



Gynecomastia in Severe Celiac Disease After Treatment with a Gluten-Free Diet

Hugh James Freeman*

Department of Medicine (Gastroenterology), University of British Columbia, Vancouver, BC, Canada

*Corresponding Author: Hugh James Freeman, Department of Medicine (Gastroenterology), University of British Columbia, Vancouver, BC, Canada.

Received: August 16, 2024

Published: August 28, 2024

© All rights are reserved by **Hugh James Freeman**.

Abstract

A 29-yr-old man with diarrhea and weight loss was diagnosed with clinically severe celiac disease. He was treated with a gluten-free diet leading to resolution of his diarrhea and rapid weight gain along with improved small bowel biopsies. During his dietary treatment, he had also purposefully consumed approximately 5000 added calories daily. Subsequently, bilateral gynecomastia developed leading to an extensive list of negative endocrine investigations. Gynecomastia complicating or associated with adult celiac disease is exceedingly rare. A re-feeding syndrome appeared to cause transient “physiologic” gynecomastia. This spontaneously resolved within weeks and did not recur. Physicians prescribing gluten-free diets should be aware of this unusual complication, particularly in severe disease reflected in significant weight loss. This re-feeding syndrome appears to be more likely to occur if there is a significant supplementation of the gluten. Celiac disease is a small intestinal mucosal disorder that may present clinically with diarrhea and weight loss together with typical, but non-specific histopathological changes in small bowel biopsies.

Keywords: Celiac Disease; Gynecomastia; Re-feeding Syndrome; Gluten-free Diet Treatment

Introduction

This spontaneously resolved within weeks and did not recur. Physicians prescribing gluten-free diets should be aware of this unusual complication, particularly in severe disease reflected in significant weight loss. This re-feeding syndrome appears to be more likely to occur if there is a significant supplementation of the gluten. Celiac disease is a small intestinal mucosal disorder that may present clinically with diarrhea and weight loss together with typical, but non-specific histopathological changes in small bowel biopsies [1,2]. A gluten-free diet usually results in resolution of diarrhea and improved small bowel mucosal architecture and function [3]. As a result, weight gain usually occurs because of improved nutrient absorption.

In celiac disease, adverse effects of gluten-free diets are generally not detected [4]. However, these may occur. For example, in some reported studies [5,6], increased, possibly significant levels of some heavy metals in blood and urine have been noted, including both celiac disease patients as well as in normal controls. These metals include mercury, lead and cadmium [5,6].

Adverse effects of gluten-free diets have focused on the benefits of therapy, especially in celiac disease. Other effects [7], even obesity, have been recorded in celiacs and their non-celiac relatives attributed to “behavioral” changes in families consuming a gluten-free diet. Further in-depth studies are needed to define the long-term changes resulting from gluten-free diets.

Case Report

A 29-yr old man was referred for evaluation of diarrhea and weight loss. His diarrhea began almost 4 years earlier. Initially,

his diarrhea was episodic, never bloody, but irregular, with an estimated frequency of about 2 to 3 times daily. Over the most recent 6 months, however, his diarrhea increased in frequency and was accompanied by the development of weight loss but no abdominal pain. He noted his “health-focus” with daily use of multivitamins with a diet consisting largely of wheat and carbohydrate products. He was a university graduate with a degree in physical education. Although he was currently unemployed, he lived with his father and described daily physical activity, jogging up to 10 km. There was no prior medical history or family history of intestinal disease. Physical examination showed a well-appearing but thin man, almost 6 feet (70 inches) (or, 177 cm), but with no definite features of malnutrition. Weight was 60 kg (or, 132 pounds).

Blood studies revealed a hemoglobin of 133 g per L (normal, 140 to 180), serum iron 8 umol per L (normal, 7-23) with 14% saturation (normal over 20) and a slightly prolonged prothrombin time of 14.4 seconds (normal, 10.0-12.5). An abdominal ultrasound was normal. Upper GI endoscopy revealed normal appearing mucosa but duodenal biopsies showed changes of severe villous atrophy with crypt hyperplasia and intra-epithelial lymphocytosis, characteristic of untreated celiac disease [1-3]. A gluten-free diet was initiated. In follow-up, it was estimated that he also consumed a daily dietary intake of 5000 calories.

After 3 months, weight had increased to 70 kg and his diarrhea had resolved. Repeat blood work was normal with a hemoglobin of 146 g per L, normal iron studies and normal coagulation status. Electrolytes and renal function were normal. Repeat duodenal biopsy showed normalization of villous architecture. However, he complained of bilateral breast tenderness and swelling. Examina-

tion revealed palpable and tender breast tissue prompting referral to an adult endocrinologist. He denied any past history of gynecomastia, including during puberty. At that time, he did recall some acne on this face and neck, but not in recent years. There was no history of impotence, symptoms of possible thyroid dysfunction or family history of endocrine disorder.

Examination was otherwise normal with normal male genitalia and testes [8], a normal neurological examination and normal extremities with no evidence of edema. Blood studies for serum estradiol, testosterone, prolactin, thyroid screening and beta-HCG were normal, all suggestive of “physiological” gynecomastia associated with re-feeding and weight gain on the gluten-free diet. A review at 6 months and 1 year revealed clinical resolution of his gynecomastia.

Discussion and Conclusion

This report focuses on a young man presenting with diarrhea and weight loss attributed to biopsy-defined celiac disease. During the early course of his treatment with a gluten-free diet, he unexpectedly developed gynecomastia. Gynecomastia has rarely been associated with celiac disease *per se* [9] and, in the present case, likely reflected improved absorption and rapid weight gain on a gluten-free diet rather than a new “autoimmune”-related complication or direct association with celiac disease. Rapid weight gain, in this case after treatment with a gluten-free diet, may suggest another, as yet potential adverse effect of a gluten-free diet, “physiologic” gynecomastia, here associated with the so-called re-feeding syndrome [10,11]. Gluten-free diets have been well documented to reverse alterations in small intestinal architecture in celiac disease and, as a result, improved nutrient absorption with weight gain. Normalization of some indirect markers of nutritional status (hemoglobin, serum iron and others) usually also occurs [12,13]. Interestingly, treatment with a gluten-free diet in children with celiac disease may also lead to “behavioral” changes in eating habits for the affected child and their families with more stable food eating, labeled by others a more “obesogenic” environment, including consumption of more junk food with added snacks and candies [7]. The present patient’s diet also appeared to change in his bid to improve his health status with consumption of an estimated 5000 calories per day that accompanied his clinical improvement. This change may have also impacted the appearance of his post-treatment gynecomastia, likely physiologically reflective of caloric re-feeding and enhanced nutrient uptake.

The re-feeding syndrome likely occurs in celiac disease following treatment more often than is currently appreciated, especially

if the disease initially appears to be clinically severe. After initiation of treatment with a gluten-free diet, careful follow-up is important. Although the appearance of the re-feeding syndrome among hospital inpatient populations is often appreciated within days of onset of re-feeding (often after courses of infused parenteral nutrition solutions), most patients with celiac disease will likely be managed in an office or ambulatory setting, making recognition of the re-feeding syndrome more difficult. Conceivably, in the present patient, a superimposed high caloric intake may also have played a critical role in the appearance of this re-feeding syndrome and eventual clinical detection of gynecomastia. Other previously described clinical features associated with the re-feeding syndrome [10,11], including potentially serious electrolyte deficits, were not evident here.

Clinical suspicion of a re-feeding syndrome requires that further evaluation be considered especially in males beyond the age of puberty, especially if there is no obvious explanation. Alterations in the androgen-estrogen ratio and the effects of growth hormone, prolactin, and other factors affecting the aromatase enzyme should be excluded. Obesity, drugs, hypogonadism, liver and renal failure, thyroid disease, Klinefelter’s syndrome and neoplastic disorders (e.g., testicular tumors) should be considered [8,10,11,14]. In the present report, having excluded each of these, an adverse effect of a gluten-free diet in celiac disease with a superimposed high caloric intake was suspected as the likely cause. In time, his gynecomastia

Bibliography

1. Freeman HJ. “Pearls and pitfalls in the diagnosis of adult celiac disease”. *Canadian Journal of Gastroenterology* 22 (2008): 273-280.
2. Freeman HJ. “Role of biopsy in diagnosis and treatment of adult celiac disease”. *Gastroenterology and Hepatology Bed to Bench* 11 (2018): 191-196.
3. Freeman HJ. “Mucosal recovery and mucosal healing in biopsy-defined adult celiac disease”. *International Journal of Celiac Disease* 5 (2017): 14-18.
4. Freeman HJ. “Adverse effects of gluten-free diets”. *International Journal of Celiac Disease* 6 (2018): 71-73.
5. Raehsler SL, Chuong RS, Marietta EV, Murray JA. “Accumulation of heavy metals in people on a gluten-free diet”. *Clinical Gastroenterology and Hepatology* 16 (2018): 244-251.
6. Patel NK and Lacey BE. “Another reason to avoid a gluten-free diet”. *Clinical Gastroenterology and Hepatology* 16 (2018): 184-185.

7. Levrn N, *et al.* "Obesogenic habits among children and their families in response to initiation of a gluten-free diet". *European Journal of Pediatrics* 177 (2018): 859-866.
8. Pizza C, *et al.* "Clinical presentation, management and follow-up of 83 patients with Leydig cell tumors of the testis: a prospective case-cohort study". *Human Reproduction* 34 (2019): 1389-1403.
9. Gliberman H, *et al.* "Gynecomastia in a patient with celiac disease". *Journal of Pediatric Endocrinology and Metabolism* 2002 (15): 103-104.
10. Ponzo V, *et al.* "The refeeding syndrome: a neglected but potentially serious condition for inpatients. A narrative review". *Internal and Emergency Medicine* 16 (2021): 49-60.
11. Kanakis GA, *et al.* "EEA clinical practice guidelines-gynecomastia evaluation and management". *Andrology* 7 (2019): 778-793.
12. Freeman HJ. "Iron refractory or iron resistant iron deficiency anemia in adult celiac disease resolves with a gluten-free diet". *International Journal of Celiac Disease* 6 (2018): 26-29.
13. Freeman HJ. "Iron deficiency with anemia in adult celiac disease: complication or presenting clinical feature". *International Journal of Celiac Disease* 10 (2022): 1-4.
14. Ayyavoo A. "Gynecomastia". *Indian Journal of Pediatrics* 90 (2023): 1013-1017.