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Dietary substitution therapy of prostate cancer patients: A possible noninvasive treatment

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ABSTRACT

Signs for adrenal involvement coupled with synergistic bio-modulating metabolic factors formed the incitement to empirically develop noninvasive curative treatment modalities for the treatment of prostate cancer (pCA). Adrenal *zona reticularis* (ZR) cells are involved in the etiology of prostate cancer. Dietary supplementation containing missing natural metabolic factors compensating the etiologic metabolic deficiency causing pCA may activate ZR feedback reactions and arrest progression of pCA. This paper presents a full formula that has been found useful as dietary substitution therapy of prostate cancer patients. The specific dietary compensation could prevent recurrence of disease, arrest pCA progression in patients, cure bone metastases, regress soft tissue metastases and prostate gland without causing apoptosis. It may also have prophylactic potential! Good prognostic traits to specific dietary treatment display increased Follicle Stimulating Hormone (FSH), prolactin (PRL) and SHBG levels, while DHEAS and PSA decline as serine, one of the ingredients in the formula, causes substrate inhibition. With PSA exceeding 15ng/ml, intermittent short time total androgen ablation [Zoladex 3.6 mg + Androcur for only 10 days] is prescribed in synergy with this powder. Hormone treatment intervals can be extended to several months until ZR feed-back reactions have regained FSH-levels. There is now a new incentive for screening, since pCA can primarily be treated in a non-invasive way using specific dietary supplementation, economically, and without causing side effects. This physiological dietary treatment is easy to administer in ambulatory practice, response and prognosis can be evaluated by laboratory tests.

Keywords: prostate cancer etiology, adrenal dysfunction, noninvasive therapy, prophylaxis, curative dietary supplementation

INTRODUCTION

Carcinoma of the prostate gland (pCA) represents an age-linked hormone dependent disease, lacking noninvasive curative treatments, as well as a comprehensible etiology. Huggins and Hodges have already demonstrated in 1941[1] that the progress of pCA can temporarily be arrested for some years, following castration. This generated a dramatic shift in the hormone balance, which was not though usually curative and recurrent pCA appeared after 1-3 years. Endocrinologists had by 1945 discovered that adrenal dihydroepiandrosterone (DHEA) could be transformed into testosterone, and this reaction was thought to cause recurrent pCA. Consequently Huggins and Scott also performed bilateral adrenalectomies on patients who suffered recurrent disease, after orchiectomies.[2] All patients died in a short time but this important finding was over-looked; the last biologically active organs which had managed to keep these pCA patients alive had actively been removed. Attention was not paid to the fact that this lethal outcome revealed the central position adrenal glands exert in regulating pCA. This postulation is supported by the observations that: (A) Adrenal zona reticularis cells proliferate markedly following orchiectomy.[3] These adrenal cells were bluish, and had a strong green fluorescence. Castration usually provokes a significant increase in the patients' serum FSH-levels, ranging from 60 to 120 IU/L, as PSA-levels decrease. (B) Upon autopsy the number of ZR cells had noticeably decreased in patients succumbing to pCA. (C) The same marked decrease in the number of ZR cells is seen in emasculated male pigs, as they are gelded at two weeks after birth for the sake of taste. (D) The low incidence of pCA in eunuchs. (E) The hormonal effect from ingestion of extracts procured from ZR cells harvested from healthy castrated boars caused an increase in PRL, with a concomitant decrease in DHEAS level. (F) The rapid lethal outcome if pCA patients – after orchiectomy are adrenalectomized (i.e., the final extirpation of the patients life saving ZR cells). The third cell-layer in the adrenal, zona-reticularis, seems to produce these controlling but still unspecified biological chemical neuroendocrine factors.[3] One increases FSH, the other PRL levels via the hypothalamus. This physiologic cell regulatory organ cycle is schematically illustrated in Figure 1.

Cancer can be regarded as a complex metabolic deficiency disease. The rare spontaneous cures of cancer represent, according to Dr. W.M. Cole, 1974, "The metabolic triumph of the host".[4] Supporting this postulation bio-immunotherapy had significantly ($p < 0.01$) improved the survival rate in 127 patients suffering from metastasized renal adenocarcinoma.[5] This combined biologic and immunologic therapy is still functioning.[3] With prostate cancer active immunisation using autologous tumour vaccines was not found successful, since PSA is not a regular tumour marker,[6] but a serine protease metabolite. Forced

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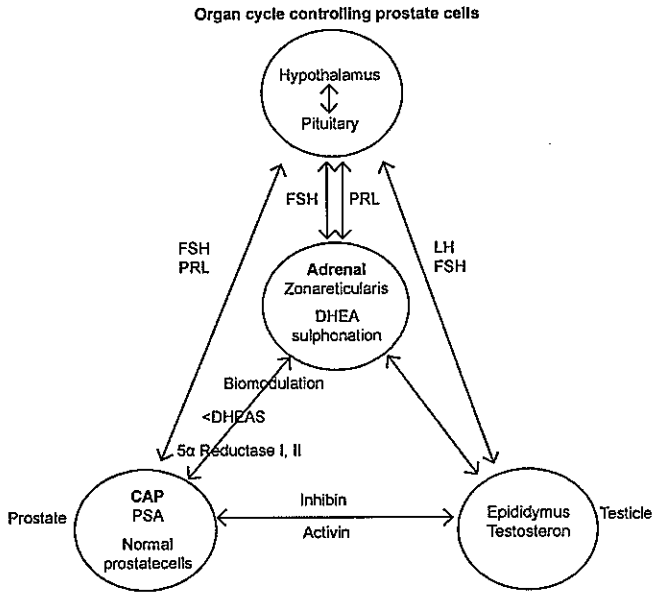

Figure 1 | Initially increased FSH or PRL are good prognostic signs and should always be analyzed when pCA is found by screening tests as if these are at increased levels, invasive treatments can be avoided. These unknown human adrenal biological factors harbored in the zona reticularis can be activated for their stimulatory effect on the pituitary. If these biological factors can be characterized, it could lead to a biological compensatory medical treatment for pCA.

to omit the use of autologous tumour vaccines in pCA patients, the option was to try to empirically delineate the specific natural metabolic components needed to activate this clinically favourable ZR feedback reaction. As no suitable analytic laboratory technique existed to detect the regulatory complexes, a wide variety of hormonal and clinical responses caused by natural dietary components were explored for decades,[7] aided by electron microscopy (EM) in pCA patients suffering from various forms and stages of prostate cancer. Mitochondria were detected to be involved in the healing process.[8] Patients who initially had a PSA over 15ng/mL were placed on intermittent short time androgen ablation therapy. No patient was placed on solely deferred treatment because it was regarded unethical, as the progress of pCA seemed to be arrested by nontoxic alimentary means. Metabolic deficiencies tend to be aggravated as a function of time. If not actively compensated it may lead to malignant transformation and recurrent disease.[9]

MATERIAL AND METHODS

Selection of subjects

A non-random selection from a pool of approximately 70 different cases of prostate cancer patients suffering from different stages and forms of pCA including rare cases initially diagnosed from soft tissue metastases formed the study group, starting in 1986. Many patients had already in 1985 been placed on standard therapy at the Helsinki University Central Hospital, Department of Urology when this non-toxic supplementary adjuvant dietary therapy trial was started. Suspicion for pCA arose from regular screening tests, verified by TRUS guided needle biopsies, incidentally also by TURP. Further risk-factors for pCA were a PSA velocity of over 0.4 ng/ml/month, a big prostate volume, usually verified by multiple cores, guided by TRUS, MRI, or CT.

Dietary bio-modulation schedule

Based on informed consent and permission by the ethical committee, various cases were offered the patented dietary supplementation of The Institute for Bio-Immunotherapy Helsinki in addition to the regular treatment for pCA. Since all alimentary components prescribed were natural nontoxic ingredients (listed in Table 1) and fairly inexpensive (2-3€/day), we were able to enlist different interesting cases to participate in this supplementary, non-invasive adjuvant treatment, although our patients knew that the duration eventually would extend over decades. To improve patient compliance the supplements were procured as two different ready-made powders.[9] They could be stored for extended times at room temperature. One powder contained the pertinent pure amino acids (Degusa, Germany) and trace-elements, the other holding all central nervous lipids [CNS prion-free lipids] in a dry micro-capsulated form, weighing 20g, but equivalent to 50g of CNS. Alternatively patients were offered canned CNS-lipids [Neurofood (220g) Ltd., Helsinki 00200] to be mixed with assorted fruits for the sake of taste. Recommended daily dose levels were 1-2 powders per day for powder No 1, but only twice a week of powder No 2 containing the CNS-lipids, each costing only ≈ 2 €.

All laboratory tests were performed on serum of patients according to calibrated national standard techniques at the Vita Laboratory, 00150 Helsinki. Serum growth factor assays for activin and inhibin were performed using standard test-kits based on an enzymatic immunological method.

For trace metal analysis, Proton-induced X-ray emission (PIXE) was performed, using 2.4 MeV protons from the 2.5 MV Van de Graaff Accelerator of the University of Helsinki and detecting characteristic X-rays.

Light microscopy (LM) was performed on ZR cells during dietary therapy and LHRH hormone therapy, or after orchiectomy. EM studies on prostate cancer cells were performed when the dietary supplements had caused the patients PSA to decline rapidly.

Table 1 | Dietary bio-modulation schedule* for the treatment of prostate cancer patients

- Oral administration of each (2-5g/day) of the respective L-amino acids: Arginine, Aspartic acid, Glutamic acid, Glycine, Lysine, and Serine taken in connection with meals.
- Essential trace element salts prescribed orally as biologically active ions at dose levels of few milligrams (1-3mg/day); Chromium ($CrCl_2.6H_2O$): 6mg (=1.17 mg Cr), Molybdenum ($Na_2MoO_4.2H_2O$): 4mg (=2mgMo), Rubidium ($RbCl_2.6H_2O$): 12mg (≈ 4mg Rb), Tin ($SnCl_4.5H_2O$): 4mg (=1.35mg Sn), Strontium ($SrCl_2.6H_2O$): 12mg (~ 4mg Sr), Vanadine (Na_2VO_4. 4 H_2O): 6mg (= 2.5 mg V), Wolfram (Na_2WO_4. 2 H_2O): 4mg (=2.3mg W), plus 45mg Manganese (Mn)/day.
- Small physiological amounts of vitamins: A,B,C,D,E,K, folic acid and lycopene
- A diet containing prion-free neurogenic lipids (equivalent to 50g of healthy brain tissue, twice/week) was recommended to improve lymphopoiesis and the immune defence of patients. The diet was purchased and canned by Neurofood Ltd., Helsinki 00200 Finland; available also in dry microcapsulated form as ready-made powders
- All these dietary ingredients can be mixed together in yoghurt or ice-cream or as a daily nutritional ration utilising pre-packed powders [No 1 & 2]
- Dose-levels are adjusted based on the clinical response as measured during the therapy, and also correlated to the patients' body weight.

*This dietary schedule is the intellectual property of The Institute for Bio-Immunotherapy Ltd., Helsinki 00200, Finland

Due to the marked increase in serum levels of FSH and PRL seen in favourable prognostic cases, linked to declining PSA-levels, the response caused by subcutaneous injection of human FSH (Serono), or FSH releasing peptide, a 14 amino-acid peptide, Sigma, Chem. Corp. F 7892, were tested in some patients. Only in one patient was injection of human PRL (Luteotropic hormone, LTH Sigma Chem. Corp. L 7009) tried.

Clinical results

Some instructive case reports are presented to help colleagues to evaluate the prognostic features, if they practise this novel biological treatment. The composition of this complex, but specific dietary supplementary therapy evolved over 25 years from empirically recording clinical symptoms, and shifts in patients' serum levels of FSH, LH, PRL, DHEA, DHEAS, SHBG, Ferritin, and PSA (% free/total). These patients were either on solely dietary therapy, or on dietary substitution combined with hormone therapy.[9] A positive trend was usually characterized by an increasing level of FSH, LH, PRL, SHBG, while DHEA, DHEAS, and PSA decreased (as Ser caused substrate inhibition of PSA), although the free percentage of PSA could increase.

A favourable clinical response caused by the specific components of the metabolic substitution is recorded as an increase in the patient's FSH, and especially as a decrease of his DHEAS level.[9] Such a favourable clinical response was interpreted as a successful activation of a feed-back reaction caused by adrenal zona reticularis (ZR) cells, which via the patient's hypothalamus and pituitary triggered this change in the hormone levels.

The central position of the adrenal gland was expressly evidenced in an orchiectomized patient as seen in Case 1. PSA had declined to immeasurable levels after orchiectomy, in 1993, but the FSH-level rose to an excessively high level, 120 IU/L. Upon MRI no pituitary adenoma was found, but both adrenal glands were evenly hyperthrophic. A diagnostic laparatomy performed on his left adrenal revealed that his gland had expanded from a selective marked proliferation of zona reticularis (ZR) cells (Case 1). These bluish cells did not seem to be endocrine (secreting), but they had a strong intracellular green fluorescence, something like the GFP proteins, found by 2008 Nobel laureate, Dr Osamu Shimomura.[21] This patient lived for over 11 years at home but succumbed to bone metastases at a time before we had realized the need for strontium, eventually also for zinc, and rubidium supplementation for patients with bone metastases.

The laboratory profile of this orchiectomized patient with an excessively high FSH level and enlarged adrenal glands is given case 1.

His FSH (IU/L) was 120 (Normal range: 1-9), LH (IU/L) was 53.8 (Normal range: 2.5-12), PRL (mU/L) was 228 (Normal range: 50-300), DHEA (nmol/L) was 3.2 (Normal range: 3-17), DHEAS (µmol/L) was 1.9 (Normal range: 1.9), Testosterone (nmol/L) 0.8 (Normal range: 9-38), Inhibin (pg/mL) <7.8 (Normal range: ~60), Activin (pg/L) 330 (Normal range: 300-500), S-Ferrit (µg/L) 65 (Normal range: 16-253), SHBG (nmol/L) 48 (Normal range: 15-55), and PSA (ng/mL) <1 (Normal: <4). His bilateral adrenal hypertrophy was caused by proliferation of ZR cells, his PSA and inhibin levels became almost immeasurable, as in all castrated patients, while DHEA and DHEAS were low, as well as testosterone, due to the orchiectomy.

Case 2: In pCA patients diagnosed by screening, dietary compensation of their etiologic metabolic deficiency has stopped the progress of the disease. The clinical effect of this specific non toxic natural dietary supplementation is furthermore linked to a dose response, but not on a homeopathic level. Screening for pCA got a new incentive as progression could be arrested by dietary means without side effects. In a 54 year old man, diagnosed in 1996 to have pCA, PSA had increased from 4.7ng/ml to 6.7ng/ml in 3 months, with a Gleason score of 6-7. He was scheduled for prostatectomy but opted to try only the biological dietary treatment, as presented in Table 1. He started to ingest a high dose of serine, 10g every day, in addition to all the other natural supportive ingredients as listed. In six month his PSA had decreased to 3.1ng/mL. He was then allowed to decrease the intake of Ser to only 5g/day. In 6 months, his PSA started again to rise to 3.6ng/mL. He was then reallocated to the higher intake of Ser (10g/d), and responded well as his PSA fell to 2.9ng/mL. This positive dose-response kept his disease stable for six years on continuous supplementation. Administration of arginine was then temporarily stopped for only three months. During this short selective depletion his PSA increased from 6.6 to 7.7ng/mL. This led to prostatectomy, in July 2002. The extirpated prostate gland revealed that the Gleason score had decreased to 4 (from 6-7 previously) and that the tumour volume had diminished. The pCA had been arrested for seven years without side effects, and economically. Based on this clinical result, we suggest that the pCA patients diagnosed by screening should primarily be offered dietary supplementary treatment controlled by all our regular laboratory tests to monitor the effect.

Case 3: To elucidate the clinical effect of dietary substitution EM was performed on pCA cells

EM studies on pCA cells reacting to specific dietary, and hormone treatment revealed that pCA cells were seen to be *surrounded by transformed organ-specific mitochondria* as PSA normalized due to combined therapy. The effect of dietary supplementation, plus a Zoladex 3.6 mg injection was used because PSA was initially > 15ng/ml. PSA decreased rapidly to normal levels in a physiological way and was seen to be generated by organ specific mitochondria, without causing apoptosis.

In six weeks his positive clinical response showed a marked decrease in PSA (53.7 – 3.7) although his testosterone increased, (5.7 – 11.1), while both DHEA (2.1- < 2.0), and DHEAS (1.5 - 1.3) decreased, but FSH (4.2 - 7.8, IU/L) as well as testosterone (5.7 - 11.1) rose. Testosterone increased although PSA decreased (as in Case 5a).[10] Due to this positive clinical response a biopsy was taken from the same lobe

Case 1

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
Normal range										
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	300-500	16-253	15-55	<4.0
120	53.8	228	3.2	1.9	0.8	<7.8	330	65	48	< 1

which previously had revealed a Gleason score 7. In EM the tumour cell nucleus is seen to be surrounded by several transformed mitochondria (Fig. 2). Two of them seem to empty their electron dense material, (as enzymes are activated by metal ions), into the tumour cell nucleus without rupturing the cell membrane, nor causing apoptosis.[8] With this good response his general clinical condition had also improved.

Case 4: Short time intermittent hormone therapy can prevent triggering a hormone refractory state

Hormone refractory prostate cancer (HRPC) is caused by too effective hormone therapy, e.g. exemplified as orchiectomy, or caused by LHRH analogue injections repeatedly administered for three months may provoke HRPC but this androgen insensitivity is not brought about by selection of a hormone refractory cell clone. Our special "short time" intermittent hormone therapy schedule supported by ingestion of the bio-modulating prostate powders has sustained the curative adrenal feed-back reaction for decades. Dietary supplementation combined with short time intermittent LHRH treatment can prevent HRPC.

Laboratory assay profiles during short time intermittent total androgen ablation reveal characteristic fluctuations in hormone profiles. Short-time intermittent LHRH treatment, i.e Zoladex 3.6mg, + Androcur 50mg x 2/day for only 10 days was practiced to prevent a painful flare-up reaction and to preserve the effect of the hormone treatment. Androgen ablation was given with three to four months of intervals in synergy with constant dietary supplements, has not exhausted the ZR feed-back reaction. It has resulted in stable disease for over 11 years, while preventing dangerous induction of HRPC.

The next LHRH analogue injections could be delayed due to synergy with dietary supplementation. Adrenal feed-back reactions had time to react seen as FSH increase to 15.3 IU, with also PSA to 14.5 ng/ml (in this case) before the next round of, short time, complete androgen ablation therapy was repeated. Patients in this short time combined intermittent hormone therapy schedule, supported by metabolic components compensating the etiologic metabolic deficiency have led to stable pCA, for decades. The patients adrenal feed-back activity has thus not been exhausted by too intensive androgen ablation,

Figure 2 | EM showing the nucleus of a prostate cancer cell into which transformed mitochondria insert their electron dense material into the tumour cell nucleus when it is forced back into normal healthy function, without causing apoptosis. The normalization of the PSA-level led to stable disease, Magnification 10,000 times in EM (reproduced from Ref. 8).

inordinately striving for a PSA nadir, but leading to a fatally low FSH, < 1 IU/L.

Case 5a: Initially idiopathically elevated FSH-levels may prevent malignant transformation of prostate cells.

This patient had a pathologic PSA-level for 5 years with yearly negative needle biopsies until the sixth year when an aggressive Gleason score of 8 was finally revealed.

He responded to a combined dietary and LHRH (Zoladex 3.6 mg) treatment in some months, with declining PSA, DHEA, DHEAS and FSH-levels, although FSH still remained over a normal level. PSA decreased while testosterone increased (6.7-10.0), the testosterone myth [10]? Patients who present a pathological PSA, (29.8) but with negative needle biopsies for pCA should be tested for their FSH since an idiopathically high level (75.0 IU/L), initiated by the adrenals can

Case 3. To elucidate the clinical effect of dietary substitution EM was performed on pCA cells

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	300-500	16-253	15-55	<4.0
4.2	4.5	269	2.1	1.5	5.7			130	61	53.7
7.8	6.9	151	< 2.0	1.3	11.1			149	55	3.7

Case 4. Hormone levels fluctuate in a typical way as pCA responds to combined intermittent treatment

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
A. Intermittent short time complete androgen ablation, Zoladex 3.6mg with cyproteronacetate for only ten days										
15.2	16.1	993	3.8	2.4	6.4	75	410	1500	45	13.4
B. One month later with Androcur for only 10 days around the Zoladex 3.6mg injection, to avoid a flare-up.										
4.2	7.3	1490	2.5	1.6	5.8	72	430	1100		2.5
C. Three months later in dietary supplementation the activated adrenal feed-back had increased FSH, and PSA										
15.3	17.7	1520	2.2	< 0.8		76	500	993		14.5

conceal the malignancy for years. These patients respond to combined metabolic and intermittent endocrine therapy. FSH should always be measured in pCA patients.

Case 6: Prostate cancer patients with initially high PRL-levels.

Patients with an initially high PRL-level seem also to have a stable disease, although FSH and LH are fairly low, while inhibin may surprisingly exceed the activin level. DHEA is low and decreasing during therapy, DHEAS may decline to an immeasurable level, while PSA is very low but with 29% in free form.

In other cases, if FSH decreases to under 1 IU/L while PRL increases it heralds a brooding HRPC, but in good stable cases as this DHEA, DHEAS and PSA stay low or decrease. The unexpected reversed shift in the relative content of the growth factors, inhibin over activin is not understood. It does not seem to represent a bad prognostic sign - but ZR specifically activates only PRL and not FSH.

Case 7: An orchiectomized patient succumbing to pCA

This patient with PSA 92.6 ng/ml [T4NxM1] was orchiectomized in November 1994 and his PSA fell to 5.7-5.3 ng/ml in 1995, in our combined therapy, but he slowly developed multiple bone metastases in an era when the importance of Sr, Rb & Zn substitution was not yet realized. Patients succumbing to pCA due to over-intensive androgen ablation show dangerously depressed FSH and LH levels, to < 0.1 IU/L. A simultaneous strong compensatory increase of PRL indicates that the pituitary gland is not exhausted, but his adrenal glands have lost their capacity to activate FSH. His markedly increased PRL to 1060 mU/L is, in vain, actively trying to save this lethal exhaustion. DHEA and DHEAS would have been depressed if the prognosis had been good, but they were high (7.2 & 6.8 respectively) as in pCA with Gleason scores of 8-10.

This patient died 8 hours after this blood sample was taken. The high ferritin is probably linked to mitochondrial activation requiring iron to activate certain beneficial enzymes in mitochondrial cristae.[8]

Case 8: Patients with bone metastases have been cured.

Case 5a.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
75	33	224	20.9	2.3	6.7			20	38	29.8
Four months later while ingesting two prostate powders per day plus CNS-lipids (Neurofood with fruits, 100g /week)										
13	0.1	122	2.9	1.5	10.0	(TSH 9.8)		50	34	2.8

Case 5b: This patient lived for 8 years with high FSH in stable disease - but died of heart failure.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
18.6	13.4	242	6.3	3.9	7.6	66	790	133	27	14.4
18.0	12.8	241	4.0	3.3		83	550	86		13.0

Case 5c: This patient was found incidentally by TURP but stayed for years in stable disease.

27.2	11.8	144	7.8	5.0	16.0	73	430	38	49	<0.3
27.0	11.0	162	5.3	4.2	16.0			34	49	<0.4

Case 5d: Is a healthy male without any signs of pCA, or other ailments except for a high FSH-level.

14.1	7.2	125		1.6				32	32	0.57, 30%

Case 5e: Was also completely healthy devoid of other ailments or urinary distress, but had high a FSH

24.9	13.8	180		0.5				155	55	2.07, 24%

Case 6: Prostate cancer patients with initially high PRL-levels.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
2.3	3.9	392	3.4	1.1	12.9	187	92	55	46	< 1.0
2.1	2.4	566	2.8-2.4	-<2	<0.8	9.8-8.9		44	37	1.7/ 29%

Case 7: An orchiectomized patient succumbing to pCA

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
<0.1	<0.1	1060	7.2	6.8	0.6			2145	-	364 /17%

Multiple bone metastases may be cured by specific dietary supplementation, following castration (total removal of testicular tissue and, not only by epidydectomy). This pCA patient with elevated PSA, 30.0 ng/ml, was diagnosed with aggressive prostate cancer and multiple bone metastases in 1992. Orchiectomy was performed but he had still hurting metastases when our supplementary treatment started in 1993. The intensive bone pain was alleviated in six months from full dietary supplementation including the intake of strontium, rubidium (7mg/day) and zinc (40mg/ day) and CNS-lipids. His general condition improved markedly. All bone metastases disappeared after four years of dietary treatment, in 1996. There has not been any recurrent disease during the follow-up, now for over 18 years. He is living at home in excellent clinical condition.

His elevated FSH-levels have been a constant finding, though levels have fluctuated for 19 years (the range has been indicated). LH-levels are also elevated after castration in as in all pCA patients who respond, evidenced as declining PSA-levels. Extremely low levels for DHEA and DHEAS (<2.0 % <0.8) are also seen, indicating a good prognosis effected by the dietary supplementation. All our other castrated pCA patients have died, if not placed on our specific dietary supplementation.

Case 9 & 10: A special form of occult pCA was diagnosed from soft tissue metastases – not from the prostate gland.

The high PSA-level in the biopsies from soft tissue metastases revealed that they come from the prostate gland. A peculiar shift in growth factors as in pCA with initially high PRL-levels was also seen in these cases. A special characteristic for these was extremely high activin and PSA levels. Activin levels could be 3-5 times over the normal upper levels of 500 pg/ml, 2900 and 1850 pg/ml respectively, and for PSA, 10070.0 and 246.0 ng/ml, but fortunately these patients also responded to our combined treatment. These special concealed forms of pCA also had bone metastases and were diagnosed by biopsies from neck and head metastases. With case 9 the PSA was 10,070 ng/ml but decreased to 5.3 ng/ml in 6 months in combined intermittent androgen ablation and dietary therapy. Case 10 had a PSA of 246 ng/ml which declined to 2.1 ng/ml in 8 weeks following our combined dietary and intermittent LHRH therapy (Zoladex, 3.6mg, Androcur for 10 days).

Cases 9&10 seem to represent a different form of pCA (neuroendocine?) but patients respond to our combined LHRH analogue, and supportive dietary therapy.

DISCUSSION

Activation of adrenal zona-reticularis cells by natural functional dietary components can regulate the hormone balance preventing the progress of pCA and preclude recurrent disease and may possibly also act as a preventive remedy. The positive effect of economical biological alimentary substitution, aimed to compensate the etiological metabolic deficiency causing pCA, has stopped bone metastases, and even cured patients, without side-effects. All patients diagnosed with pCA should therefore be tested for their response to dietary treatment in the early phase of their disease while there is a good chance to achieve a biological curative effect, and try to avoid un-physiological invasive standard therapies.[11] If this specific dietary supplementation induces positive prognostic signs that can be measured by standard laboratory tests, one would even be entitled to avoid starting immediate standard hormone therapies, especially if the patient's PSA is still < 15 ng/ml. This biological option should be used as our standard treatments usually cause a lot of both physical and mental side effects, with deterioration of the patient's family life, as well as the general quality of life,[11,12] in spite of the fact that standard therapies don't even guarantee a cure. To improve patient compliance with this supplementary treatment modality, ready-made powders containing all necessary alimentary factors were produced. They have a long shelf life at room temperature and cost only € 2-3 per day because they merely contain natural non-toxic functional food components. Owing to these positive clinical

Case 8: Patients with bone metastases have been cured

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-50	<4.0
30-67	16-37	95-159	< 2.0	< 0.8	1.0	< 7.8	330	99-109	58-61	<0.1

Case 9. Diagnosed from soft tissue metastases but react to combined therapy and short time androgen ablation

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA ng/ml
1-9	2.5-12	50-300	3.0-17.0	0.5-8.0	9-38	~60	~500	16-253	15-55	<4.0
5.1	<0.1		2.4	1.8	<0.8	25	2900	1164		10,070
Combined hormone & dietary therapy led to complete rejection of neck metastases and to normal PSA										
6.2	<0.1					22	2650	316		5.3

Case 10. Responded to our combined biological and short time hormonal (Zoladex 3.6mg Androcur) treatment

FSH	LH	PRL	DHEA	DHEAS	Testost	Inhibin	Activin	S-Ferrit	SHBG	PSA
1.9	<0.1	222	4.0	<0.8	1.2	34	1850	2499	165	246.0
Combined hormone & dietary therapy improved health, decreased activin- ferritin- & PSA-levels										
0.74	<0.1	212	2.2	<0.8	1.2	33	1770	493	151	2.3

results with biological compensation no, watchful waiting nor active surveillance should be recommended without active biological efforts to ethically prevent the progress of pCA[13] as the risk for malignant transformation increases as a function of time. The study plan for the ERPC trial is at fault since patients lack dietary supplementation, which explains why there is only a limited improvement on survival from prostatectomy over deferred treatment[12] as in neither group no active compensation of the deficiency has been tried. The pCA may thus proceed, since prostatectomy removes only the symptoms of pCA.

Descriptive epidemiology indicates that the probable causes of pCA are determined rather on environmental[15] than genetic factors, and demographic studies point to the effect of dietary habits. Long empiric studies were obligatory, since no analytic tests were available which could delineate which natural nutritional factors were able to physiologically compensate this complex metabolic deficiency, causing pCA.[3] A positive trend was evidenced by an increase in FSH, LH, PRL, SHBG, while DHEA, DHEAS, and PSA decreased, although the free percentage of PSA could increase.

Bio-immunotherapy for metastasized renal cancer is still clinically functioning[3,5,7] because renal cancer cells contain tumour antigens, at variance with serine protease (PSA), which is a metabolite and not a true tumour marker. Due to this, autologous vaccines for pCA did not improve the clinical results and their use were therefore discontinued in 1995.[6]

EM studies on pCA cells in healing were performed to further analyse the reason for the positive clinical effect caused by functional alimentary components. The curative effect was not due to apoptosis. The nucleus of the malignant cell was surrounded by transformed mitochondria, as shown in Figure 2, of which some injected their electron dense material (metallo enzymes) of their cristae into the nucleus of the tumour cell, as pCA cells regained healthy transcription, without apoptosis.[7,8]

With improved diagnostic tests such as, e.g. PCA3,[16] EPCA-2,[17] PSA velocity, and prostate volume, MRI, CT, TRUS eventually aided by analyses for genetic predisposition etc,[18] we should be able to decrease the need for excessive needle biopsies (12 cores)[19,20] as it causes fever infections and need for injections of anesthetics, resulting in fewer histopathological samples which will turn out to be much cheaper. Biopsies may spread malignant cells outside the prostate, with fewer bloody interventions it may thus decrease the incidence of over 35% of the biochemical relapses seen even after radical prostatectomies.[19] One single well directed core - to reveal the Gleason score - would suffice. This form of bio-modulating therapy would anyway be the same disregarding the eventual number of focuses of cancer present in the prostate gland. The tumour load does not seem to be crucial.

A serious adverse effect was observed when a patient on his expressed demand got DHEA, 25mg per day because his serum level was markedly depressed. DHEA administration is definitely contraindicated since he developed intensive pain, and died in three weeks. Excessive hormone mono-therapy with Casodex®, or using LHRH analogues repeatedly, given in three months duration, can dangerously decrease FSH-levels to under 0.1 IU/L, leading to HRPC heralded by a simultaneous increase in PRL-levels (to > 600 mU/L). HRPC does not represent a clonal selection of hormone refractory prostate cells, but indicates exhaustion of the adrenal feed-back reaction! Attempts to passively increase the FSH-level by injections of human FSH, (75 -150 IU /day) can fleetingly decrease PSA-levels, but would be too expensive as a continuous treatment.[9]

The shift in the relative content of the growth factors inhibin and activin may indicate that the etiological metabolic aberration representing different metabolic forms causing pCA. After orchiectomy inhibin decreased to < 7.8 pg/ml, while activin stayed at a normal level (Case 3). Surprisingly this shift was also seen during normal pregnancy and in post-menopausal healthy females on estrogen substitution (using only 50µg plasters). In patients with high PRL, inhibin levels could unusually exceed that of activin (187/92 pg/ml, Case 6). In forms of occult pCA, diagnosed from soft tissue metastases (Case 9 & 10) the activin level could be excessively elevated (inhibin 25 pg/ml while activin was at, 2900 pg/ml). Rare forms of metabolic aberrations seem to exist in pCA, but fortunately they seem to react to biological therapy. Complete regression of bone metastases caused by this specific dietary supplementation may require the total removal of the testicular tissue, as it possibly excretes an unknown ZR inhibitor.

Bio-modulation of pCA may represent a form of epigenetic regulation, as natural components create shifts in the clinical outcome and phenotype expression articulated as a cure. Recurrent disease may appear, if this specific physiological supportive therapy is stopped. One form of this regulation may also be expressed as shifts in malignant transcription seen as regression of Gleason scores, as in Case 4.

The increased incidence of pCA, has already reached over 300,000 new cases per year in the European Union. In the USA over 180,000 patients were diagnosed and over 27,000 died in severe pain caused by bone metastases last year.

CONCLUSION

A biological, economical and non-invasive treatment modality is needed.[13] Screening has now got a new incentive, since pCA can be treated by dietary supplementation. The adrenal gland has a central position in prostate cancer etiology and its ZR-cells can biologically be activated and thus shield the patient from progressive prostate cancer without causing apoptosis and numerous side effects,[11,12] nor deterioration of the life quality. One should measure FSH and DHEAS to evaluate prognosis and the Gleason score. These specific functional alimentary formulae can be improved to more precisely suit individual patient requirements.

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