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Halted Progression of Soft Palate Cancer in a Patient Treated with the Paleolithic Ketogenic Diet Alone: A 20-months Follow-up

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Abstract *Introduction:* Myoepithelial tumor of the soft palate is associated with rapid progression and poor outcome. The standard care includes surgery with optional radiotherapy and/or chemotherapy. *Case report:* Here we present a case with myoepithelial tumor of the soft palate where the patient denied conventional treatment options. Instead, the patient started the paleolithic ketogenic diet which resulted in a halted progression of the tumor as evidenced by imaging follow-up. Currently, the patient is on the diet for 20 months, without symptoms and side effects. *Conclusion:* We conclude that the paleolithic ketogenic diet was effective and safe in this patient.

Keywords: *soft palate tumor, myoepithelial tumor, paleolithic diet, ketogenic diet*

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1. Introduction

Otto Warburg was the first to suggest that cancer emerges from abnormal cellular metabolism [1]. He postulated that key points in tumorigenesis include impaired oxidative phosphorilation, compensatory glycolysis and aerobic fermentation [1]. Utilization of fat for energy ultimately relies on the mitochondria and the associated metabolic pathways. Tumor cells, with dysfunctional mitochondria are unable to use ketones but largely depend on glucose for energy [2,3]. Based on this, adopting a ketogenic diet, which represent a shift from carbohydrates toward fat, has been repeatedly suggested as a promising option to treat cancer [3,4].

Encouraging studies in cancer patients with the ketogenic diet include a landmark study from 1995 reporting long-term survival in two children with brain tumor [5] and another case report which reported halted progression of glioblastoma for a few months [6]. In recent years several group studies have been carried out using the ketogenic diet in cancer. Overall, these studies did confirm that the ketogenic diet is relatively safe [7,8] and may diminish side effects associated with chemotherapy and/or radiotherapy [9]. However, as regards hard clinical endpoints, such as survival, no clear evidence is coming from these group studies supporting that the ketogenic diet is indeed beneficial. In the study of Schmidt et al. [7] and that of Fine et al. [10] advanced cancer patients were put on the ketogenic diet. In both studies [7,10] there was a tendency for halted disease progression in those patients adhering to the diet. However both studies were limited in follow-up duration with three and one months. In the ERGO study recurrent glioblastoma patients were put on the ketogenic diet but all patients progressed while on the diet [8]. In a retrospective study of Champ et al. [11] six glioblastoma patients were on the ketogenic diet for 3-12 months. Survival benefit was uncertain, however, one patient showed no signs of recurrence at 12 months of diet therapy. In patiens with tuberous sclerosis tumor progression was not halted by the ketogenic diet [12]. In the most recent study the ketogenic diet resulted in tumor regression in those patients with early stage cancer [13]. This study was however limited in duration too.

An assessement of the available patient studies shows that there are two features common to all of them. First, the dietary therapy was used following and/or concurrently with radiation and/or chemotherapy. Second, all studies used the classical version of the ketogenic diet which is based on vegetable oils and/or also included dairy, formula feeding or supplements.

Ketosis is often viewed as an evolutionary adapted state in humans [14]. In their study Schmidt et al. [7] also cite Steffanson who studied and proposed the traditional diet of the Inuit which is actually an animal meat-fat diet [15]. The most comprehensive overview on the animal meat-fat diet is provided by gastroenterologist Voegtlin [16], who is rarely cited in the context of the ketogenic diets. Considering ketosis as evolutionary adapted state combined with the knowledge on the diet of ancestral people [17], we propose that an ideal therepeautic diet in cancer would also rely on animal fat instead of vegetable-based oils used in previous clinical trials.

Accordingly, the authors of the present study are using a diet based on animal meat and fat, similar to that

proposed by Steffanson [15] as well as Voegtlin [16]. In an attempt to distinguish this diet from both the classical ketogenic as well as the diet termed paleolithic in a series of clinical studies [18] and books [17], we refer the diet as paleolithic ketogenic. Previously we have published cases of type 1 [19,20], type 2 diabetes [21], epilepsy [22,23], Gilbert's syndrome [24] and Crohn's disease [25] where we successfully applied the diet. Here we present a case with soft palate tumor of myoepithelial origin, an aggressive cancer type, where using the paleolithic ketogenic diet without any conventional treatment modalities resulted in halted progression of the tumor for 20 months, while producing no symptoms or side effects.

2. Case Report

The 60-year-old patient was non-smoker and denied alcohol consumption. For the six months before diagnosis she had been feeling a lump in her soft palate which was asymptomatic and did neither cause airway obstruction nor dysphagia. The mass was firm and without ulceration. Biopsy was taken on on 31 Oct 2014 and histopathology showed myoepithelial carcinoma (Grade 2 tumor). The MRI on 20 Dec 2014 showed a well-circumscribed and non-infiltrative mass measuring 36x33x27 mm arising from the left soft palate. The tumor was staged as T2,N0,M0. Knowing the malignicity of such tumors, the patient was offered radical surgery and palatal lift prosthesis which she did not accept. The patient did neither received chemotherapy nor radiotherapy.

3. Paleolithic Ketogenic Diet

We first met the patient in December 2014, shortly after diagnosis onset. We recommended the paleolithic ketogenic diet which the patient started instantly. The paleolithic ketogenic diet is an animal meat-fat based diet with a fat:protein ratio of approximately 2:1 and with a plant content less than 30% (in volume). In the diet, consumption of red and fat meats over lean meats as well as organ meats are encouraged. In the first six months the patient followed the most strict form of the diet: a full meat-fat diet. From July 2015 on, she was allowed to eat small amounts of vegetables with a frequency of ≤2 times a week. From this time on she was also allowed to drink coffee in moderation as well as to use small amounts of honey for sweetening. No calorie restriction was applied but the patient was suggested to eat when hungry and then to eat until satiation. Typically the patient had two meals a day. The patient regularly used urinary ketone strips which indicated sustained ketosis. Altogether, the patient exhibited a high level of dietary compliance as assessed by laboratory parameters (Table 1) and patient feedback. The patient was followed by personal visits every three months. In between she was followed by e-mail and phone calls. At the time of writing the manuscript the patient is on the diet for 20 months.

Table 1. Laboratory measurements during follow-up ont he paleolithic ketogenic diet

	17.04. 2015	25.09. 2015	30.10. 2015	25.11. 2015	26.02. 2016	17.06. 2016	21.07. 2016	normal range
WBC (G/l)	4.32	5.22	4.37	4.34	3.5	3.9	3.6	4-10
RBC (T/l)	4.32	4.47	4.31	4.58	4.48	4.65	4.55	4-5.6
Hgb (g/l)	126	129	126	130	130	135	132	120-160
Hct (%)	0.371	0.381	0.371	0.387	0.402	0.411	0.403	0.36-0.46
Thrombocyte (G/l)	232	217	244	230	192	213	211	120-350
CRP (mg/l)	-	1.4	1.9	2	1.6	2.9	1	< 5
ESR (mm/h)	14	14	26	25	18	27	25	1-30
Total protein (g/l)	-	71.7	66.7	67.2	65.7	71.5	70.4	66-83
Carbamid (mmol/l)	7.2	8.4	6.2	6.2	8.7	6.9	8.7	2.8-7.2
Creatinine (µmol/l)	51.5	50.1	40.1	45.8	40.6	44.7	44.1	45-84
Sodium (mmol/l)	137	140	139	140	141	138	138	136-146
Potassium (mmol/l)	3.7	3.9	3.7	4.2	3.5	4	4	3.5-5.1
LDH (U/l)	-	246	230	249	259	245	253	208-378
GOT (U/l)	18	15	15	17	16	19	18	< 31
GPT (U/l)	19	16	17	18	17	-	26	< 34
GGT (U/l)	14	15	13	13	13	13	14	< 38
ALP (U/l)	-	67	60	-	-	64	-	30-120
Iron (µmol/l)	11.6	11.2	10.3	11.8	11.3	13	12.4	10.7-32.2
Uric acid (µmol/l)	213	301	318	267	199	-	187	155-357
Glucose (mmol/l)	4.4	4.9	4.7	4.6	4.9	6	5.8	3.5-6
Calcium (mmol/l)	2.29	2.27	2.24	2.31	2.3	-	2.33	2.2-2.65
Magnesium (mmol/l)	0.85	0.83	0.81	0.84	0.81	0.79	0.85	0.77-1.03
T. chol. (mmol/l)	9.5	8.3	8.6	8.6	9.6	9.4	9.4	3.9-5.6
HDL chol. (mmol/l)	2.04	1.97	1.93	2.11	1.98	2.21	2.44	1.15-3
Triglyceride (mmol/l)	0.71	0.87	0.67	0.64	0.72	0.68	0.6	0.5-1.6
Fibrinogen (g/l)	-	-	4.7	4.5	3.5	4.7	4.1	2-4
Urinary ketones	++	++	+++	++	+	++	+	

Abbreviations: WBC: white blood cell count, RBC: red blood cell count, Hgb: hemoglobin, Hct: hematocrit, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, LDH: lactate dehydrogenase, GOT: glutamate-oxaloacetate transaminase, GPT: glutamate-pyruvate transaminase, GGT: gamma-glutamyl transferase, ALP: alkaline phosphatase,
T. cholesterol: total cholesterol, HDL chol.: high density lipoprotein, LDL: low density lipoprotein. – indicates that a given parameter was not measured.

4. Laboratory Data

Laboratory workup was performed seven times during the follow-up which indicated a high level of dietary adherence (Table 1). Glucose levels averaged 5 (±0.6) mmol/l. Renal and liver function as well as ions were normal. Inflammatory markers CRP and ESR (erythrocyte sedimentation rate) were in the normal range while fibrinogen was mildly elevated on some measurements. Cholesterol was elevated while triglyceride was low. Urinary ketone was positive on each workup.

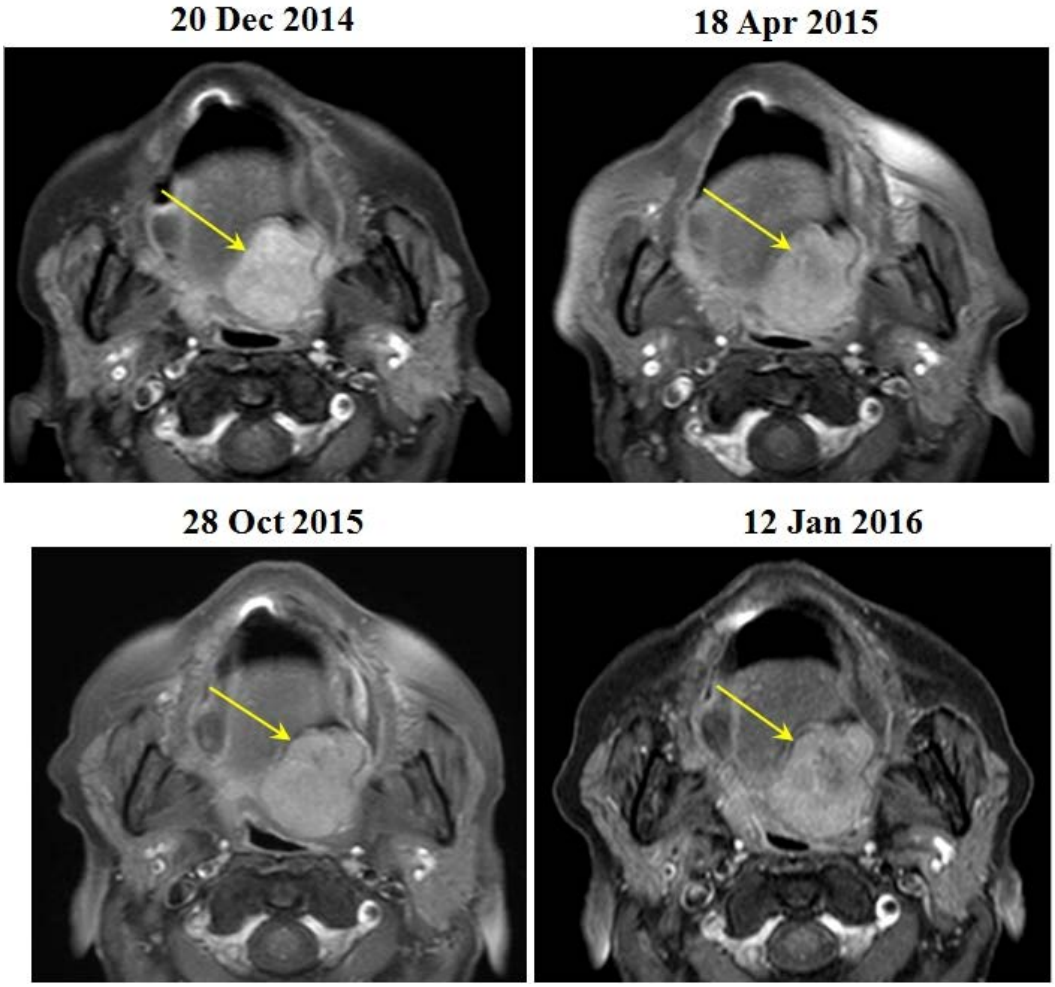

Figure 1. Subsequent MRI scans showing the tumor in left soft palate. The first one (on 20 Dec 2014) was performed at diagnosis onset. The three subsequent MRI were performed during follow-up on the paleolithic ketogenic diet

5. MRI Imaging

Three follow-up MRI examinations were carried out which indicated a minor decrease in tumor size. The first follow-up exam, on 18 Apr 2015, showed no change in tumor size (36x33x27 mm) while the two subsequent MRI examinations (on 28 Oct 2015 and 12 Jan 2016) showed a decreased tumor size (33x27x24 mm). No enlarged lymps nodes were seen on either MRI exams.

6. Condition and Symptoms

The patient was highly motivated and so it was relatively easy for her to maintain the diet.

The patient reported no side effects of the diet but improved physical fitness and well-being. Currently she is on the diet for 20 months. Subjectively she feels that the tumor diminished. At diet onset she weighted 68 kg and was 165 cm tall (BMI=25). Currently she weights 63 kg (BMI=23).

7. Patient Consent

Written informed consent was obtained from the patient for publication of this case report.

8. Discussion

In animal models the ketogenic diet has been shown to have antitumor effects [3]. In the human literature several benefits have been associated with the ketogenic diet including imrovement in quality of life [7] as well as a decrease in therapy-induced side effects [9]. Yet, apart from an early study from 1995 [5], no reports are available on long-term survival benefit associated with the diet. The ketogenic diet is generally proposed as an adjunct to conventional treatments to enhance their effectivity. At the same time, as also pointed out by Seyfried [26], chemotherapy and radiation may induce necrosis and inflammation both of which elevate extracellular

glutamate and glucose concentrations and thereby may contribute to cancer progression. Cortocosteroids, which are frequently administered along with radiation therapy, also contribute to this process [26]. As a result, conventional treatments may turn counterproductive and may also conteract the beneficial effect of dietary carbohydrate restriction [26]. As far as we know, our case study is the first one in the literature where a ketogenic diet is used as a stand-alone therapy in cancer. This study is also the first in using a ketogenic diet based on animal meat and fat instead of the classical version based on vegetable oils and dairy. We assume that both factors might have significantly contributed to the success achieved in the present case.

Myoepithelial tumors are rare tumors accounting for less than 1 % of all salivary gland tumors [27]. In this tumor type surgery is the first choice of treatment with optional postsurgical radiotherapy and/or chemotherapy [28]. Myoepithelial tumors typically exhibit extensive growth and infiltration to adjacent tissues [28]. Overall, prognosis for myoepithelial tumors of the head and neck is poor with the 3- and 5-years survival of 59% and 32%, respectively [27]. Incomplete surgery is known to be associated with an even worse outcome [27]. Halted progression and the absence of tumor-associated symptoms in our case represent a much better outcome than could be expected based on the statistics of this tumor type.

The patient showed excellent dietary adherence as also shown by laboratory workups. Her laboratory parameters are similar to that seen in our other patients on the paleolithic ketogenic diet with other diseases [19,20,21,22,23,24,25].

We opine that, beyond maintaning ketosis, avoiding vegetable oils, dairy as well as other non-paleolithic food items all represent key factors in the successful management of this case. As we showed in a previous case study, the paleolithic ketogenic diet was also more efficient in reducing symptoms as compared with the popular version of the paleolithic diet [24]. Non-paleolithic components (e.g. milk and dairy, grains) of the classical ketogenic diet and that of the standard diet have been suggested to increase pathological intestinal permeability [17]. Accordingly, in our previous case study on Crohn's disease, we showed that pathological intestinal permeability had normalized while on the paleolithic ketogenic diet [25]. Such a normalizaton of intestinal permeability was not seen in a study using a much more popular and indulgent version of the paleolithic diet [29]. Importantly, increased permeability of the intestine and that of other membranes was suggested to play a role in the cancerous transformation of normal tissues [30]. In addition, while the classical forms of the ketogenic diet has been described to induce side effects including diarrhea, constipation, deficiency of magnesium, iron and other vitamins [31], the paleolithic ketogenic diet results in no such side effects.

We assume that the paleolithic diet may be of superior effectiveness while having no side effects as compared to the classical ketogenic diet in cancer management. It is our opinion that such a preferable effectivity/side effect profile of the paleolithic ketogenic diet can only be explained evolutionarily. We assume that the paleolitic ketogenic diet is the evolutionary adapted diet itself for humans.

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Conflict of Interest

The authors declare no conflict of interest.

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