

Biotin Deficiency Caused By Long-Term Raw Egg Consumption: A Case Report

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The objective of this case study is to describe dietary methods to aid in the management of a biotin deficiency due to long-term raw egg white consumption..

CLINICAL FEATURES

Biotin deficiency is considered rare and can result from different mechanisms such as an acquired deficiency, consumption of raw egg whites, parenteral nutrition without biotin, and innate errors of biotin metabolism. This case report describes the management and symptomatic improvement of a biotin deficiency due to long-term raw egg white consumption with supplementation and dietary management.

INTERVENTION AND OUTCOME

After adhering to biotin supplementation and dietary modifications for 4 weeks, this patient experienced a complete resolution of all signs and symptoms associated with a biotin deficiency.

CONCLUSION

A case of biotin deficiency through chronic consumption of raw egg whites was successfully treated with biotin supplementation and revised dietary management.

Keywords: Biotin Deficiency, Nutrition, Egg Whites, Supplementation

INTRODUCTION

There are numerous food sources for biotin, and it is found in every living cell in minute amounts. Biotin is absorbed via facilitated diffusion from the diet and in addition, there is some synthesis of biotin by the gut flora. It remains unclear whether biotin synthesis by gut microorganisms contributes importantly to the total biotin absorbed. In general, biotin found in food of animal origin is more available than that of foods from plant origin. However, and most relevant to this case report is the interaction between raw egg whites and biotin. Biotin can be rendered unavailable by avidin (a glycoprotein) that is found in raw egg white. Research studies on determining what symptoms may be present with a biotin deficiency use raw egg white (in powder form) due to its effectiveness as avidin binds with very high affinity.¹⁻⁴ This led to the disorder “egg white injury” when referring to a biotin deficiency caused by consuming raw egg white.¹

Biotin is a B complex vitamin that is considered essential for carboxylases in the human body that support processes

in the cell including gluconeogenesis, amino acid metabolism, and fatty acid synthesis.⁵⁻⁸ The Food and Nutrition Board (FNB) of the United States does not have either Estimated Average Requirement (EAR) or a Recommended Dietary Allowance (RDA) for biotin due to many foods containing biotin.⁹ However, an Adequate Intake (AI) has been established for biotin at 30 mcg/day for male and female adults.⁹ While most foods contain some biotin, foods that contain the most include organ meats, fish, eggs, meat, seeds, nuts, and some vegetables.^{10,11} Biotin is not considered a nutrient of concern as the average intake in the United States ranges from 30-70 mcg/day.^{10,12}

In general, in a normal human population, a true biotin deficiency in the absence of other nutrient deficiencies is rare.¹³ Clinical findings of frank biotin deficiency include periorificial dermatitis, conjunctivitis, alopecia, ataxia, hypotonia, ketolactic acidosis/organic aciduria, seizures, skin infection, and developmental delay in infants and children.^{14,15} However, there is a general lack of dermatologic literature describing skin features in this deficiency. Children affected most show a macropapular eruption typically described as scaly and erythematous, especially in moist and periorificial areas.¹⁴ In addition, the alopecia can also include the eyebrows and eyelashes which is a distinction since many will associate the deficiency with simple hair loss.¹⁴ However, the exact mechanism by which biotin produces this remains unknown.

Biotin deficiency results from different mechanisms such as an acquired deficiency, such as consumption of raw egg whites, parenteral nutrition without biotin, and innate errors of biotin metabolism.^{15,16} The two identified innate errors of metabolism are a holocarboxylase deficiency and biotinidase deficiency.¹⁵⁻¹⁷ Biotinidase deficiency is well studied. In fact, most signs and symptoms of deficiency were obtained from people lacking normal biotinidase. A deficiency of this enzyme results in decreased absorption of biotin and the inability to recycle free biotin.¹⁸

It should be appreciated that biotin does have known interactions with other molecules. One of the major biotin-drug interactions is with anticonvulsants. Biotin requirements may be increased during anticonvulsant therapy. The anticonvulsants primidone and carbamazepine inhibit biotin uptake into

brush-border membrane vesicles from human intestine.¹⁷ Long-term therapy with anticonvulsants increases both biotin catabolism and urinary excretion of 3-hydroxyisovaleric acid.¹⁸ Phenobarbital, phenytoin, and carbamazepine displace biotin from biotinidase, possibly affecting plasma transport, renal handling, or cellular uptake of biotin.¹⁹ In addition, lipoic acid competes with binding to the sodium-dependent multivitamin transporter (SMVT).¹⁹ Due to this it is hypothesized that it may potentially decrease the cellular uptake of biotin.¹⁹ This is an important finding as evidence has clearly indicated that the SMVT is the major biotin uptake system that operates in intestinal and liver cells.²⁰

This case report describes a patient with a biotin deficiency who inquired about alternative management of the condition through dietary and lifestyle changes. The patient was consuming 5-8 raw egg whites a day for 16 months. Biotin supplementation at 5 mg/day and a revised dietary regimen were recommended. After adhering to both supplementation and dietary modifications for 4 weeks, the patient experienced a complete resolution of signs and symptoms consistent with the presentation of a biotin deficiency due to long-term raw egg white consumption.

CASE REPORT

A 23-year-old male sought treatment for a constellation of symptoms including thinning of hair on the head and body, scaly red rashes around the nose, conjunctivitis, seizures, and hearing loss. The subject reported seeing both his primary care physician and a neurologist for treatment of his condition. Neither the Primary Care Physician (PCP) nor the Neurologist was able to provide a precise diagnosis. Extensive lab testing was performed that was all unremarkable. Treatment had consisted of a topical prescription of corticosteroid cream for the rashes, antibiotic eye drops for the conjunctivitis along with antihistamines, no treatment was provided for the seizures or hearing loss. The subject stated overall good compliance with these recommendations and some improvement in both the rashes and conjunctivitis only.

The subject had first experienced some of this symptomatology in early 2018. The symptom onset was gradual and began primarily as dermatological including red scaly skin rashes and dermatitis. The initial treatment from the PCP was topical steroid cream which was partially effective. Symptomatology progressed to conjunctivitis and some hair thinning in mid-2018. Treatment from the PCP was antibiotic eye drops and antihistamines for conjunctivitis. No treatment or diagnosis was rendered for the hair thinning. In late 2018 the subject began to experience bouts of hearing loss in the

right ear. This was confirmed with an additional visit to the PCP, but no treatment was rendered. The subject was diagnosed with a sensorineural hearing loss in the right ear. Patient was referred to a Neurologist and the hearing loss was confirmed in addition to some paresthesia in the left arm. No specific treatment was rendered. The labs ordered were unremarkable. In early 2019 the subject who was a student, had a seizure during a lecture. This occurred again the following week while the patient was attending class at school.

The subject was a student in my classroom during the first seizure. Later that week during a lecture on micronutrients in which we were discussing B vitamins and specifically biotin, the subject's girlfriend raised her hand and stated that many of the signs and symptoms of a biotin deficiency were present in her boyfriend. The subject stated he had been eating approximately 5-8 raw egg whites a day for the last 16 months. The subject asked if he could receive a consultation and became a patient in early 2019.

In early 2019, the subject expressed a genuine concern over the lack of progress in their condition. The total number of symptoms had increased over the last year and had continued to progress. The subject sought alternative management for their signs and symptoms and wanted an extensive review of nutritional factors that could be related to this condition. The subject was very concerned about the progression of symptoms and especially the seizures and lack of progress and diagnosis of their condition. The subject became a patient in early 2019.

HISTORY, EXAMINATION, AND LABORATORY FINDINGS

The review of systems indicated a healthy male with no major abnormalities detected beyond his previous symptomatology. A family history of cardiovascular disease and cancer was present on both sides of the family. The patient reported two hospitalizations related to the seizures that occurred at school. The patient was in the hospital for 24 hours for extended monitoring after each seizure. The labs were unremarkable. The patient denies any other current or past pathologies. The patient indicates normal bowel movements, at least once a day. The consistency, according to the patient's description, appears normal. Urination, both frequency and color as reported by the patient, appeared within normal limits.

A complete physical exam was completed with the patient's PCP prior to consultation. A nutrition exam was performed. Observation of the patient during the consultation revealed a healthy Caucasian male that was intelligent with



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full cognitive function. Patient is a full-time student. His physical presentation appeared muscular without any obvious abnormalities beyond the previous signs and symptoms (red scaly rashes, conjunctivitis, right sided hearing loss, left arm paresthesia, and hair thinning). Patient is of normal weight for height. The patient does perform regular physical exercise such as resistance training six days a week for approximately 90 minutes. The patient describes their overall activity level as active.

The patient is 5'11" and weighs 198 lbs. Blood pressure values were within the normal range (right arm 122/79 mm HG, left arm 118/80 mm HG). Patient is right hand dominant. The temperature was normal (98.3 F). The body mass index indicated 27.6 which is considered overweight. However, skinfold anthropometry (7 site) indicated a result of 14%, which falls under the fitness category (healthy).

Diet history was performed through a free online program called Cronometer.²¹ The patient was instructed to enter 4 days of food intake, 3 weekdays and 1 weekend day. Maintenance calories were calculated with Aragon's TEE equation (11.5 x lean body mass in pounds). The results of the 4-day food record indicated overconsumption of energy on all 4 days recorded. The amount of overconsumption ranged from 400-700 calories, with the largest variation seen on the weekend day. This was expected as the patient is attempting to put on more weight and is part of his overall program to increase muscle. The patient exhibited a tendency to have multiple meals throughout the day with small high protein snacks throughout the evening right up until bedtime. The patient is meeting recommended daily intake (RDI) for some vitamins and minerals except for calcium, fiber, iron, potassium, folate, and vitamin D. Beverage intake includes adequate amounts of water, or carbonated water, and black or green tea. The patient does not consume coffee and his estimated daily caffeine intake from the food diary was 120 mg a day. The patient denies using any nutritional supplementation. Patient reports that he is not currently on a diet, nor has he used a particular dietary strategy for health.

The overall dietary picture indicated a poor variety of nutrient dense food with inclusion of many high protein foods (red meat, chicken, Greek yogurt, cottage cheese, whey protein, raw eggs). Processed food consumption was high although they were typically fortified with many of the vitamins and minerals that would have been lost in processing. The patient eats out regularly. The frequency of fast-food intake, on average, was 4 times a week. The patient does not routinely cook full meals at home. Most meals are prepackaged and frozen. The patient does indicate occasional gastrointestinal problems. The patient has not completed a

food journal to illuminate which foods may be associated with the GI problems.

Laboratory values were provided by the patient from a previous visit to his PCP. Laboratory values for the CBC were within normal limits. The blood lipid profile was unremarkable. The patient had a thyroid panel completed which was all within normal limits. Kidney function tests were unremarkable.

WORKING DIAGNOSIS AND TREATMENT PLAN

The patient is currently lacking a definitive diagnosis. It was determined from the information provided that the patient most likely had a biotin deficiency due to excessive long-term raw egg white consumption. While the patient does not normally take any nutritional supplements, they were willing to take a biotin supplement for a trial of treatment along with complete removal of all raw egg whites from the diet.

METHODS USED TO TREAT AND OUTCOMES

The patient was instructed to begin a symptom diary to make a record of the prevailing symptoms and any improvement or resolution. The patient was provided extensive information about signs and symptoms of a biotin deficiency and the interaction of raw egg whites on biotin absorption. As the patient sought treatment for signs and symptoms related to biotin deficiency only, major dietary changes were not recommended during this trial of treatment. The patient was encouraged to seek additional nutritional counseling at the end of this trial of treatment for overall dietary improvement.

The supplementation regimen was biotin at 5 mg/day for 4 weeks. Dietary management consisted of a complete removal of all raw egg-white consumption. It was indicated that based on a previous case study a very high oral dose was necessary for rapid symptom resolution. This was important because a 5 mg/day dose of biotin is substantially higher than the AI for adults which is 30 mcg/day. There is no evidence that high levels of biotin are harmful or cause toxicity as excess is excreted in the urine.⁹

RESULTS OF TREATMENT

The patient was experiencing red scaly rashes, conjunctivitis, right sided hearing loss, left arm paresthesia, and hair thinning prior to treatment with the 5 mg/day biotin supplement and the revised dietary management consisting of a removal of all raw egg whites. After adhering to these rec-

ommendations' symptom reversal was rapid. In less than a week, there were no signs of dermatitis, red scaly rashes, or conjunctivitis. Within 2 weeks on follow-up the appearance of tiny new hairs was apparent on the scalp and areas of the body in which hair thinning was experienced. At 4 weeks, the patient no longer had paresthesia in the arm or hearing loss. The patient indicated full compliance with all recommendations and the symptom resolution is consistent with adherence. After symptom resolution at week 4, biotin supplementation ceased. Dietary analysis indicated the patient was exceeding the AI for biotin from food. The patient was encouraged to cook all eggs and to refrain from consumption of raw egg whites in the future.

DISCUSSION

While biotin deficiency is considered rare, this is an important opportunity to appreciate that deficiencies can and still do occur even within one of the world's largest economies. According to data from the Centers for Disease Control and Prevention about 10% or less of the general population had nutritional deficiencies related to vitamins and minerals in the United States.²³ However, biotin is found in many foods, and Americans are receiving more than sufficient biotin in the United States that either meets or exceeds the AI.^{10,12} In this particular case study, the primary issue was not a frank deficiency of biotin due to diet, but rather a unique interaction between raw egg whites and biotin. Lack of knowledge of this interaction led to a biotin deficiency.

The exclusive feature of this case study is the presence of one food, raw egg whites, and the corresponding biotin deficiency that is considered very rare. The deficiency of biotin due to long-term raw egg white consumption is well understood and is called "egg white injury".^{24,25} Consumption of raw egg whites on a regular basis causes a biotin deficiency due to the avidin glycoprotein present in the uncooked egg white.²² Avidin tightly binds to biotin and renders it unavailable for intestinal absorption.²² Conversely, cooking eggs denatures avidin, thus making it unable to tightly bind dietary biotin.²² In this case study, the patient was consuming approximately 5-8 raw egg whites every day for 16 months.

Biotin deficiency will lead to variable clinical presentations. While this patient experienced red scaly rashes, conjunctivitis, hearing loss, hair loss, paresthesia, and seizures there are other important signs and symptoms of a biotin deficiency that should be appreciated. While the dermal manifestations of a biotin deficiency are due to impaired fatty acid metabolism which includes symptomology such as hair loss (alopecia) and periorificial dermatitis; scaly, red rash around the orifices, i.e., eyes, nose, and mouth ("biotin-

deficient face"), conjunctivitis, and skin infections.²⁶⁻³⁰ Neurological symptoms of biotin deficiency include hypotonia, seizures, ataxia, numbness and tingling of the extremities, mental retardation, and developmental delay in children. The patient may also show depression, lethargy, and a history of hallucinations. Other neurological abnormalities include optic atrophy and sensorineural hearing loss if the condition is left untreated.²⁶⁻³⁰ Intestinal symptoms may also develop in patients with biotin deficiency, such as nausea, vomiting, and anorexia.²⁶⁻³⁰ Other biotin deficiency presentations include ketoacidosis, lactic acidosis, and organic aciduria.³¹

Biotin deficiency is reversible and can be treated with oral biotin supplements as they have high bioavailability. Typically, a dose of 5 mg/day is given for all forms of biotin deficiency.²⁴ While biotin deficiency due to raw egg white consumption is rare, it can have serious consequences. It is important to be aware of the potential risks associated with consuming raw egg whites and to ensure adequate intake of biotin through a balanced diet or supplementation if necessary.

CONCLUSION

A patient presenting with signs and symptoms consistent with a biotin deficiency was consuming 5-8 raw egg whites a day for 16 months. After adhering to both supplementation (5 mg/day) and dietary modifications (removal of raw egg whites) for 4 weeks, the patient experienced a complete resolution of signs and symptoms consistent with the presentation of a biotin deficiency due to long-term raw egg white consumption.

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