CASE REPORT

Stable improvement in classical B-cell chronic lymphocytic leukemia with dietary interventions: A personal experience

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Abstract

If the lymphocyte count is still low enough, the first part of the wait-and-see approach for asymptomatic Rai stage 0 classical B-CLL can be used to find out if the lymphocyte counts follow an exponential growth curve. If they do, the whole food, plant-based (WFPB) diet intervention can be started.

KEYWORDS

B-CLL, dietary intervention, hematology, lifestyle medicine, oncology, plant-based diet, whole food

1 | INTRODUCTION

A remarkably consistent and stable reversal of progressive Rai stage = 0, B-CLL was found after starting a whole food, plant-based (WFPB) diet intervention replacing the wait-and-see approach. The number of asymptomatic years may increase with this regimen and eventually may delay or even prevent the start of systemic intensive treatment.

Lifestyle medicine has great therapeutic and financial (savings in health care costs) potential, especially in cardio-vascular disorders and metabolic diseases like type II diabetes mellitus.[1] The impact on the course of specific cancers is controversial.

The link between food and cancer was suggested already in the mid-1800s and has been extensively studied ever since.[2-5] Based on such studies Campbell et al advised to eat "whole food, plant-based".[6,7]

In 2010, a large, prospective study was published that followed 525 982 men and women during more than 11 years.[8] During that period 1129 persons developed chronic lymphocytic leukemia (CLL) or small cell lymphocytic lymphoma (SLL). In these 1129 cases, a suggestive, positive association between body mass index (BMI > 25) and development of CLL/SLL was found. This finding suggests a possible link between food and CLL/SLL, because the BMI has everything to do with eating behavior: while excessive eating and drinking of a typical American diet results in a high BMI, the eating of unprocessed, plant-based food goes together with a substantially lower body weight and BMI. When BMI is linked to development of CLL/SLL in some way, the role of dietary intervention in the course of disease could be interesting.

In support of the latter notion, some in vitro experiments have shown that plant-based food may suppress the growth of certain cancer cells. After eating a vegan diet for 1 year, the blood drawn from these individuals suppressed cancer cell (including breast, prostate, lung, and colonic cancer) growth nearly eight times better than blood drawn from those eating a typical American diet.[9]

To our knowledge, no study has been conducted concerning the link between plant-based, whole food diet and the chance to develop CLL, without lumping the data of CLL and SLL patients.

Patients with Rai stage 0 B-CLL (only peripheral blood lymphocytosis) are managed with a wait-and-see policy. To introduce a dietary intervention in this early stage of disease might have an impact on the course of disease. By advising such intervention, there is nothing to lose and, possibly, much to gain.

2 | CASE HISTORY

2.1 | Subject

A Caucasian male born in 1946 was found to have an asymptomatic elevated leukocyte count of 13.2×10^9/L (normal value 4.0-11.0) and serum cholesterol of 6.6 mmol/L (normal value < 6.5) at routine check-up in week 0 of Figure 1. This was February 6, 2009. No further action was taken. In week 144, knee surgery was planned and at preoperative screening, leukocyte count was 31.8×10^9/L while lymphocyte count was elevated to 27×10^9/L (normal value 1.00-3.50). He was diagnosed to have asymptomatic classical B-CLL, Rai stage 0.

The patient had no concurrent disorders other than B-CLL, for example, no type II diabetes mellitus, no hypertension, no hormonal disorders, and no concomitant medication. The patient history was unremarkable as well, and the family history was negative for CLL. The patient was a nonsmoker. This habit has not been changed since. Bodyweight 80.3 kg. BMI 24,5 (normal value 18.5-25).

The usual approach of "wait-and-see" was started with clinical and laboratory follow-up examinations by the hematologist every 3 months for the first year. The five leukocyte counts during week 0 till week 196 resulted in an exponential growth curve with an 8% increase every 3 months ($y = 13.401e^{0.0057x}$; $R^2 = .9919$). Figure 1 shows the extrapolated curve (broken line), presuming the progression would follow the same pattern. If the actual lymphocyte counts would follow the extrapolated line, systemic treatment would probably have started in week 450. The patient was not happy with this prospect. As a research biologist, he performed a literature search in peer-reviewed journals for promising treatments and/or interventions. He decided to start dietary intervention to try to get his lymphocyte counts down. This was discussed with and approved by the hematologist/oncologist.
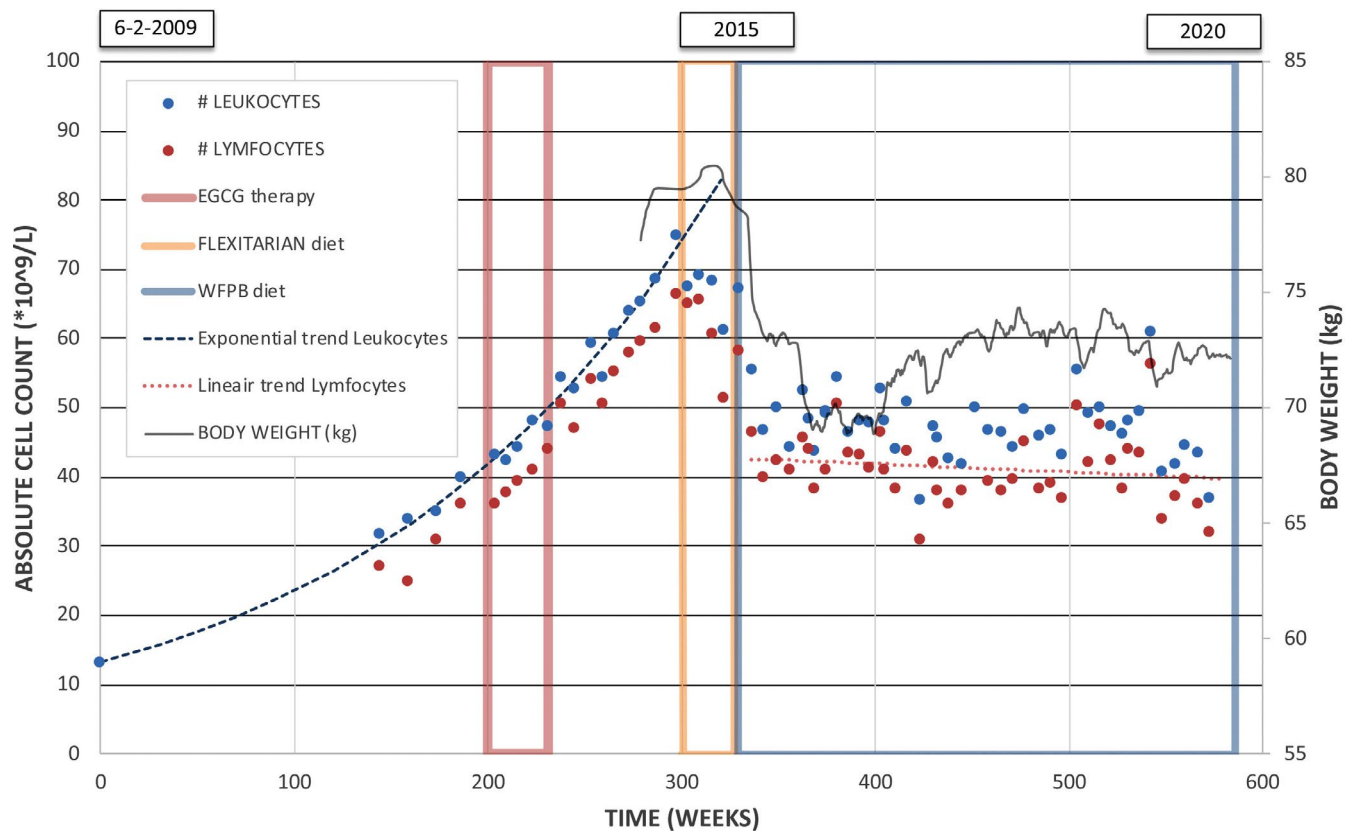

FIGURE 1 Course of disease related to three dietary interventions. The remarkably consistent and stable reversal of the progressive CLL co-occurring with a sharp decrease in body weight (gray line) after starting the Flexitarian diet (yellow box) followed by the Whole Food Plant-Based (WFPB) diet intervention (blue box). Initially, the leukocytes (blue dots) follow an exponential growth curve that is depicted by the black, broken line fitted through the first 5 measurements and extrapolated; $y = 13.401e^{0.0057x}$; $R^2 = .9919$). (Note: In week 0, no lymphocyte count was available in the hospital records. Therefore, the leukocyte counts were used for fitting and extrapolating the exponential growth curve. This is considered a good proxi since the lymphocyte counts tend to follow the leukocyte counts, albeit a little lower). The epigallocatechin gallate (EGCG) therapy (pink box) had no effect whatsoever: the leukocyte (blue dots) and lymphocyte (red dots) counts did not deviate from the extrapolated curve. After the reversal of the progressive CLL, the lymphocyte counts (red dots) stabilized around a mean of 41×10^9/L (SD = 5). A linear trend with a slightly downward slope (see the red, dotted line; $y = -0.0118x + 46.623$; $R^2 = .0293$) was fitted through the lymphocyte counts following the reversal. The body weight curve (gray line) depicts a moving average of onethird of the measurement points

2.2 | Methods

Peripheral blood leukocytes and lymphocytes counts as well as hemoglobin level were measured every 6 weeks in order to enable a close evaluation of the dietary interventions. A consistent diversion from the exponential growth curve into a horizontal line was considered a significant effect. Furthermore, the total cholesterol and some other metabolic parameters were checked regularly, such as cholesterol HDL, cholesterol LDL, hemoglobin, platelets, urine micro albumin, triglycerides, sodium, potassium, calcium, fasting glucose, folic acid, vitamin B12, vitamin D (250 H), creatinine, ferritin, glycohemoglobin (HbA1c), omega-3 fatty acids, iron, zinc, iodine, vitamin B2, in order to check for potential shortages or excesses as a result of the dietary interventions. In addition, the clinical check-ups for lymphadenopathy and spleen size by the hematologist were continued every 6 months. The weight (kg) was measured daily (naked and unburdened in the early morning before breakfast and after going to the toilet). A daily diary was kept with notes on infections, concurrent illness, and violations of the intervention. During observation period concurrent disorders, for example, hypertension, type II diabetes mellitus, hormonal disturbances, or comedication did not occur, nor did patient go through any lifestyle changes other than diet-related ones, for example, exercise. The following two trials were carried out one after the other.

TABLE 1 Details of daily food intake during the whole food, plant-based (WFPB) diet from week 329 onwards

Description	Time	Quantity
Breakfast:	8:00	
Almond milk (unsweetened)		100 mL
Fresh smoothy (with almond milk, kiwi, fruits of summer, apple, orange, few leafs of mint, handful of spinach, teaspoon Spirula)		⅓ liter (1 glass)
Limewater (1 lime squashed in glass of water) with 1 capsule of stomach acid inhibitor		⅓ liter (1 glass)
In between:	9:30	
(selfmade: oats, nuts, cranberries, cinnamon) with almond milk		200 mL
Cruesli		88 g (5 full tablespoons)
Tea		2 cups
Coffee time:	11:00	
Fresh vegetable/fruit juice/smoothy (with several juiced vegetables blended with 2 tablespoons of linseed, 1 banana or avocado, tomatoes and a handful of spinach)		⅓ liter (1 glass)
Limewater		⅓ liter (1 glass)
Lunch:	13:00	
Selfmade ryebread		2 slices
With tomatoes, avocado, or cucumber and sandwich spread		2 knives
Limewater		⅓ liter (1 glass)
Teatime:	15:30	
Fresh vegetable/fruit juice/smoothy (with several juiced vegetables blended with 2 tablespoons of linseed, 1 banana or avocado, tomatoes and a handful of spinach)		⅓ liter (1 glass)
Limewater		⅓ liter (1 glass)
Dinner:	18:00	
Whole food, plant-based dinner		1 plate
Limewater		⅓ liter (1 glass)
Coffee time:	20:00	
Tea		2 cups
TV time:	22:00	
Mixed nuts (unroasted, not salted)		110 g (handful)
Limewater		⅓ liter (1 glass)
Bedtime:		
Vitamin B12		1 tablet (1000 µg)
Total		Appr. 2511 kcal/day

2.3 | Trial 1: epigallocatechin gallate (EGCG)

This was a trial of daily, oral Polyphenon E (antioxidant EGCG) as described in the phase-2 trial in patients with asymptomatic, Rai stage 0-II CLL.[10] From week 200 to 230, EGCG was taken orally in the same way as described[10] (see box "EGCG therapy" in Figure 1).

2.4 | Results of trial with EGCG

Lymphocyte and leukocyte counts were not affected by the 7-month trial with EGCG; they continued to follow the exponential growth curve fitted through the first five leukocyte counts (Figure 1, broken line). So, the antioxidant EGCG appeared not beneficial. James Watson even argued that nutrition and pills that are rich in antioxidants increase the chance to get cancer or type II diabetes mellitus, instead of decreasing it.[11]

2.5 | Methods of trial 2: whole food, plant-based (WFPB) diet

The second trial concerned a change from the regular diet (with lots of processed food and animal protein) to a WFPB diet as described in the Campbell plan [6] starting with a transition period.

During week 300-329, a "flexitarian" diet was followed first (see box "flexitarian diet" in Figure 1). The diet consisted of vegetarian food five times weekly, no red meat, twice weekly a little piece of fat fish, hardly any dairy products, no cookies and instead once daily a little piece of dark chocolate (72%), no desserts, no alcohol in the evening but instead fresh fruit juice.

After the transition period, from week 329 to 573, all animal proteins and processed food were excluded, including alcohol and coffee (see box "WFPB diet" in Figure 1). Furthermore, daily vitamin B12 (1000 μg) was taken orally. Details of the daily consumptions during the WFPB diet are presented in Table 1.

2.6 | Results of WFPB diet trial

After closure of trial 1, the lympho- and leukocyte counts continued to follow the extrapolated, exponential growth curve, and in week 297, immediately before the start of trial 2, the lymphocyte count was higher than ever (66.4×10^9/L), the weight was above 80 kg, and the BMI was 24.5.

In week 300, the flexitarian diet was started. Remarkably, the lymphocyte counts immediately diverted from the exponential growth curve and with some ups and downs had decreased by week 329.

In view of the considerable drop in cell counts, the subject's social environment became motivated and prepared to reorganize the eating patterns even further: From now, the Campbell-WFPB diet was strictly and completely followed.[6]

The next two lymphocyte counts nosedived and in week 342, the lymphocyte count was below 40×10^9/L: a decrease of 40% since the highest value in week 297. The weight curve had nosedived as well to 73.8 kg (see Figure 1). The BMI was down to 22.5. Without concomitant medication, the cholesterol had gone down from 6.6 to 4.2 mmol/L.

The following 4.5 years the lymphocyte counts stayed down and varied around a mean of 41×10^9/L (SD = 5). The dotted line fitted through the lymphocyte counts from week 342 onwards is near horizontal and shows a tiny downward slope ($y = -0.0118x + 46.623$; $R^2 = .0293$; see Figure 1).

In Figure 1, a number of outliers can be seen above the dotted line and one below. It is interesting to note that there were always clearcut physical reasons for these outliers, that were absent at the other count moments closer to the fitted line. These physical reasons were infections, illnesses, or violations of the diet. The first two are only to be expected. The violations of the diet are interesting. The first time this occurred during a holiday in the last 3 weeks preceding the count. As an experiment in triplo, this violation was repeated two more times during other holidays with the same result. After the holidays, the violations were stopped and the counts went down again.

A striking additional nosedive in bodyweight occurred around week 360 from 73 kg to a minimum of 68.5 kg while the subject was pale and felt dizzy every day. A full physical examination was done by the general practitioner, which turned out to be normal. Therefore, the suspicion rose that the complaints and the decrease in bodyweight could be related to the nutritional changes. Campbell had reported that a USA male citizen of 77 kg on a standard American diet eats on average 2400 kcal/day and a Chinese male citizen of 77 kg on a diet with mostly plant-based food eats 3000 kcal/day.[7] The WFPB diet in trial 2 amounted to appr. 2511 kcal/day (see Table 1). To make a long story short, three changes were made from week 368 onwards. First, much more kcal per day (>3000 kcal/day) was taken in. Second, 25 g of plant-based protein powder with all the essential amino acids was added daily to the smoothy. And, third, the number of times food was taken in was brought down to three per day in order not to disturb the biorhythm[12,13]: breakfast, lunch and dinner, and no food after 20:00 pm. Pretty soon the complaints disappeared and over time the bodyweight curve gradually increased and stabilized again around 73 kg (see Figure 1).

3 | DISCUSSION

3.1 | Is the effect of the WFPB diet on the course of CLL generalizable?

The remarkably consistent and stable reversal of the steady progression of the CLL after starting the WFPB diet intervention is a highly interesting phenomenon and deserves further research to replicate these findings. Three approaches to that end may be used.

First, stop the special diet, closely evaluate the effect on the lymphocyte counts and, in case of renewed progression of CLL, follow this up by a restart of the special diet. In fact, in some way, this approach, although rather temporarily, has been used in the present case report in the experiment in triplo concerning a violation of the diet in the analysis of the outliers (as mentioned in the "results of WFPB diet trial" section). Three times the lymphocyte counts increased significantly and decreased again after the restart of the complete WFPB diet.

The second approach would be to evaluate the effects of this diet in at least several patients with CLL. "Two of the arguments leveled against the use of single subjects—uniqueness and chance relationships—can be readily tested and easily rejected", according to Denenberg[14] (p. 279). If a pattern of change in one subject is replicated in another subject that is like an experiment in duplo and "eliminates the problem of uniqueness within an individual." As for chance relationships, "it is necessary to find only one or two additional cases to reject the null hypothesis that the population proportion is zero"[14] (p.279).

And third, a formal trial with larger number of individuals needs to be done "to obtain a reliable estimate of the population proportion with a relatively small standard error".[14]

Finally, a placebo effect cannot be ruled out completely, but the rise after temporarily stopping the diet and immediate drop after resuming, appears very suggestive of a real effect instead of placebo. Furthermore, there was no placebo effect in the first trial of the present study.

3.2 | Why "whole" food?

Cordain et al[15] described that (a) our food has changed substantially, (b) our genome has not yet been able to adapt to these changes (evolutionary discordance theory), and (c) excessive consumption of that "new food" resulted in the so-called diseases of affluence, that are the leading causes of mortality in the Western World. The ultra-processed food that was introduced during the last 50 years is part of the problem.[16,17] Hunter-gatherers and other non-Westernized people do not eat that new food (yet) and are (almost) not afflicted by the diseases of affluence.[15]

3.3 | Why plant-based food?

In the seventies, a nationwide survey of death rates from 12 different kinds of cancer in more than 2400 Chinese counties and 880 million (96%) of their citizens produced an atlas showing areas displaying high frequencies of certain types of cancer whereas in other areas these were almost nonexisting.[18] Huge differences between counties were found of up to a factor 100. A follow-up study was started by China in cooperation with Cornell University, USA, and Oxford University, England, that came to be known as the "China Study".[19] Blood samples and questionnaires were collected for 6500 Chinese citizens in 65 different counties, producing data on lifestyle, diet, and illnesses. Two groups emerged out of the analyses: 1) the affluent (mainly in cities) that ate more animal proteins and fat (extravagant portions of pork, beef, and lamb) and suffered from different types of cancer, coronary heart disease, and type II diabetes mellitus; and 2) the poor, -mainly in rural areas-, who had insufficient nutrition and poor hygiene and mainly suffered from infectious diseases, metabolic and endocrine disease other than type II diabetes mellitus, and diseases of pregnancy.[7,19]

In experiments with rats that were given the carcinogen "aflatoxin," the link between excessive eating of animal protein (casein) and cancer was shown by two independent research teams.[7,20,21] The "critical level" of dietary protein intake was approximately 10%.[21,22] The growth of cancer tumors could be turned on and off in the same animals with a diet rich respectively poor in animal protein.[23] In contrast, plant protein (gluten, the protein of wheat) did not promote cancer growth.[24]

Until recently it was a mystery why other mammals could eat red meat without such adverse health consequences as found in humans, that is, increased risk for cancers, type II diabetes mellitus, cardiovascular diseases, infections, kidney disease, liver disease, respiratory disease, and cerebral vascular strokes.[25] Varki et al found that red meat and dairy products contain the sugar N-glycolylneuraminic acid (Neu5Gc) which is naturally present in other mammals but not in humans. Consequently, the regular consumption of red meat and dairy products causes an immune reaction to the foreign sugar in humans, producing antibodies leading to chronic inflammation, and in the end possibly leading to malignancy. Varki et al genetically engineered mice in such a way that they did not produce Neu5Gc naturally anymore: These mice developed cancer when they were fed the sugar.[26] In the current case report, it is interesting to see that the lymphocyte counts started to drop when the flexitarian diet (without red meat) was started in trial 2, as described in the methods section.

Gibson reported differences in the expression of certain leukocyte gene profiles between Maroccan people living in cities with complex diets of urban cultures (high in animal fat and protein) versus people living in remote areas with simple diets of rural cultures (low in animal fat and protein).[27,28]

3.4 | What might be the implication for clinical practice?

The indolent and often spontaneously remitting course of CLL is well known. Using the wait-and-see approach for asymptomatic Rai stage 0 classical B-CLL, it is difficult to predict the exponential increase of lymphocyte counts and possible rapid development of progression to more advanced stages of disease. One possible scenario for intervention with the proposed diet is this. If initial lymphocyte counts are still low (let's say $<100 \times 10^9$/L), clinical and laboratory follow-up examinations by the hematologist every 3 months for the first year of a wait-and-see approach can be used to find out if the lymphocyte counts follow an exponential growth curve. If they do, the WFPB diet intervention could be started with the aim of increasing the duration of asymptomatic Rai stage 0 CLL. It might prevent or at least delay systemic treatments. The patient should receive some kind of support in the transition to the new lifestyle. Considerable experience with support for changes in lifestyle already exists in the management of type II diabetes mellitus.[1]

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

FXP: was the patient in this case, and as a research biologist searched the peer-reviewed literature for promising interventions, collected and processed the data, and wrote the first draft of this paper. JR: facilitated the project by ordering blood measurements every 6 weeks and assisted in writing the paper.

ETHICAL APPROVAL

Ethical approval was not applicable since the first author was the patient in this case.

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