene expression, pattern recognition stimulates cytokines & macrophages in CRS

GH deficiency in Chronic Rhinosinusitis Patients

- May 2004-2008
- Total 79 patients, age 30-77, 64 Female, 15 Male
- 54% (42/79) had chronic sinusitis
- 180% had either/or both a history of environmental mold exposure or positive environmental mold plate testing; 42% had positive mold plate testing, 1% had positive history of mold exposure
- Mold Plate average colony count 21 colonies (normal 6-4)
- Trichothecenes 7 of 8 tested were positive, ITT - grp, IGF1 average 208.5 (normal 88-249 ng/ml)
- 51% HGH deficient (40/79)
- 75% ACTH deficient (59/79)
- 81% 1º or 2º Hypothyroid (64/79) (Free T3 must be 3.7-4.2 to be fungicidal)
- 44% had HGH, ACTH, and TSH deficient (39/79)
- 18% Fatigue, Cognitive Dysfunction, A Significant mold exposure
- 49% Vitamin D Deficient
- 73% Food Allergy with 30% Gluten Intolerance
- 73% GERD with IgG Candida Allergy and Visible Candida on Tongue Base

Mold(s)

- IgG -
- Soybean       5
- Peanut         5
- Wheat      0
- Milk, cow’s  0
- Gluten       1
- Egg yolk    1
- Egg white    0
- Corn (food)  0
- Chicken      0
- Beef          0
- Soybean       5
- Peanut  1
- Milk, cow  0
- Gluten    1
- Egg yolk  1
- Egg white  0
- Corn  0
- Chicken  0
- Beef  0

Food(s)

- Soybean       5
- Peanut         5
- Milk, cow’s   2
- Gluten           3
- Egg yolk       5
- Egg white    5
- Corn (food)   3
- Chicken        5
- Beef             5
- Soybean   0
- Peanut     1
- Milk, cow  0
- Gluten  1
- Egg yolk  1
- Egg white  0
- Corn  0
- Chicken  0
- Beef  0

Total for the Room:

- Alternaria alternatus              0
- Aspergillus fumigatus                  1
- Candida albicans                                 0
- Cladosporium herbarum              0
- Cephalosporium acremonium      0
- Epicoccum purpurascens      1
- Fusarium oxysporum                   5
- Geotrichium candidum              5
- Alternaria alternatus         5
- Aspergillus fumigatus             3
- Candida albicans                           5
- Cladosporium herbarum              5
- Cephalosporium acremonium      5
- Epicoccum purpurascens      5
- Penicillium notatum               5
- Mucor racemosus  6.6 ug/mL 0
- Helminthosporium halodes    0
- Fusarium oxysporum             0
- Epicoccum purpurascens       0
- Cladosporium herbarum          0
- Cephalosporium acremonium    0
- Candida albicans                   0
- Aspergillus fumigatus            1
- Alternaria alternatus              0
- Mucor racemosus                        4
- Penicillium notatum               1
- Helminthosporium halodes          5
- Fusarium oxysporum                   5
- Candida albicans                           5
- Aspergillus fumigatus                  3
- Alternaria alternatus         5
- Mucor racemosus                                    0
- Penicillium notatum                0
- Helminthosporium halodes          0
- Fusarium oxysporum                  5
- Candida albicans                               0
- Aspergillus fumigatus                  3
- Alternaria alternatus              0
- Mucor racemosus                                    0
- Penicillium notatum                0
- Helminthosporium halodes          0
- Fusarium oxysporum                  5
- Candida albicans                               0
- Aspergillus fumigatus                  3
- Alternaria alternatus              0
- Mucor racemosus                                    0
- Penicillium notatum                0
- Helminthosporium halodes          0
- Fusarium oxysporum                  5
- Candida albicans                               0
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2 Pts. with GHD, 1 with CRS & 1 w/o, both with systemic inflammation, so innate immune activation is independent of the mechanism of CRS (IgG & H5-13-INF-γ) so >4.8mill.

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Mycotoxins found in 170 mold exposed patients in Am Urine sample*

- Over 400 mycotoxins known
- >60% were positive to 1 or more of 10 Trichothecenes
- 30% were positive to 1 or more Aflatoxins (B1, B2, G1, G2 Ochratoxin)
- Mycotoxins produce non specific symptoms headache, fatigue, irritability, difficulty concentrating, mucous membrane irritation, chest tightness, skin irritation

*Bill Rea 2007

GH Dosage

- Start with 0.2 – 0.3mg, adjust down if adverse symptoms, balance with Thyroid, Cortisol to improve GH tolerance
- If no symptoms adjust by IGF1 level in 2 months
- Do not exceed 6mg/day
CHRONIC SINUSITIS IS THE MOST FREQUENTLY OCCURRING CHRONIC DISEASE IN THE US

Superantigen Disease Mechanism

Super antigens activate 30% of total T-cells vs. .01% or 3000 X more T-cell activation

This causes systemic toxicity, e.g. affecting every system

TCR Vß motifs similar for SEB & Fungi because IgE to both were always found together in CRS nasal polyps, so MRV vaccine helpful

Known superantigens are: S. aureus enterotoxin (SEB), Epstein-Barr virus, retrovirus associated with breast cancer, Type 1 diabetes, multiple sclerosis, psoriasis, rheumatid arthritis, Alternaria, Bipolaris spicifera, many other molds

Once Vß TCR site is deformed, pt. is susceptible to multiple hypersensitivities to chemicals & drugs, food, bacteria, fungi

Schubert, M. 2001

Super Antigen Interaction with TCR MHC 2 Molecule

Transfer Factor

- Discovered by Sherwood Lawrence 1949, PBL lysate from infected pt. transfers immunity to non immunized patient
- TF is Released by Helper T-Cells
- Binds to specific Antigens (fungi-Bacteria) which are on the surface of infected body cells
- TF makes new Helper T-cells, Natural Killer cells, Macrophages
- Increases TH1 cytokines (TNF & INF-γ) to increase cellular immunity~ Lymphocytes to TH-1 Cells ~ Macrophages
- Lowers TH2 interleukins L1-4, IL-5, IL-13 to lower B cells and antibody immunity

AFS Resolves After Transfer Factor
Transfer Factor Endoscopic Photos Before & After Vaccine

Vaccine Resolves Chronic Sinusitis, Polyps & Mucin in 2 wks

Sinus Infection Resolves After Transfer Factor

Transfer Factor Results