Tracy L. Brobyn
Patrick J. LaRiccia

Case Report: A Multifactorial Integrated Systems Approach in the Successful Treatment of Primary Amenorrhea

Abstract

A 22-year-old female, having failed standard medical assessment and treatment for a primary amenorrhea, experienced menarche with the establishment of regular and recurrent menstrual cycles after global integrative medicine assessments and interventions: Autonomic Response Testing, Neural Therapy, Acupuncture, Low Dose Immuno-therapy, Homeopathy, heavy metal reduction with chelation and laser energetic detoxification and dietary change. Such a multi-factorial approach to chronic disease deserves research attention.

Introduction

The etiology of primary amenorrhea can be complex. Many functional physiologic systems influence the normal onset of menses. By definition, primary amenorrhea includes patients with the following conditions: 1) no menses by the age of 14 with normal growth and development of secondary sexual characteristics or 2) no menses by the age of 16 regardless of presence of normal growth and normal secondary sexual characteristics[1,2], Normal menarche requires a functional hypothalamic-pituitary axis, a functional ovary and a patent outflow tract[1]. Once pregnancy is ruled out ascertainment of the presence of a uterus is mandatory. Absence of a uterus indicates congenital issues such as mullerian agenesis or androgen insensitivity disorders.

When a uterus is present, the etiology of primary amenorrhea is in one of three categories: 1) normogonadotropic hypogonadism (i.e. normal Estradiol, FSH and LH levels), 2) hypergonadotropic hypogonadism (i.e. low estradiol and elevations of FSH and LH) and 3) hypogonadotropic hypogonadism (estradiol, FSH and LH all are low)[2]. Although these categories are useful, gonadotropin levels may not always follow these guidelines depending on the disorder. It is important, when considering primary amenorrhea, to always consider causes of secondary amenorrhea during the evaluation[3].

Category 1 disorders present with normal sexual characteristics and include outflow obstruction issues such as imperforate hymen or transverse vaginal septum. These cases are estimated to make up approximately 20% of cases of primary amenorrhea[1].

Category 2 disorders involve anomalies of the gonads whereby folliculogenesis does not occur despite the release of FSH. Subsequent lack of gonadal estradiol release leads to a reduction in the negative feedback loop involving estradiol and FSH, thus FSH is elevated. Patients in category 2 are likely to have a reduction in secondary sexual characteristics on exam or evidence of hyperandrogenism. Gonadal dysgenesis can often be attributed to congential syndromes such as Turner's or Swyer's[1]. Poly cystic ovarian syndrome (PCOS), although typically seen as a common cause of secondary amenorrhea, is a multifactorial endocrine disorder that can present as a form of primary amenorrhea in this category. FSH/LH and estradiol levels may all be normal in PCOS, therefore, the disorder is characterized by hyperandrogenism found on either clinical or laboratory examination[3]. Other causes of primary gonadal failure include damage to the ovaries in childhood as a result of infection such as mumps or toxicity from chemotherapy. Disorders in category 2 make up the majority of cases of primary amenorrhea accounting for up to 50% of cases[1] although a recent case series from India placed mullerian anomalies at 47% of the 102 cases of primary amenorrhea studied[4].

Category 3 which is due to the disorders with central anomalies of the hypothalamic-gonadal axis accounts for approximately 30% of primary amenorrhea cases. These disorders include central anomalies of the hypothalamic-pituitary tract such as cranial tumors/pituitary adenomas; anatomic defects such as empty sella syndrome; inhibition of pulsatile GnRH as can be found in cases of excessive exercise; malnutrition and stress. Systemic diseases which can lead to disruption of the axis such as hypothyroidism, chronic renal failure or Cushing's disease can also be grouped in this category, however these disorders can also be found to have normal levels of gonadotropins[2]. Although disorders in category 3 are rarely present prior to puberty, they still need to be considered in cases of primary amenorrhea[1].

Autonomic response testing

"Autonomic Response Testing (ART)"[5,6], is a form of applied kinesiology. Applied kinesiology (AK) is a form of manual muscle testing in which an interpretation is made regarding the response (weakness, no change, or strengthening) of a muscle to manual testing. The interpretation informs the assessment of the patient and the prediction of positive, negative, or neutral responses to therapies. Different forms of applied kinesiology can give different results[6]. There are no published studies that have evaluated ART's reliability and validity. We hope this case study will prompt such studies. Our clinical experience with ART as an assessment tool has been very positive.

The usefulness of different versions of AK can be likened to different antibiotics. Although antibiotics are designed to inhibit or kill micro-organisms, their effectiveness depends on the clinical situation in which they are applied and is determined by the outcomes resulting from their use in real life clinical situations. Like different forms of AK, the success or failure of a given antibiotic cannot be generalized to other antibiotics without further clinical evaluations specific to those other antibiotics. One can also liken the assessment aspects of the various forms of applied kinesiology to diagnostic tests that vary in regard to sensitivity, specificity, positive predictive value and negative predictive value.

In a systematic review of AK studies (ART was not included in the review) by Hall et al[7], it was unable to draw clear conclusions and recommended studying applied kinesiology utilizing a pragmatic study design. Schwartz et al[8], recently published a negative study wherein no distinction was made regarding the various forms of AK. Based on the study's description of how the applied kinesiology was performed, it is clear that ART was not specifically evaluated. No designation was given as to which form of AK was being tested[9].

Neural therapy of scars and teeth

"Neural therapy" is an injection technique that was developed during the early 1900s in Germany by Walter and Ferdinand Huneke. The premise behind this therapy is that scars and other types of damaged tissue can lead to over excitation of efferent neurons within the autonomic nervous system resulting in so called "interference fields"[10,11],which can result in symptoms such as nausea, vomiting or pain[10,11,12,13]. Neural Therapy treats the presence of inference fields via injection of procaine. The solution is injected intradermally into active scars as well as through the use of clustered 0.5 cm intradermal blebs (also known as quaddels) over generalized areas of interference[10,11]. Interference fields resulting in pain/dysfunction in bodily locations remote to the interference field location is not an unknown physiologic idea and has been described within the conceptualizations of referred pain and osteopathy[10,11]. In our presented case, the patient had interference fields on the lower legs, chest, nose and gums.

Heavy metal body burden therapies: exposure avoidance and chelation

The level of lead or mercury in a person's blood may be considered within normal limits based on the most currently accepted norms. However, there exist individual differences in sensitivity to toxic substances. The important questions are: does the patient's current body burden of a toxin have anything to do with the current health? Will reduction of total body burden improve the patient's state of health? Will desensitization techniques result in clinical improvement? The body burden can be reduced by avoidance of exposure or active intervention (e.g. chelation) to eliminate toxins from the body. Occasionally a person dies of or becomes ill from peanuts or shell fish exposure. These events are rare in the general population as a whole. Thus, peanuts and shell fish are not removed from the market because of the low prevalence of hypersensitive people. It is not inconceivable that individuals vary in their sensitivity to various levels of heavy metals such as mercury and lead.

If one checks for toxic levels of heavy metals in every patient the number of positive tests would be low based on our current reference standards. However what if we could check for a person's individual sensitivity. ART appears to permit this type of evaluation. Patient A with emotional lability may have a mouth full of mercury amalgam fillings, removal of which results in no clinical improvement. Patient B with emotional lability may have only two mercury amalgam fillings, but removal of the two amalgam fillings has a rapid dramatic clinical response. The difference in response has to do with the individual's sensitivity to their own total body burden of mercury. Our clinical experience indicates that ART allows us to determine the sensitivity of patients to their current body burdens of toxins. One of the reasons for publishing this retrospective case review is to encourage the research community to examine ART closely and for other integrative medicine practitioners to publish their own clinical case reports in order to encourage further research.

Ionic footbath

Our clinical experience indicates that an ionic footbath is of use in detoxification from heavy metals. We believe the foot bath promotes increased excretion of toxins in the stool or in the urine. There is limited research that has been done in this area. We use a device called the *Ion Cleanse* by A Major Difference, Inc, 7318 S Revere Pkwy, Ste B-7, Centennial, Colorado. There is a paucity of research on this and similar

devices[14,15]. More research is called for.

Low Dose Immunotherapy (LDI) and Low Dose Allergen Immunotherapy (LDA)

Low Dose Allergen Immunotherapy (LDA) developed by William Schrader M.D., and Low Dose Immunotherapy (LDI), developed by Ty Vincent M.D., are treatments whereby large groups of antigens are delivered to a patient sublingually or subcutaneously in an effort to build immune tolerance to said group of antigens[14,15]. Very low concentrations of these antigens will stimulate the production of T regulator cells which are responsible for suppressing "allergic" reactions which can often progress to pathologic autoimmunity[15]. LDA has largely been used to treat food sensitivities, however, Dr. Vincent has expanded on Dr. Schraders work to include mixtures for chemicals, environmental irritants/pollens as well as pathogens such as Borrelia, Varicella and Streptococcus thought to play a pivotal role in the development of autoimmunity[17]. It has been proven especially useful in our practice for food sensitivities as well as herpes viruses such as Varicella. Our practice has modified Dr. Vincent and Dr. Schrader's original methods by tailoring the base concentrations of the immune mixtures to the individual patient using ART testing resulting in the use of higher C dilutions. As an example, where upon initial treatment of a patient might include using the original base concentration of a mixture, for example 4C, we generally find patients to test positively on ART with more dilute concentrations such as 10C to 15C. We have experienced excellent results using these modifications and rarely observe exacerbations of patient symptoms which become a much stronger possibility using initial treatment with the more concentrated base mixtures.

Laser energetic detox (LED)

Laser Energetic Detox (LED) is a detoxification technique wherein a biophoton is illuminated over a patient's body such that all major acupuncture control points are stimulated. The light is passed through a vial containing a homeopathic form of a toxin as it is swept over the entire body. Given that all cells are in communication with each other energetically, the cells respond by dumping that toxin into the interstitium and the circulatory system where it is eventually eliminated through either micturition or defecation. The body will eliminate that toxin in over the next 24.5 hours. LED was developed in Germany and brought to the US by Dietrich Klinghardt, however there remains very little formal research on this technique[16].

History of present of illness

We present the case of a 22-year-old G0P0 female dental hygienist who sought treatment at our multi-disciplinary, integrative medicine clinic in New Jersey for a case of primary amenorrhea. The patient initially presented to our practice in June of 2016 with complaints of amenorrhea without the use of oral contraceptives or some other form of hormonal intervention. She was concerned that given her lack of menses without the use of hormones that she would be unable to have children in the future. Her LMP was in March of 2016 after which she had stopped her oral contraceptives. She denied history of obesity, hirsutism or acne nor was she taking any medications. The patient also complained of a "red flaky and very itchy" rash of the hands bilaterally. She noted that the rash would get worse after wearing medical gloves for work although the rash had been present prior to exposure to gloves. In fact, the rash had been present for several years and she had undergone a consultation with a dermatologist. A skin biopsy was performed on the dorsum of her hand which was unrevealing and she was treated with a topical steroid. The itching often would wake her from sleep. Also present on review of systems was a history of significant fatigue since high school which was sometimes bad enough to cause her to miss out on social events with family or friends. The patient noted that she would generally need to take a nap during the day. She also reported some mild anxiety and occasional trouble falling asleep which would occur approximately twice a week.

The patient initially presented to her gynecologist for amenorrhea in 2009 at the age of 16 whereupon she was found to have a normal exam including Tanner staging, breast development, weight and pelvic/physical exam. A work-up was completed prior to hormonal therapy which included a normal pelvic ultrasound and blood work, all within normal ranges were: thyroid panel, lipids, fasting glucose and FSH/LH levels. She denied undergoing any form of glucose tolerance testing. The patient denied any history of eating disorder or malnourishment at that time or at any time. She was not participating in any significant athletic behavior. Following an oral progesterone challenge, the patient had withdrawal bleed, however, she continued to experience amenorrhea unless bleeding was induced via oral contraceptives or other form of hormonal therapy. At that time, she was diagnosed with polycystic ovarian syndrome despite normal hormone levels and no signs of androgenization. The patient sought the care of three different gynecologists over the next several years all of whom prescribed either oral contraceptives or medroxyprogesterone. The patient experienced several side effects from the oral contraceptives over the years including acne, weight gain, depression and generally "not feeling myself". As of March 2016 she discontinued all forms of hormonal therapy due to these intolerable side effects. For the last several years the patient has been seeing a chiropractor regularly.
Past medical history: Concussion at age 9.
Past surgical history: All 4 wisdom teeth removed.
Social history: Denies any history of drug use and rarely uses alcohol. The patient is a non-smoker. She is not sexually active.

Medications: None.
Drug allergies: None
Family history: Unremarkable other than her father has a history of slight hypothyroidism.
Physical exam: The patient's physical exam was essentially normal consistent with her previous physician evaluations including normal secondary sexual characteristics. ART testing revealed the following abnormalities: positivity for nickel, mercury, aluminum and hydroxy-aluminum. Interference fields were discovered over the ovaries, the left ear piercing and bilateral knee scars. Herpes type I was also positive on ART testing.

Visit #1 – Initial visit

Neural therapy was performed on the knee scars as well as the left ear piercing. The patient was started on Blue Ice fish oil to treat her herpes type I; and chlorella (Chlorella pyrenoidosa, Biopure, Bellevue, Washington) 15 tablets three times a day to treat mercury sensitivity. She was also started on a concentrated form of cilantro (Herbpharm) for mercury; 2 full droppers 3 times per day in warm water or tea. ART indicated that these remedies would be beneficial. Acupuncture was recommended at this visit, however the patient reported a needle phobia and therefore acupuncture treatment was deferred to the next visit.

Visit #2 – 25 days following visit #1

The patient had not yet started the supplements due to concern over side effects interfering with an upcoming vacation. Her eczema over the hands was unchanged and she still had not menstruated. ART testing again was positive for nickel, aluminum and mercury. The patient underwent a laser energetic detox for mercury at that visit and acupuncture which included master skin point of the right ear as well as the following points bilaterally: Kidney 3 (KI3), Spleen 4 (SP4), Pericardium (P6), Stomach 25 (ST25), Stomach 36 (ST36). Although a full Chong Mo/Yang Ming approach was attempted, the patient could only tolerate the listed points due to her needle phobia[17]. The patient was continued on Blue Ice fish oil, chlorella and cilantro.

Visit #3 – One month and 18 days following visit #1/24 days following the previous visit

The patient noted that she had experienced some improvement in her eczema on hand. At this visit, the patient's mother recalled that the patient had two episodes of a rash in the area of the perineum at the age of 8 which at that time was diagnosed as shingles. ART testing was negative for nickel and mercury. Given the history of rash at age 8, testing for varicella virus was performed via ART and was positive over the pelvis. A pelvic sonogram was ordered. (patient's last study was 5 years prior). Acupuncture was performed at the Nogier phase 2 and 3 ovary points in the ears bilaterally. The patient was started on a homeopathic for herpes zoster in light of the ART finding of varicella. Neural therapy was again performed on the patient's ear piercings. Acupuncture point Govering Vessel 20 (GV20) was successfully implemented to ease some of the patient's needle phobia. Acupuncture was then performed on the following bilateral points: ST30, KI3, SP4, P6, Large Intestine 4 (LI4), ST36. Conception Vessel 2 (CV2) and CV3 were also piqured to complete the Chong Mo/Yang Ming treatment. The patient was continued on Blue Ice fish oil, chlorella and cilantro.

Visit #4 – Two months and 12 days following visit #1/24 days following the previous visit

The patient noted continued improvement in her eczema, but amenorrhea persisted. ART testing was positive for varicella zoster and aluminum over the pelvis. The patient's pelvic ultrasound was normal. Acupuncture was performed at the following sites bilaterally: KI3, SP4, P6, LI4, ST30, and ST36. Also the following acupuncture points were used: CV2, CV3. GV20 was again used to curb the patient's anxiety. The patient continued the fish oil, cilantro and chlorella and the Varicella Zoster homeopathic remedy.

Visit #5 – Five months and 15 days following visit #1/three months and 3 days following the previous visit

For the first time in the patient's life she experienced her first normal period spanning 6 days without the need for hormonal intervention and in the subsequent calendar month experienced another normal period spanning 5 days. In addition, she reported significant improvement in her hand eczema. ART testing revealed continued presence of aluminum over the pelvis only and general testing of aluminum was negative. Varicella testing was also negative on ART testing. Acupuncture was performed at the following sites bilaterally: SP4, KI3, ST25, PC6, LI4. CV2 and CV3 were also used and the patient underwent an ionic foot bath for further detoxification at this visit. Cilantro was continued as was chlorella and Blue Ice fish oil.

Visit #6 – Six months and 19 days following visit #1/one month and 4 days following the previous visit

Patient noted some re-occurrence of her hand eczema after eating walnuts the night before her visit but otherwise the eczema was noted as much better since seeking treatment at our office. She had begun a regular menses on the day before this visit and missed a period the previous month after two consecutive months with normal menstrual periods. ART testing revealed aluminum only over the pelvis. She was continued on cilantro and was prescribed an ionic foot bath every other week. A Chong Mo/Yang Ming treatment was used with the following points: SP4, KI3, PC6, LI4, ST36, SP13 bilaterally. GV20 was no longer necessary as the patient had grown accustomed to acupuncture. The

patient continued the fish oil, cilantro and chlorella.

Visit #7 – Seven months and 16 days following visit #1/28 days following the previous visit

The patient did not have a period in February yet. ART revealed continued aluminum over the pelvis despite the ionic foot baths every other week and continued cilantro. ART revealed interference from the 2 right sided ear lobe piercings. Neural therapy was performed on those scars. The frequency of ionic foot baths was increased to once a week and the following acupuncture was performed: SP4, KI3, PC6, LI4, ST36, SP13 bilaterally; and CV2, CV3. A positive predictive response to cilantro, EDTA and vitamin K was elicited on ART. The patient continued the fish oil, cilantro and chlorella.

Visit #8 – Nine months following visit #1/42 days following the previous visit

The patient experienced normal periods in February and March. ART revealed continued interference from the right sided ear lobe piercings and these were treated with neural therapy. Aluminum was negative throughout including directly over the pelvis at this visit. Acupuncture was again performed using bilateral SP4, SP13, KI3, PC6, LI4, ST36; and CV2, CV3; using Chong Mo/Yang Ming. The patient reported that her eczema is improved. The patient continued the fish oil, cilantro and chlorella.

Visit #9 – Eleven months and 22 days following visit #1/two months and 23 days following the previous visit

At this visit, the patient reported she did not have a period in April or May. She reported that she had a cold and possibly might be more stressed lately. ART testing revealed negative aluminum, however her knee scars and right earlobe piercing revealed interference fields. These were treated with neural therapy and acupuncture was done on the following points: SP4, KI3, PC6, SP13, LI4, ST36 bilaterally CV2, CV3. Nogier ovary points in phase 1 were piqured on the ears bilaterally. The patient was re-started on cilantro as she had run out since last visit. The patient continued the fish oil, and chlorella.

Visit #10 – Fifteen months and 3 days following visit #1/three months and 11 days following the previous visit

The patient reported significant stress over the summer due to the sudden death of her grandfather. This may have contributed to a lack of menses in August and September. The patient did have a menstrual period in July. ART testing revealed a recurrence of varicella zoster as well as interferences from the knee scars and right ear lobe piercings. These scars were once again treated with neural therapy while the varicella was treated with low dose immunotherapy (LDI). ART food testing was performed at t his visit revealing a gluten sensitivity, therefore low dose antigen(LDA) treatment was also used. The patient was placed on a gluten-free diet. Further ART testing tested positive for depleted uranium (definition for this toxin can be found at https://en.wikipedia.org/wiki/Depleted_uranium). Chong Mo/Yang Ming was again performed for acupuncture with the following: bilateral SP4, KI3, PC6, SP13, ST25, ST36; and CV2, CV3. An ionic footbath was also performed and laser energetic detox was scheduled for depleted uranium. Mercury was detected over the right ovary via ART and therefore chlorella was continued.

Follow-up between February 2018 and April 2019

The patient has a period approximately every month although she might occasionally miss a cycle especially if she experiences significant emotional stress. We continue to perform acupuncture every 3-4 months and treat her food sensitivity with LDA and varicella with LDI when ART is positive for varicella. She tries to avoid gluten.

Discussion

We present a case of a 22-year-old G0P0 female with a history of primary amenorrhea initially presenting for evaluation at the age of 16 with normal physical exam, normal weight, normal laboratory values and an absence of androgenization. Based on the etiologic categorization of primary amenorrhea as was initially defined in the introduction, our patient would fall into category 1 normogonadotropic hypogonadism (i.e. normal Estradiol, FSH and LH levels), however she had normal anatomy, normal pelvic sonogram and no evidence of imperforate hymen on exam. She was diagnosed with PCOS presumably as a diagnosis of exclusion. The fact that she was able to undergo a withdrawal bleed following a progesterone challenge indicated adequate estrogenization of the endometrium. The patient underwent several years of standard medical treatment which mainly included the use of oral contraceptives.

The patient presented to our integrative medicine practice at the age of 22 in an attempt to determine the primary underlying etiology of her amenorrhea and achieve menses without pharmaceutical intervention. She underwent evaluation via autonomic response testing (ART) which detected mercury, aluminum, aluminum hydroxide, depleted uranium, several scars acting as interference fields, herpes simplex I, varicella virus, and gluten sensitivity. Using a multi-factorial regimen which included: neural therapy, body acupuncture, ear acupuncture, supplements, homeopathy, gluten avoidance, LDA, LDI, and laser energetic detox (LED), we were able to achieve menarche without the need of hormonal intervention after 2 months (it would have to be more than 2 months as visit 4 occurred at 2 months and 12 days after the first visit. No menses were

Table 1: Treatment Timeline

Visit Number	Findings on ART	Treatment given during visit	Treatment prescribed	Noted improvement
1: Initial Visit	• Nickel • Mercury • Aluminum • Hydroxy-aluminum • Herpes Type I • Knee scar and ear piercing • Ovaries bilaterally	•Neural therapy performed on knee scars and ear piercings.	• Blue Ice fish oil • Chlorella • Cilantro	Not Applicable
Visit 2: 25 days following visit #1	• Nickel • Mercury • Aluminum	•Laser Energetic detox for Mercury •Body Acupuncture •Auricular acupuncture	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro	•No changes in skin or menses
Visit 3: One month and 18 days following visit #1/24 days following previous visit	•Varicella Zoster •Virus detected over pelvis •Negative Mercury testing •Negative Nickel testing	•Auricular acupuncture •Neural therapy to ear piercings •Body Acupuncture	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro •Varicella Zoster homeopathic remedy •Pelvic Sonogram advised	Modest improvement in hand eczema but persistent amenorrhea.
Visit 4:Two months and 12 days following visit #1/24 days following previous visit	•Varicella Zoster virus detected over pelvis •Aluminum over the pelvis only	•Acupuncture	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro •Varicella Zoster homeopathic remedy	Continued improvement in hand eczema but persistent amenorrhea
Visit 5:Five months and 15 days following visit #1/Three months and 3 days following previous visit	•Aluminum over the pelvis •Varicella negative	•Acupuncture •Ionic footbath·	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro	Patient experienced two normal menstrual periods without the help of hormonal intervention for the first time in her life.

Visit 6: Six months and 19 days following visit #1/One month and 4 days following previous visit	•Continued aluminum over the pelvis	•Acupuncture Ionic footbath	•Ionic footbath every alternate week. •Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro	Eczema much improved overall. No menses in previous month but occuring on time for current month.
Visit 7: Seven months and 16 days following visit #1/28 days following previous visit	•Aluminum over the pelvis •Ear piercings •Positive predictive response to cilantro, vitamin K and EDTA on ART	•Neural therapy performed on ear piercings •Acupuncture	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro •The frequency of Ionic foot bath increased to every week	No menses during this month yet.
Visit 8: Nine months following visit #1/Forty-two days following previous visit	•Aluminum over the pelvis now negative •Ear piercings positive on ART	•Neural therapy performed on ear piercings. •Body acupuncture	•Continue Blue Ice fish oil •Continue Chlorella •Continue Cilantro	Regular cycles since last visit. Eczema is improved.
Visit 9: Eleven months and 22 days following visit #1/Two months and 23 days following previous visit	•Knee scar and ear piercing	•Neural therapy performed on ear piercing and knee scars. •Body acupuncture Auricular acupuncture	•Re-start cilantro •Continue Blue Ice fish oil •Continue Chlorella	No menses since last visit (i.e. has missed 3 cycles). She thinks she has a cold and is experiencing more stress and has run out of cilantro
Visit 10: Fifteen months and 3 days following visit #1/Three months and 11 days following previous visit	•Knee scar and ear piercings •Herpes Zoster •Gluten •Depleted Uranium •Mercury over the right ovary	•Neural therapy performed on ear piercing and knee scars. •Body acupuncture •Auricular acupuncture •LDI •LDA •Ionic footbath	•Continue chlorella •Schedule laser energetic detox for depleted uranium •Gluten free diet was initiated.	Patient had one menstrual period since last visit which occurred 3 months ago. Patient notes significant stress secondary to grandfather's sudden death. Eczema is controlled.
Follow-up visits between February 2018 and April 2019		•Body acupuncture •LDI •LDA	•Avoid gluten	Menses have been essentially monthly but she may miss an occasional cycle if she is under stress.

Abbreviations: ART- autonomic response testing; EDTA – Ethylenediaminetetraacetic acid, LDI – Low Dose Immunotherapy, LDA – Low Dose Antigen Therapy

reported at visit 4 of treatment. This would indicate that the etiology of the patient's amenorrhea would most likely be related to a combination of factors. Future research is needed to determine the contribution of the individual factors and their possible interactions.

Although there is a paucity of literature revealing an association between heavy metals and ovulatory disruption in humans, it is well established in animal models that lead, mercury, cadmium, and polyaromatic hydrocarbons are responsible for interference of follicular growth including decrease in ovarian weight, follicle numbers and increase in follicle atresia[18,19]. One study in humans concluded that hair follicle content of Hg is inversely associated with lower oocyte yields and follicle number in IVF patients[20,21] while a similar study revealed that women with Hg concentrations above the EPA reference level of 1 ppm also had lower oocyte yields[21]. It is important to note that this patient works as a dental hygienist/assistant and although her office is mercury-free she is still put at higher risk of exposure due to the aerosolization of previously existing amalgam fillings in the dental patients she works on.

An argument could be made that given this patient's normal gonadotropin levels and normal anatomy, disruption would have had to occur at the level of the hypothalamic-pituitary axis. Like ovulatory disruption, there is a scarcity in the literature regarding this issue. One study using NHANES data reported an inverse association between Hg in the blood and LH levels in women (LH was inversely correlated with Hg detection, P value of 0.056)[22] while drinking water containing sodium arsenite exposure in rats revealed lowered levels of LH and FSH[23].

Although there were no studies linking herpes and amenorrhea in our literature review, there has been precedence for the use of homeopathy in the treatment of amenorrhea[24]. In addition, our patient was found to have gluten sensitivity on ART. Gluten sensitivity would generally not be considered as severe a condition as fulminant Celiac Disease, however, there is strong precedent in the literature for regulation of irregular menses and improvement of fertility through a gluten free diet in cases of Celiac[25,26]. One case report in particular highlights a patient with primary amenorrhea in which the ultimate cause was, in fact, Celiac disease[27].

Clearly this is a complex case with a multifactorial etiology. It is not clear, therefore, which intervention was the primary factor in restoring the patient's menstrual cycles. Furthermore, retrospective case reports remain at the bottom of the research hierarchy. However, this case is typical of the chronic patients we treat at our integrative medical practice and it highlights our belief that addressing all factors in the presentation of a chronic disease is necessary in order to achieve resolution of pathology.

Conclusion

A multifactorial integrated systems approach incorporating ART assessment resulted in a successful outcome. Further research is needed to determine the contribution and synergy of the multiple factors addressed.

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Tracy L. Brobyn, MD, FAAFP, DABMA
(Corresponding Author)
The Chung Institute of Integrative Medicine
Assistant Clinical Professor, Rowan School of Osteopathic Medicine,
Department of Family Medicine, Won Sook Chung Foundation,
110 Marter Ave. Moorestown, NJ 08057 856-222-4766
Email: tbrobyn@gmail.com
Patrick J. LaRiccia, MD, MSCE
Penn-Presbyterian Medical Center Won Sook Chung Foundation
Adjunct Scholar Center for Clinical Epidemiology and Biostatistics,
Perelman School of Medicine, University of Pennsylvania,
51 N. 39th St, Philadelphia, PA 19104 215-662-8988
Email: lariccip@mail.med.upenn.edu