Chiropractic Management of a Patient With Chronic Fatigue: A Case Report

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Abstract

Objective: The purpose of this case report was to describe the examination and management of a patient with chronic fatigue.
Clinical Features: A 34-year-old woman presented to a chiropractic clinic with complaints of fatigue and inability to lose weight for 2 years. When tested, she was found to have high serum thyroglobulin antibodies, low serum vitamin D_3, low saliva dehydroepiandrosterone-sulfate, and low saliva total and diurnal cortisol.
Intervention and Outcome: The patient was placed on an anti-inflammatory ancestral diet and given recommendations to decrease the aerobic intensity of her exercise routine. On the basis of the result of conventional and functional laboratory tests, she was prescribed a treatment plan of targeted supplementation. After 12 weeks of application of dietary, lifestyle, and supplementation recommendations, the patient reported experiencing increased energy and weight loss of 15 pounds. Her thyroglobulin antibodies returned within reference range, salivary cortisol increased and closely followed the proper circadian rhythm, and dehydroepiandrosterone-sulfate increased.
Conclusions: This report describes improvement in a patient with chronic fatigue with the use of nonpharmaceutical polytherapy involving dietary changes, lifestyle modification, and supplementation. (J Chiropr Med 2016;15:314-320)
Key Indexing Terms: *Adrenal Insufficiency; Hypothalamic Dysfunction Syndromes; Hashimoto Thyroiditis*

Introduction

Fatigue is a common symptom seen in clinical practice; however, it is difficult to define, measure, and specifically relate to the chief complaint within the clinical encounter. Because of its subjective nature, clinicians often ignore fatigue as a symptom and rely on objective findings to steer the diagnosis. Evaluation and management of patients who experience fatigue as their major or only complaint could then be difficult for the clinician.[1]

Fatigue frequently is a major part of the complex pathophysiology of the presenting patient. Fatigue can be described broadly as being either acute and self-limiting or chronic and debilitating.[2] Fatigue is also categorized as being peripheral or central in origin. Peripheral fatigue is caused by peripheral neurotransmitter imbalance and causes impairment in the peripheral nerves and muscular contraction. Central fatigue relates to abnormalities of neurotransmitter balance within the central nervous system and is often present with psychological complaints, such as anxiety and depression.[3] Without proper and ample focus on fatigue as a symptom, the underlying problem may not be identified, and multiple medications, including antidepressants, antipsychotics, and benzodiazepines, could be prescribed. Long-term use of these and other medications could prolong fatigue and affect the patient to the point that chronic fatigue syndrome (CFS) and other chronic conditions could develop.[4]

Chronic fatigue syndrome is characterized by persistent fatigue that may be associated with many other debilitative conditions.[5] Chronic fatigue syndrome is not necessarily caused by exertion and not usually relieved by rest.[6] Common symptoms of CFS include sudden onset of an infectious-type illness, subsequent chronic and debilitating fatigue, pharyngitis, and postexertional malaise.[7] As the cause of CFS is still not known, and its multifaceted mechanism is not understood, effective treatment is difficult.[8] Treatment of CFS conventionally has been restricted to cognitive behavioral therapy and medication.[9] The effectiveness of medications, including antidepressants and immunomodulatory agents, has not been confirmed.[10] There is a growing body of research that supports acquired abnormalities of the hypothalamic-pituitary-adrenal (HPA) axis, including decreased levels of cortisol, enhanced cortisol negative feedback, and blunted HPA axis response in patients with CFS.[11] Reduced activity of the HPA axis and, thus, the hyposecretion of cortisol has been associated with fatigue, although a temporal association has not yet been established.[12]

Chronic fatigue syndrome also has a distinct inflammatory component that can aggravate many of its symptoms and associate it with other endocrine and immunologic disorders that

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Paper submitted January 6, 2016; in revised form August 5, 2016; accepted August 5, 2016.
1556-3707

http://dx.doi.org/10.1016/j.jcm.2016.08.006

are often seen in clinical practice. Chronic fatigue syndrome has been associated with cytokine abnormalities,[12,13] which are very likely indicative of immune activation and pathogenic inflammation. Furthermore, objective fatigue symptom scores in CFS have been significantly correlated with levels of proinflammatory cytokines.[14]

Hypothyroidism is characterized by decreased levels of the thyroid hormone (thyroxine [T_4] and triiodothronine [T_3]) or normal levels of the thyroid hormone but with elevated, and sometimes compensatory, thyroid-stimulating hormone (TSH). Symptoms may include dry skin, poor memory, slow thinking, muscular weakness, muscle cramps, cold intolerance, puffy eyes, constipation, hoarseness, and fatigue. The overall prevalence of hypothyroidism is between 4% and 10% of the general population.[15]

Hashimoto thyroiditis (HT), an autoimmune condition that attacks the thyroid gland by an immune process mediated by cellular T-helper 1 (Th1), commonly results in hypothyroidism. Hashimoto thyroiditis occurs in 0.3-1.5 per 1000 individuals worldwide and is more predominant in females, with gender prevalence ratios of 5–20:1.[16] Symptoms of HT include weight gain, depression, anxiety, sensitivity to cold, and chronic fatigue.[17] Diagnosis for HT is made by testing TSH, free T_4, free T_3, thyroid peroxidase antibodies (anti-TPO), and thyroglobulin antibodies (anti-TG). Diagnosis may be assisted by performing ultrasonography of the thyroid gland, where a mild goiter is sometimes present.[18] Conventional treatment for HT includes life-long replacement of hormone levels, by levothyroxine, triiodothyronine, or desiccated thyroid extract.[19] With regard to nonpharmacologic intervention, a systematic review and a meta-analysis showed an association with routine supplementation of selenium and not only a reduction of anti-TPO but also an improvement in well-being and mood.[20] Immune-endocrine interaction via the HPA axis has also been proven vital for HT, even though its onset and course are insidious. Human studies have demonstrated that physiologic stressors induce various immunologic changes, either directly or indirectly, through the nervous and endocrine systems. These changes in immune function may contribute to autoimmune inflammation in patients who have been already diagnosed or are genetically predisposed to HT. Physiologic stressors, in various forms, can be one of the environmental factors for thyroid autoimmunity, including HT.[21]

There are few cases in the literature describing chiropractic management of chronic fatigue with the use of a polytherapeutic approach. Therefore, the purpose of this case report was to describe the examination and management of a patient with chronic fatigue.

Case Report

A 34-year-old female presented with complaints of chronic fatigue, inability to lose weight, and mood swings. The patient reported to the chiropractic physician that she had been having these symptoms for 2 years. She also complained of bilateral breast tenderness around the time of her menstruation for the last 4 months. The patient described experiencing increased anxiety when driving on bridges over the past 2 years. Her fatigue had worsened over the past 3 weeks, and since then, she had stopped her 6-days-a-week running regimen and her caffeine supplement.

Table 1. *Patient Information Pre- and Post-Treatment*

Patient Information	Initial Visit	12 Weeks Post-Treatment	Reference Range
Weight (lb)	164	149	
BMI	28.1	25.6	18.5–24.9
Vitamin D_3 (pg/mL)	16.8	89.8	18–78 pg/mL
Anti-TG (IU/mL)	225.0	51.0	<116 IU/mL
TSH (mU/mL)	2.645	1.706	0.3–5 mU/L
T_4 free (ng/L)	1.2	1.5	0.8–1.8 ng/dL
T_3 free (pg/mL)	2.9	3.4	2.3–4.2 pg/mL
DHEA-S (ng/mL)	1.92	8.78	2–10 ng/mL
Cortisol – morning (nM/L)	8.8	14.9	13–24 nM/L
Cortisol – noon (nM/L)	4.3	6.2	5–8 nM/L
Cortisol – afternoon (nM/L)	3.1	3.7	4–7 nM/L
Cortisol – nighttime (nM/L)	2.4	2.6	1–3 nM/L
Cortisol sum (nM/L)	18.6	27.4	23–42 nM/L
Cortisol-to-DHEA-S ratio	9.69	3.12	5–6

Anti-TG, thyroglobulin antibodies; *BMI,* body mass index; *DHEA-S,* dehydroepiandrosterone sulfate; *T_3,* triiodothronine; *T_4,* thyroxine; *TSH,* thyroid-stimulating hormone.

A review of her systems included past medical history of trigonocephaly at 8 months of age as well as 3 pregnancies and vaginal deliveries with no miscarriages or abortions. She had had no abnormal Pap test results. The patient had a family history of diabetes, thyroid problems, and seizures. She reported current history of nasal congestion, earaches, voice hoarseness and coughing, snoring, and excessive thirst. She denied being depressed or feeling down. The patient denied taking medications, nutritional supplements, and herbal supplements.

Upon examination, her blood pressure was 106/64 mm Hg, pulse 61 beats per minute, temperature 96.9°F (36.1°C), weight 164 lb (74.4 kg), and height 5 feet 4 inches (162.6 cm). She initially had a body mass index of 28.1. Her general physical examination was unremarkable, with the exception of a left-sided nontender prominence on the thyroid, which was consistent with thyroid nodules and goiter.

Thyroid ultrasonography was ordered on the basis of the physical examination findings, along with a complete blood count, comprehensive metabolic panel, TSH, free T_4, free T_3, reverse T_3, anti-TG, anti-TPO, lipid panel, C-reactive protein, antinuclear antibodies, and serum vitamin D_3 and B_{12}. A saliva adrenal function panel, which included samples of cortisol measured 4 times daily, and dehydroepiandrosterone-sulfate (DHEA-S) measured twice daily, was also ordered because of her complaint of fatigue.

The patient's thyroid ultrasound image was consistent with a multinodular goiter with no dominant cystic or solid

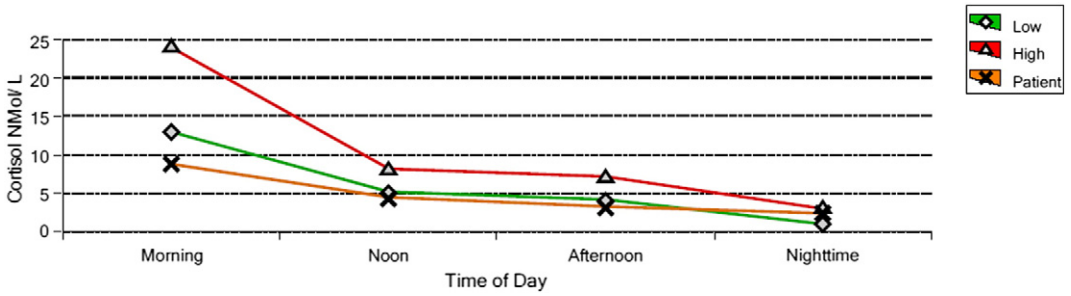

Fig 1. *Patient cortisol levels before treatment.*

lesions. Her blood tests were unremarkable with the exception of high anti-TG at 225 IU/mL (normal: <116) and low vitamin D_3 at 16.8 pg/mL (normal: 18–78). The patient's saliva adrenal function panel revealed low cortisol levels of 8.8 nM/L (normal: 13–24) at morning, 4.3 nM/L (normal: 5–8) at noon, 3.1 nM/L (normal: 4–7) at afternoon, and 2.4 nM/L (normal: 1–3) at nighttime and cortisol sum 18.6 nM/L (normal: 23–42). She tested low for DHEA-S at 1.92 ng/mL (normal: 2–10) (see Table 1 and Fig 1).

The patient was given options for treatments with explanation of the known risks, benefits, and side effects of each type of management, including anti-inflammatory diet, lifestyle changes, targeted supplementation, and endocrinologist referral. The patient declined the endocrinologist referral and stated that she wanted to manage her condition without the use of medication.

The patient was placed on a supplement treatment plan with a high-dose multivitamin to maintain or improve micronutrient status, 3 g ascorbate to serve as a cofactor for adrenal function, 3 g essential fatty acid (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) to help revert hypothalamic inflammation, and 10,000 IU vitamin D to assist in T-helper cell (Th) balance in autoimmunity. Specific to the adrenal function panel results, the patient was placed on the following supplement treatment plan of liquid tinctures: 2.4 mg sublingual DHEA 3 times daily, 18 mg sublingual pregnenolone 3 times daily, and 350 mg sublingual licorice root extract (7.2 mg Glycyrrhizin) upon waking to increase the patient's cortisol levels because of the reduced levels occurring throughout the day.

The patient was also instructed to follow an anti-inflammatory ancestral diet that excluded bread, cereal, refined carbohydrates, inflammatory fats and oils, and included high-micronutrient nuts, seeds, fruits, and vegetables as well as lean red meat, fish, or eggs. It was emphasized that a usual meal should consist of fruits and vegetables occupying two-thirds of the plate and lean meat, fish, or eggs occupying one-third of the plate. The patient was counseled to reduce her aerobic workout intensity and also to reduce aerobic exercise time by 30 minutes to decrease demand on the adrenal glands for cortisol production and reduce exhaustion. The patient was advised to increase her strength training time to compensate for the reduction in exercise time. The patient agreed to follow this treatment plan for 12 weeks. She also agreed to repeat blood work and adrenal function panel at the end of the 12-week period.

The patient returned after following the prescribed plan for 12 weeks. Repeat blood work and adrenal function panel had been performed at the time of this visit. She reported that her nasal congestion, earaches, voice hoarseness, snoring, and excessive thirst had resolved 6 weeks into the treatment. She also reported that her breast tenderness and anxiety upon driving over bridges had been significantly alleviated. She stated that her energy had increased and that no signs of anxiety, high blood pressure, or fast heart rate were experienced as side effects of the supplements. At this visit, she weighed 149 lb (67.6 kg), with a body mass index of 25.6.

The patient's blood and saliva tests were repeated at the same 12-week interval between her visits. Her test showed her vitamin D_3 levels at 89.8 ng/mL and anti-TG at 51 U/mL. Her TSH decreased 2.645 IU/mL from her initial visit to 1.706 IU/mL. The patient's adrenal function panel showed cortisol levels within reference ranges for morning, noon, and nighttime, with levels of 14.9, 6.2, and 2.6 nM/L, respectively. The afternoon cortisol level was still low, but it, too, had improved to 3.7 nM/L. Her cortisol sum increased to 27.4 nM/L. Her DHEA-S level was within reference range at 8.78 ng/mL (Table 1; Fig 2).

The patient stopped visits with the attending physician, and no further follow-ups occurred. The patient gave consent to have her personal health information published.

Discussion

This case illustrates the importance of appropriate testing, including conventional blood tests, which showed positive thyroglobulin autoantibodies in this case, and also functional medicine tests, such as the adrenal function panels used for this patient. The presentation of fatigue was also significant in this case. Fatigue in this patient was a sign of an inflammatory milieu, not only specific to the thyroid gland but also central to the HPA axis and the corresponding hypocortisolism. This HPA axis dysfunction may have been the central driver for

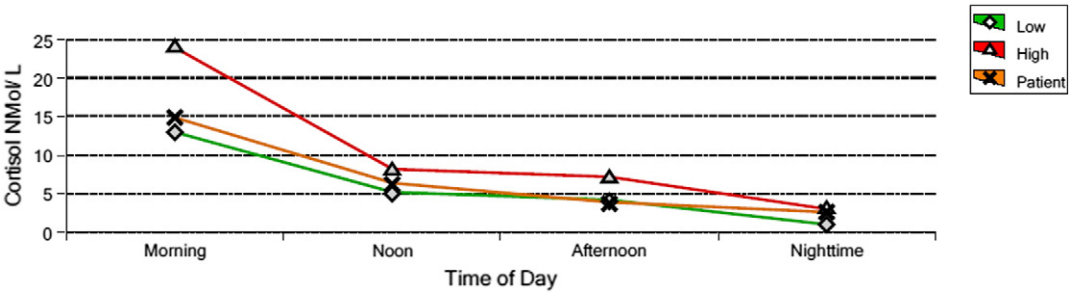

Fig 2. *Patient cortisol levels 12 weeks after treatment.*

the patient's HT, which could have amplified the fatigue and inability to lose weight.

Additionally, cytokines produced during inflammatory diseases such as HT modulate hormone production and conversion. The activity of 5′-deiodinase type I, which converts T_4 to T_3, is known to be regulated by proinflammatory cytokines in the thyroid and the liver.[22] Therefore, by reducing the inflammatory environment of the body, conversion of T4 to T3 may be rendered more efficient.

There may be question on the reliability of salivary cortisol testing in clinical practice and whether salivary cortisol could be used as a surrogate for serum total cortisol. Researchers have found that salivary cortisol measured with a simple enzyme immunoassay can take the place of, and is actually preferable over, serum total cortisol for the assessment of HPA activity.[23] Additionally, multiple salivary cortisol measures across the diurnal curve effectively evaluate HPA axis tone with similar between-visit reliabilities. This consistency makes it feasible to perform population-based studies with this testing to reflect not only chronic disease but also successful treatment in relation to changes in the HPA axis dynamics.[24] However, the interpretation of saliva cortisol results was seen to be limited because of inconsistencies in measurement practice.[25]

Analysis of the HPA axis in this patient, in the form of cortisol and DHEA-S measurements, was important not only with regard to her complaint of chronic fatigue but also in association with her inflammatory and autoimmune milieu. The HPA axis may have a strong modulation effect on the Th1 and Th2 activity balance. Th1 and Th2 cells direct different immune response pathways. Th1 cells drive cellular immunity, and Th2 cells drive humoral immunity. Overactivation or dominance of Th1 activity can drive an autoimmune response, especially if a genetic predisposition present.[26] A dominant Th1 immune response may explain, at least in part, the appearance of HT in the patient. The HPA axis, in secreting cortisol as an adrenal hormone, helps shift the cytokine pattern from a proinflammatory Th1 pattern to an anti-inflammatory Th2 pattern.[27] Patients with an inflammatory or autoimmune condition, such as HT, may benefit from HPA axis normalization, as in the patient in this case. There is evidence that the HPA axis plays a relevant role in controlling excessive inflammatory reactions.[28] In addition to the normal function of the HPA axis assisting in the cytokine shift from Th1 to Th2, supplementation with vitamin D_3,[29] EPA, and DHA[24] may have also helped alleviate the inflammatory autoimmune activity in the form of HT in this patient. Vitamin D deficiency has been seen to have an association with thyroid autoimmunity,[30] and supplementation of vitamin D has been seen to decrease autoimmune antibodies.[31] Eicosapentaenoic acid and DHA have a specific reversion effect on hypothalamic inflammation, which may aid in the function of the HPA axis, especially in overweight individuals.[32] Ascorbate has been seen to be a functional cofactor for both the adrenal cortex and the medulla in the production of cortisol, DHEA, epinephrine, and norepinephrine.[33] To have physiologic effects on the HPA axis, including the brain and the adrenal glands, and also to treat a patient with inflammation, as described in this case study, therapeutic dosages of 3 g ascorbate have been used with limited side effects.[34,35] In addition to the normalization of HPA measures, recommending an anti-inflammatory ancestral diet[36,37] likely assisted in decreasing thyroid autoimmunity.[38]

Normalization of HPA axis function was also assisted by specific targeted supplementation based on adrenal function panel results, each with its own mechanism. Licorice root was used to increase the cortisol level by increasing the half-life of the hormone.[39] To replace low levels of the hormone, DHEA was used, as it is a hormone precursor that can functionally assist the production of cortisol and other adrenal- and extra-adrenal–based hormones as one of its precursors.[40] Therapeutic pregnenolone has been used to decrease apoptosis and inflammation, modulate the HPA axis, and positively modulate N-methyl-D-aspartate receptors.[41,42] Therapeutic use of pregnenolone and DHEA has been proposed to be used in clinical trials.[43]

The nature of the treatment for this patient should be given due consideration. The patient was not treated with a single supplement, dietary change, or other intervention but was placed on natural medicine polytherapy. The polytherapy described in this case included general nutritional support, targeted supplementation, dietary changes, and lifestyle modifications; the patient declined the endocrinologist referral. Polytherapy has been widely described in clinical

pharmaceutical literature[44-46]; however, polytherapy studies in nutritional medicine have been performed only on a small scale,[47] even though the use of nutritional medicine polytherapy has lower side effects. This research phenomenon may have resulted from researchers wanting to see the effects of a single nutritional entity. However, treatment with a single nutritional entity does not match the actual intervention in and the biochemical requirements of a particular patient for resolution of a chronic disease, as is seen with the patient described in this case study report.

Limitations

The limitations of this study include the fact that it has reported findings from only one patient, and these findings cannot be applied to every patient with HT or the same symptomatology. The use of polytherapy can also be seen as limitation, because it is not possible to determine which part of the treatment had the most effect. Extenuating circumstances such as financial hardship, allergies, and limiting comorbidities may not allow patients to take all the diagnostic and therapeutic steps that this patient was able to. The patient also did not undergo repeat thyroid ultrasonography to determine if the multinodular goiter and the size of the thyroid gland had decreased. This could have provided further evidence of a pronounced change in the patient's condition. Payment for repeat ultrasonography may have been denied by the patient's insurance provider. Repeat ultrasonography after selenium supplementation for 3 months has been reported to show normalization of thyroid autoimmunity, accompanied by normalization of autoimmune thyroid antibodies.[48] No laboratory testing for celiac disease or gluten sensitivity was performed on this patient. Gluten sensitivity can promote thyroid diseases, including thyroid autoimmunity.[49] Proper testing for gluten sensitivity antibodies could have better guided treatment in this patient. Additionally, neither extended treatment nor follow-up was performed in this case after the 12th-week visit. Even though this patient's symptoms and test results improved greatly, it takes a year or more for the cortisol diurnal circadian pattern to be normalized. Because of lack of follow-up, given the patient compliance in this case, it was not determined if the thyroid autoantibodies would continue to stay low. In future case studies, case series, and clinical trials, at least a 12-months' follow-up would be appropriate to determine the long-term efficacy of this treatment approach.

Conclusions

This case study illustrates the evaluation of a 34-year-old female presenting with chronic fatigue and the subsequent resolution of HT. Using HPA axis functional testing and nonpharmacologic treatments directed toward Th1/Th2 balance, inflammation modulation, and HPA axis normalization, the patient's symptoms and laboratory findings improved at the time of her revisit. Although this study does not suggest that all patients with autoimmune conditions and CFS would respond in the same manner, this conservative approach to the treatment of chronic disease could be considered before using medications with known adverse effects.

Funding Sources and Conflicts of Interest

No funding sources or conflicts of interest were reported for this study.

This case report is submitted as partial fulfillment of the requirements for the degree of Master of Science in Advanced Clinical Practice in the Lincoln College of Post-professional, Graduate, and Continuing Education at the National University of Health Sciences, Lombard, Illinois.

Contributorship Information

Concept development (provided idea for the research): C.T.A.
Design (planned the methods to generate the results): C.T.A.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): C.T.A.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): C.T.A.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): C.T.A.
Literature search (performed the literature search): C.T.A.
Writing (responsible for writing a substantive part of the manuscript): C.T.A.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): C.T.A.

Practical Applications

- Chronic fatigue may be a common complaint that is difficult to define and evaluate in the offices of chiropractic physicians.
- Acquired abnormalities of the HPA axis have been associated with inflammation, autoimmunity, and the symptom of chronic fatigue.
- Targeted nutritional and botanical supplementation towards normal HPA axis function, anti-inflammatory dietary focus, and exercise changes may serve as a polytherapy to combat primary causes of chronic fatigue.

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