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Case Report **Open Access Journal**

Treatment of Cancers with a Novel Combination of Re-Purposed Pharmaceuticals and Some Nutriceuticals.

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Abstract
A 63 year old woman with CLL Leukaemia offered to try a novel treatment being developed at our centre. Beginning with Propranolol and Aliskiren several additional compounds were tried over time, Aspirin, Curcumin and Bromelain were retained. Over the succeeding eight years her lymphocyte count has risen slowly and was presently stable around 35,000. A few weeks ago when Bromelain was increased to 500mg pd the Lymphocytes dropped to 32.1. The patient still continues to lead a normal life with no side effects, the only complaint being tiredness. This treatment we infer to inhibit cancer growth at least.

Key words : Cancer treatment, repurposed pharmaceuticals plus nutriceuticals.

Introduction

In 2014 a 63 year old woman diagnosed with CLL leukaemia (lymphocyte count 6.6) approached our centre. Aware of the limited and non-curative treatment already available for CLL she felt there was nothing to lose by trying, through her family doctor, any other reasonable approach we might suggest.

We were then at the Gillies-McIndoe Research Institute (GMRI) which had successfully treated infants with Infantile Haemangiomas using low dose beta-blockers to inhibit the renin-angiotensin system (RAS) [1,2]. The basic idea was that the renin-angiotensin system might also be central in the growth of tumours which might be responsive to similar treatment. As the patient was already taking a beta-blocker, Propranolol was easily substituted and titered up to a total of 80mg once daily. While Propranolol had a significant effect on the leukocyte count something extra was needed and Aliskiren - a renin blocker was added. After the Propranolol and Aliskiren administration there was a decline in the lymphocyte count but gradually it returned to around its previous value. Our laboratory studies showed that when the 'classical' RAS pathway is inhibited, bypass loops such as Cathepsins B D & G, and COX2 take over its role. A wave-like response pattern in the lymphocyte counts appeared, that is common in CLL, averaging around eight [3]. To deal with the Cathepsins we added Curcumin (with piperine to increase its solubility and uptake) titered up to a dose of 300mg od. as a Cathepsin B blocker[4,5] and aspirin enteric coated 100mg bd.. Curcumin and Aspirin are both Cox2 inhibitors, aspirin also inhibits Cox1. Our data below (Table 1) of the earlier interventions over the first half of the study showed that there was a correlation of r = 0.773

(p = 0.009) (60% of the total variance) between our interventions (increasing dosages) and declines in the lymphocyte numbers. The mean of post-intervention values is significantly lower than the pre-intervention mean (t = 2.94, P = 0.016).(Used SPSS v.22) And the second-to-last entry arose from a brief withdrawal of Aliskiren leading to a lymphocyte increase from 9.6 to 10.8 declining to 8.5 when the Aliskiren was restarted.

Table1: Patient's Lymphocyte Count (per 1,000) by Treatments added or removed over time.

Date	Treatments (Mg per day)	Lymphocytes	Date	Treatments (Mg per day)	Lymphocytes
2014			2016		
06/27	Propranolol 30	6.1	01/02		6.8
07/02	Propranolol 60	6.8	02/03		8.1
08/27		6.4	03/06	Doxycycline	7.7
09/10		7.4	03/12	Doxycycline WD*	10.8
09/17		6.9	03/22		9.6
		7.9	04/18		8.4
10/17					
11/18	Enalapril 60 Propranolol 30	8.4	05/16		9.2
12/01		7.4	06/23		8.6
12/26	Enalapril WD*	8.9	07/19		9.5
2015			07/25	Metformin 500	
01/14	Aspirin 300		08/08	Metformin,1000	
01/29		7.6	08/19		9.4
03/10		8.0	09/15		9.6
03/21	Propranolol 60		10/13	Aliskiren WD*	
04/09		7.8	10/31	Metformin WD*	11.6
05/17		7.4	11/05	Aliskiren 130	
06/09		8.1	11/22		8.5
06/19	Propranolol 90		12/31		10.7
07/06		6.6	2017		
08/07		8.2	01/31		9.9
09/07	Propranolol 120	7.6	03/14		10.7
09/21	Propranolol 80 Aliskiren 150	8.0	04/13		11.9
10/20		7.8	06/20		14.2
12/01		8.0	07/27		15.0
12/19	Curcumin 600		08/31	Curcumin 1500	13.0
			10/10	Celebrex	8.6
			11/17	Celebrex WD * Aspirin 400	17.2
	*WD=Withdrawn		2018		
			01/05		15.1

Unexpected outcomes sometimes followed the introduction of new possible treatment regimes which were purportedly related to cancer decline. The inclusion of Doxycycline produced a rise in Lymphocytes from 7.7 to 10.8 in a month (2016/03/12) returning to 8.4 two months after its withdrawal. Aliskiren was withdrawn at 8.6 to allow Metformin 500mg pd to be introduced

(2016/16/06). This caused a rise to 9.6 in a month, 2 months later the dose was increased to 1000 producing in a month an increase to11.6 which upon withdrawal of all metformin and reintroduction of Aliskiren returned to 8.5 (2016/11/22).

After about three years of treatment Celebrex was substituted for aspirin as a Cox2 inhibitor. (The belief then was that Cox1 was not involved in cancer.) The result was that lymphocytes rose from a count of 8.6 to 13.9 in about three weeks so the Celebrex was withdrawn and replaced with aspirin.

At about that time (2017/10/10) Lymphocyte count became 8,600 and her Matutes score was 4. Her doubling time of 51 months compared well with a common doubling time of 12 months for typical lymphocyte counts for this cancer. Her karyotype shows 13q14.3 x 2 (homozygous) deletion. Extrapolating the likely trajectory for the progress of her condition shows a much more optimistic position than those with 13q deletions who have already been treated conventionally or are awaiting it [6].

Since then there has been a gradual rise in her lymphocyte count to a level of 35,000 after eight years of treatment. This increase in level may be related to unforeseen misadventures from a triple vaccination (Boostrix dTpa), taking melatonin (a propranolol inhibitor) for sleep regulation and a probable bite from a white tailed spider requiring steroid treatment. After each of these disruptions there was difficulty in reducing lymphocyte counts, suggesting some cancer resistance to apoptosis, thus the lymphocyte count may have been inflated by senescent cells. This was responded to using Co-Enzyme Q10 [7] (Ubiqinone then the more soluble Ubiquinol).

Recently, (18/2/2022) we substituted Quercetin (with Bromelain for solubility) for Co-Enzyme Q10 assuming, given Quercetin's reputation as an apoptosis promoter, that it might reduce the White Blood Cells (WBC) as well as the Lymphocyte count. Over nine weeks WBC remained around 42.2 but Lymphocytes declined from 35.9 to 35.0.

After leaving the GMRI we have continued treatment for another four years. With doses gradually augmented, her levels for the last five months have been around *Lymphocytes 35.0, WBC 42.3, GGT 37*. About the level traditionally used to start regular monitoring, and half the usual level to trigger chemotherapy intervention. However , three weeks ago we withdrew Quercetin because of patient's headaches and increased the Bromelain from 156mg pd to 500mg pd. Her latest levels are *Lymphocytes 32.1, WBC 39.1 and GGT 28.0*. Presumably the purported apoptosis effect of Bromelain is reducing both the senescent cells and the cancer activity [8].

Discussion

The level of GGT (28) suggests little cancer activity at present [9] (at diagnosis it was 215).

The present treatment is: Aliskiren 150mg od., Propranolol 40mg tid, Curcumin (with Piperine) 500mg tid, Aspirin (enteric) 100mg tid, Bromelain 500mg od..

Now aged 71 the patient lives alone, enjoys a normal life, the main complaint being tiredness, but she does her garden, does some voluntary work, and takes extended solo camping trips driving for up to two months throughout the country.

While this regime may or may not cure CLL, at least, it seems to inhibit the progress of the cancer with practically no side effects. From our laboratory studies we were aware that the above approach to treatment may also apply to other forms of cancer. The results by Tan et.al.[10]. helps to support this and the two studies complement each other, namely that the similar treatments used probably inhibit the progress of cancers. While other people have tried using some of these medications by themselves we are unaware of other attempts to use these pharmaceuticals and nutriceuticals together to treat cancer.

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