Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 7 Issue 9 September 2024

Case Report

Prolonged Survival in Immunoglobulin a (IGA) Deficiency and Adult Celiac Disease Complicated by Metastatic Small Intestinal Adenocarcinoma

Hugh James Freeman*

Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

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

Received: August 05, 2024

Published: August 23, 2024

Abstract

A 48-year-old male with celiac disease was treated with a gluten-free diet. Within a year, he presented with a small bowel obstruction caused by a jejunal adenocarcinoma with metastatic disease involving 7 of 13 lymph nodes. After surgical resection, a single course of adjuvant chemotherapy with 5-flurouracil and folinic acid was given. Subsequent clinical, laboratory, radiologic and endoscopic imaging follow-up studies were normal, except for a selective deficiency of immunoglobulin A. Now, over 3 decades later, his celiac disease remains in histopathological remission and there has been no evidence of cancer recurrence.

Keywords: IgA Deficiency; Celiac Disease; Gluten-Free Diet; Small Bowel Adenocarcinoma

Prior studies have detailed different malignancies in celiac disease, particularly lymphoma and adenocarcinoma in the small intestine [1-4]. If a localized small bowel carcinoma is detected, there may be an opportunity for cure of the cancer since complete resection is possible. In others with metastatic carcinoma that has already spread, long-term prognosis is likely worse but this has not been well studied. Even studies on malignancy in large series of patients with concomitant IgA deficiency *per se* are generally lacking, however, there appears to be a moderately increased risk of cancer, particularly gastrointestinal cancer, among adults with documented IgA deficiency, but not children [5]. Also an increased risk of lympho-proliferative malignancy was not observed in adults with selective IgA deficiency [5]. Interestingly, the malignancy risk was highest during the immediate time after initial diagnosis, suggesting to these investigators that this may be a reflection of a form of surveillance bias [5]. In the present report, a patient with IgA deficiency and celiac disease was complicated by small bowel cancer. Despite metastatic disease, his survival continues, now more than 3 decades following initial detection of malignancy.

Case Report

A 48-yr-old male developed vague upper abdominal bloating and intermittent burning epigastric pain in May 1994. Blood studies by his family physician were normal. Omeprazole provided temporary symptom relief but because of recurrent pain, he was eventually referred for further assessment in August 1994. His only past history was an appendectomy at age 8 yrs. Physical examination was normal. Ultrasound, computerized tomographic studies and a barium study of the esophagus, stomach and duodenum were normal. Upper GI endoscopy was normal along with gastric biopsies but duodenal biopsies suggested untreated celiac disease with crypt hyperplastic villous atrophy [6,7]. A gluten-free diet was initiated but his symptoms persisted, including weight loss. In December 1994, he presented to the same hospital surgical service with severe abdominal pain and studies showed an obstructed jejunum. A laparotomy was done with a small bowel carcinoma detected leading to surgical resection of a high grade, poorly differentiated adenocarcinoma with metastatic carcinoma in 7 of 13 lymph nodes. Liver biopsy was negative. He was treated with post-operative adjuvant chemotherapy that included 5-fluorouracil and folinic acid for 6 months from February to July 1995.

By May 1996, he was doing well with weight gain of 7 kg. He had occasional episodes of abdominal bloating, but no pain.

Radiographic studies, including chest radiographs, barium studies and computerized tomography, were normal. CA-19.9, carcinoembryonic antigen, blood counts and liver chemistry tests were normal.

Because of recurrent epigastric burning pain associated with weight loss, he was referred to our service for review in December 1997. His pain resolved with oral antacids. Of note, he reported that his 19-yr-old son had recently died from non-Hodgkin's lymphoma. Immunoglobulin results were not measured in this patient. Our referred patient had remained on a gluten-free diet. Upper GI endoscopy was normal and duodenal biopsies showed only minimal changes with intraepithelial lymphocytosis [6,7].

In 1998, he reported some looseness of his stools, however, blood studies were normal with a hemoglobin of 152 (normal, 133-165) and a white blood count of 5.8 giga/L (normal, 4.0-10.0). INR, total protein, albumin, iron studies and liver/renal chemistry tests were normal. Red cell folate and serum vitamin B12 were normal.

ANCA was negative. Immunoglobulins were normal except for serum IgA of 0.13 g/L (normal, 0.70-4.00) while IgA-tTG was measured at 1.2 Units (normal, less than 20). Upper GI endoscopy was normal with normal healed duodenal biopsies [8]. Colonoscopy and biopsies were normal.

Repeat evaluations in 2006, 2011 and 2020 were normal, including upper GI endoscopy with biopsies followed by colonoscopy with biopsies. Treatment with a gluten-free diet alone was continued, now over a quarter century since his original diagnosis of metastatic small bowel carcinoma in celiac disease.

Discussion

This report documents the development of a small bowel carcinoma in celiac disease with concomitant and selective deficiency of IgA immunoglobulin. Just after the initial diagnosis of celiac disease, extensive metastatic lymph node involvement developed. Treatment consisted of surgical resection and a single course of adjuvant chemotherapy for his malignancy along with an ongoing gluten-free diet for his celiac disease. Over 3 decades have now passed since the time of his original diagnosis with no evidence of recurrent malignant disease. Despite definition of an advanced malignancy and its very poor prognosis associated with adult celiac disease, he has survived for over 3 decades with no evidence of recurrent cancer.

Earlier studies have explored small intestinal malignancies in adult celiac disease [1-4] and have documented the frequent association of selective immunoglobulin A deficiency with adult celiac disease [9-10]. Although this has been estimated to approximate 1 in 200 celiac patients (or about 0.5%), some referral-based centres, including our own, have reported higher rates of about 3% [9-11]. Indeed rates of detection may have actually been historically higher as measurement of immunoglobulins in recent years may be more reflective of concomitant measurement of IgA tissue transglutaminase assays in celiac disease.

T-cell non-Hodgkin's lymphoma of the gamma/delta type has been previously described in selective immunoglobulin A deficiency, although the 28-year-old male may have had, in retrospect, celiac disease [12]. In another report, a 71-year-old female with IgA deficiency and celiac disease was suspected to have an occult or cryptic T-cell lymphoma based on molecular gene rearrangement studies showing a monoclonal lymphocyte population in small intestinal biopsies, but no clear histopathological biopsy evidence of lymphoma [10]. Cancer risk has also been explored in patients with IgA deficiency along with their Danish or Swedish relatives [13]; in 386 patients with IgA deficiency, no increased risk of cancer was documented nor an increased risk of cancer in their relatives. The authors concluded that immunodeficiency *per se* rather than specific genetic traits may have been more critical to cancer development [13].

Studies are still needed to further explore prognostic factors related to small bowel adenocarcinoma complicating the clinical course of celiac disease. In one recent report from France [14], for example, specific factors were evaluated in advanced metastatic small bowel carcinoma, including underlying disease, age, location and characteristics of the primary cancer, stage of disease and effects of adjuvant chemotherapy.

Conclusion

These studies may help to identify positive characteristics of long-term survivors of this devastating disease and promote an ongoing positive outlook for future survivors.

Bibliography

1. Freeman HJ. "Lymphoproliferative and intestinal malignancies in 214 patients with biopsy-defined celiac disease". *Journal of Clinical Gastroenterology* 38 (2004): 429-434.

2. Freeman HJ. "Malignancy in adult celiac disease". *World Journal of Gastroenterology* 15 (2009): 1581-1583.

3. Freeman HJ. "Intestinal adenocarcinoma in biopsy-defined celiac disease". *Acta Scientific Gastrointestinal Disorders* 6 (2023):16-18.

4. Freeman HJ. "Adenocarcinoma of the small intestine in celiac disease over more than 30 years". *International Journal of Celiac Disease* 11 (2022): 19-22.

5. Ludvigsson JF., *et al*. "IgA deficiency and risk of cancer: a population-based matched control study". *Journal of Clinical Immunology* 35 (2015): 182-188.

6. Freeman HJ. "Small intestinal mucosal biopsy for investigation of diarrhea and malabsorption in adults". *Gastrointestinal Endoscopy Clinics of North America* 10 (2000): 739-753.

7. Freeman HJ. "Pearls and pitfalls in the diagnosis of adult celiac disease". *Canadian Journal of Gastroenterology* 22 (2008) 273-280.

8. Freeman HJ. "Mucosal recovery and mucosal healing in biopsy-defined adult celiac disease". *International Journal of Celiac Disease* 5 (2017): 14-18.

9. Pallav K., *et al*. "Immunoglobulin A deficiency in celiac disease in the United States". *Journal of Gastroenterology and Hepatology* 31 (2016): 133-137.

10. Freeman HJ. "Biopsy-defined adult celiac disease and selective immunoglobulin A deficiency". *International Journal of Celiac Disease* 5 (2017): 10-13.

11. Heneghan MA., *et al*. "Celiac sprue and immunodeficiency states: a 25-year review". *Journal of Clinical Gastroenterology* 25 (1997): 421-425.

12. Ott MM., *et al*. "Abdominal T-cell non-Hodgkin's lymphoma of the gamma/delta type in a patient with selective immunoglobulin A deficiency". *American Journal of Surgical Pathology* 22 (1998): 500-506.

13. Mellemkjaer L., *et al*. "Cancer risk among patients with IgA deficiency or common variable immunodeficiency and their relatives: a combined Danis and Swedish study". *Clinical and Experimental Immunology* 130 (2002) 495-500.

14. Aparicio T., *et al*. "NADEGE Investigators. Small bowel adenocarcinoma: results from a nationwide prospective-NADEGE cohort study of 347 patients". *International Journal of Cancer* 147 (2020): 967-977.