

contain a C-terminal carbohydrate binding module, family 20, domain.³

In summary, we have identified glucoamylase I precursor in *N. crassa* CM using human scFv antibodies. Glucoamylase I precursor is recognized by IgE from some individuals with bakers' asthma and mold allergy, and its presence in vaccines expressed in *N. crassa* needs to be controlled. Besides glucoamylase, antibody NC65 recognizes α -amylase from *A. oryzae* and possibly *S. cerevisiae*, and may be useful as a tool for allergen detection.

Acknowledgments

The authors thank Dr. Elena H. Page from the Health Hazard Evaluations program of the National Institute for Occupational Safety and Health, for providing the human serum samples from bakery workers.

Supplementary Data

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.anai.2012.11.021>

Taruna Khurana, PhD*
Maggie Collison, BS*
Binh Le Haynes, BS†
Edward Cambareri, PhD†
Jay E. Slater, MD*

*Laboratory of Immunobiochemistry
Division of Bacterial, Parasitic and Allergenic Products
US Food and Drug Administration
Bethesda, Maryland
†Neugenes Corporation
Burlingame, California
jay.slater@fda.hhs.gov

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Hypogammaglobulinemia treated with infusion therapy associated with cortisol deficiency

Hypogammaglobulinemia is an inclusive term that encompasses all primary immunodeficiency states with low immunoglobulin or low antibody function. It is characterized by blighted B differentiation with faulty immunoglobulin production. Antibody deficiency characteristically leads to recurrent, often severe, upper and lower respiratory tract infections, usually with encapsulated bacteria.¹ The clinical diverseness of the disease implies that multiple immunological defects can result in the ultimate consequence of hypogammaglobulinemia. The clinical course may be complicated with various autoimmune, endocrinological disorders and malignancies.² We present 5 white female patients with hypogammaglobulinemia without decreased cortisol levels presenting with generalized fatigue and weakness.

Patient A is a 42-year-old white woman with a history of mild intermittent asthma, Hashimoto's thyroiditis and repeated episodes of pneumonia, bronchitis, and sinusitis. Laboratory workup indicated a deficiency of immunoglobulin G (IgG (602 mg/dL) and subclass 1 (367 mg/dL). IgA levels were also low (65 mg/dL), with normal IgM levels (207 mg/dL). Three-week anti-polysaccharide IgG antibody titers illustrated a less than 50% response to the major pneumococcal serotypes. High-resolution computed tomography of the thorax illustrated bronchiectatic changes. Years later she began to feel tired, fatigued, and unable to perform activities of daily living. Thyroid function tests were within normal limits; ensuing laboratory tests indicated a low AM (5 AM cortisol levels) (0.8 μ g/dL), PM (5 PM cortisol levels) (1.2 μ g/dL), high AM adrenocorticotropic hormone (ACTH) level (334 pg/dL), and minimal response to ACTH stimulation tests.

Patient B, a 50-year-old white woman with a history of hypothyroidism, asthma, and Sjögren's, presented with recurrent

nonresolving sinopulmonary infections and oral thrush. Laboratory evaluation demonstrated a low level of IgG (540 mg/dL), subclass I/III (240 mg/dL, 17 mg/dL, respectively), and low IgA (75 mg/dL) and IgM levels (37 mg/dL). The 3-week post-pneumococcal vaccine titers depicted a less than 50% response to the major serotypes. During follow-up visits she began to complain of progressively worsening fatigue, and dyspnea on exertion. Further workup illustrated low AM (0.4 μ g/dL) and PM cortisol levels (0.9 μ g/dL) and high AM ACTH levels (550 pg/dL). Resultant ACTH stimulation tests depicted minimal response.

Patient C, a 30-year-old white woman with a history of asthma and Raynaud's, presented for evaluation of frequent episodes of otitis media, bronchitis, esophageal candidiasis, and viral meningitis. Workup revealed a deficiency in IgG (427 mg/dL) and subclass I/III (192 mg/dL, 15 mg/dL, respectively), also with normal IgA (143 mg/dL) and IgM levels (172 mg/dL). The 3-week anti-polysaccharide IgG response titers to the major pneumococcal serotypes were less than 50%. In later years she started to complain of loss of energy, and weakness with resultant decreased AM and PM cortisol levels (0.44 μ g/dL and 2 μ g/dL, respectively) and minimal response to ACTH stimulation test.

Patient D, 52-year-old white woman with a history of Sjögren's and psoriasis, presented with recurrent skin, soft tissue, and sinopulmonary infections. IgG levels were low (549 mg/dL), as well as levels of IgG subclass I (261 mg/dL), III (26 mg/dL), and IV (1 mg/dL), with low IgA levels (53 mg/dL) and normal IgM levels (91 mg/dL). She also had a limited antibody response to the major pneumococcal serotypes. She began to experience severe fatigue in the ensuing years after the diagnosis, with resultant low AM and PM cortisol levels (0.07 μ g/dL, 1.4 μ g/dL), high ACTH levels, and minimal response to stimulation testing.

In patient E, a 52-year-old woman with a history of Sjögren's, peripheral neuropathy was evaluated for persistent urinary tract infections and gram-positive bacteremia. Initial laboratory tests showed low IgG levels (320 mg/dL), with normal IgA (222 mg/dL) and IgM levels (159 mg/dL). The 3-week post titers had a less than 50% response to the major pneumococcal serotypes. In follow-up visits she appeared to be lethargic and fatigued. Low levels of AM and PM cortisol (0.5 µg/dL, 0.8 mg/dL) were detected. Further workup showed high serum ACTH levels and negligible response to ACTH stimulation testing.

All of the patients presented were treated with intravenous gammaglobulin and hydrocortisone, with successful resolution of symptoms. None of the patients were on any chronic steroid therapy. They only required intermittent short courses (5–7 days) of steroids for exacerbations and were always given tapered doses of steroids to avoid complications. These patients only required oral or intravenous steroids previous to treatment of their hypogammaglobulinemia. Moreover, all of the patients we have described were symptom free, without exacerbations, only needing short-acting beta-agonist therapy, for years after being treated with intravenous gammaglobulin before presenting with weakness and cortisol deficiencies.

Accounts of these types of associations are limited to pediatric cases. Tovo et al described a 6-year-old girl who presented to the hospital with adrenal insufficiency and common variable immunodeficiency.³ Younes and Secord⁴ described an 8-year-old girl with established hypogammaglobulinemia who presented with pneumonia and adrenal crisis.

Hypogammaglobulinemia is associated with a high incidence of inflammatory, endocrine, and autoimmune conditions and malignancies. We suspect that the relationship between the 2 diseases is not coincidental but likely is caused by interactions between endocrine and the immune system. Of the 221 patients with hypogammaglobulinemia in our large suburban practice, 151 are

female, and 5 of them have been diagnosed with cortisol deficiency (3.3%). Although these patients meet the definition of common variable immunodeficiency, they appear to be less clinically involved, which may suggest the type of patients that would be associated with cortisol deficiency. Based on these data, a consideration should be made to check cortisol levels in women with hypogammaglobulinemia, ages 30 to 50 with an underlying autoimmune disorder, presenting with new or worsening fatigue or weakness.

Ali Saad, DO
Devi Jhaveri, DO
Julie Sterbank, DO
Jonathan Horbal, DO
Haig Tcheureledjian, MD
Robert Hostoffer, DO
University Hospitals
Richmond Medical Center
Allergy and Immunology Associates Inc
Cleveland, Ohio
alimsaad17@aol.com

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