Case Study: Pituitary Adenoma with Hyperprolactinemia

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Abstract

This article documents one case of a prolactin-secreting pituitary macroadenoma successfully treated using acupuncture, herbal medicine, and nutrition. The treatment was constructed using both traditional Chinese and biomedical models and their diagnostic tools and included traditional indications and scientific findings. MRI was used for initial diagnosis and to confirm resolution of the tumor. Regular prolactin levels were used as a monitoring tool during the treatment. The author discusses stress, dopamine, and kidney yang and how this influenced the treatment.

Key Words: prolactin, prolactinoma, pituitary adenoma. Chinese medicine, herbal medicine, acupuncture, dopamine

Preface

In November, 2001, a patient diagnosed with a benign prolactin-secreting pituitary macroadenoma1 sought care. A prolactin-secreting adenoma has several unusual properties which make it both easier to monitor and potentially more receptive to treatment than other types of benign tumors. There is infrequent clinical opportunity to treat a serious but potentially manageable condition such as this with Chinese medicine, so after careful consideration the care was initiated.

The first concern was safety to ensure that the patient would not be at medical risk because of delay in commencing the recommended allopathic medical treatment. Medical consequence of this condition is that excess prolactin causes amenorrhea and anovulation, which in turn leads to infertility. In addition, there is possible risk of endometrial hyperplasia due to unopposed estrogen stimulation (no progesterone due to anovulation), which, if undetected, may develop into endometrial cancer. Lastly, if the pituitary macroadenoma grows, and if it grows outside the sella, it can impinge on the optic nerve causing headaches and visual defects which may or may not be reversible.

Standard Biomedical Treatment

Dopaminergic medications to reduce PRL secretion represent the standard first line of treatment and may act to shrink the tumor. Anti-prolactin medications have a number of common side effects such as constipation, dry mouth, insomnia, nasal congestion, mood swings, and vertigo. The ability to tolerate these medications varies greatly. Less common but more serious side effects include auditory hallucinations, leukopenia, thrombocytopenia, hepatitis, and cardiac arrhythmias. This pharmaceutical course of treatment was initially proposed to the patient.

Should the dopamine agonist medication be ineffective, or the side effects too difficult to tolerate, surgical debulking is indicated. Surgery is risky, due to the tumor's location near the optic chiasm. Since recurrence rates are high at >50%, this is not generally the treatment of choice.

Benign prolactinomas do not have the same concerns that arise with malignant tumors, which can grow rapidly and metastasize. Rather, the issues are whether the prolactin levels will decline and the tumor itself will shrink. This is monitored by either utilizing an MRI or by frequent monitoring of prolactin levels through a simple and inexpensive blood test.

The physiology of prolactin secretion is unique as it is the only hormone which must be continuously inhibited and restrained throughout life except during relatively brief and infrequent lactation periods. Prolactin is inhibited by dopamine. Along with epinephrine and norepinephrine it works as an “amplifier” of the sympathetic nervous system thereby acting on mood and motivation. Monitoring prolactin levels indicates whether treatment is proceeding in the right direction. Ongoing anti-prolactin (PRL) treatment is usually required for maintenance even if the tumor shrinks. Bromocriptine, the most commonly used dopamine agonist, has been shown to reduce prolactin in 70% of patients, but the rate of tumor shrinkage is less impressive. Success rate statistics are as follows: Of patients with macroadenomas who take dopamine agonist medications, 70% achieve normal prolactin levels with this treatment and 40% of patients will achieve tumor shrinkage of ≥ 50%.

Given the above statistics, the frequency and amount of tumor shrinkage is less than optimal, even with good prolactin control. In most cases a relationship exists between prolactin secretion and tumor growth. Therefore, unlike many other types of tumors, there is a dynamic interaction between a normal, albeit altered, physiologic mechanism and the tumor. In terms of treatment strategy, this interaction was a “way in” to developing a treatment plan. Information was located pertaining to specific herbs/formulas known or suspected to inhibit prolactin.

Oriental Medicine Treatment

Rationale and Strategy

The treatment rationale began with a summary of what is known about the unique physiology of prolactin secretion and the nature and actions of dopamine. This was an important guiding principle in the treatment plan. According to Chinese medicine, the properties of dopamine identify it as an extremely yang substance. Its action is moving, warming, and motivating. It holds back and inhibits the forces of yin and blood in the transformation to breast milk. As with any yang substance, it can become overtaxed and “used up” by excessive stress and exhaustion, and the patient can present with yang deficiency signs of cold, fatigue, and dampness.

When under prolonged stress, dopamine is in high demand. Modern genetics may eventually identify differences in how individuals respond to stress or show why one person becomes depressed or develops high blood pressure and still another presents a PRL-secreting adenoma. Chinese medicine-based constitutional analysis can be utilized to understand susceptibilities to illness. In this case, the patient is clearly a fire build as she is tall, slender, has long, tapered fingers, and facial features of the fire type. The fire constitution can easily “burn out” the water element, represented here by “adrenal burn out” or kidney yang depletion.

Further analysis determined that if excess prolactin was a result of insufficient dopamine, or of insufficient action of dopamine on the pituitary, this represents a lack of yang in Chinese medicine. When yang is low, dampness accumulates and yin is un restrained. Thus the excess prolactin secretion represented unrestrained yin, resulting in galactorrhea and damp accumulation.

The root problem was yang deficiency manifesting as low dopamine. The branch problem of dampness presented as excess PRL and galactorrhea. While both needed to be addressed, for the root to flourish the branch needed restraint.
Another theoretical model used was the physiological understanding of depression. The possibility that serotonin-enhancing medications for the treatment of depression can deplete a person’s neurotransmitters which in turn creates additional emotional illness has become an accepted concept. In some cases this does happen, and the concept—if not the tool—is part of the treatment strategy in this case. The patient had been under long-term, unrelenting stress before her diagnosis and presented in an extremely high anxiety state. Perhaps under these conditions she depleted her dopamine reserves and developed a PRL-secreting tumor as a result.

Framing the Treatment

Long term treatment has specific challenges that must be directly identified to clearly frame the treatment. Both patient and practitioner must attend to these challenges so that treatment can be sustained long enough to give a fair chance for success. In this case, the patient had to contend with four main problems: 1) symptom discomfort, 2) psychological doubt, 3) fear of the illness and 4) compliance with diet and lifestyle changes, regular acupuncture, and consistent ingestion of herbs and nutritional supplements.

These four issues were addressed in the following manner:

1) Symptom discomfort was treated by addressing the “branch” with herbs and acupuncture. Remaining discomfort was addressed with reassurance and occasional use of medications but, to some extent, was endured by the patient.

2) Doubt and fear were best answered by conducting treatment with the consent of her medical team to “watch and wait.” Following the PRL levels regularly allowed for doubt to be easily managed by the objective change in the patient’s blood tests.

3) Compliance with diet, lifestyle, acupuncture, herbs, and nutritional supplementation was essential and the patient understood this from the outset. The patient was highly compliant.

In this case, if things did not go well, excellent monitoring options as well as biomedical treatment were available. Utilization of these methods alongside those of Chinese medicine allowed for a conceptual understanding that enabled treatment to proceed.

Case History Detail

November 2001: A 30-year-old woman presents with galactorrhea, itching on the breasts, and hyperprolactinemia. Blood work confirmed FSH, LH and thyroid within normal ranges, but prolactin is very high at 70mcg/L (30 is high end of normal).

Prior medical history: In 1993 a ruptured ovarian cyst was treated with surgery. Subsequent ileus due to surgical adhesions resulted in a second surgery to remove adhesions. In January, 2001, after a stressful period in her life, breast itching started, followed by a full body rash. This was resolved after one week.

Previous menstrual history: Menarche age 15. From 15 – 24 years, patient had significant dysmenorrhea with clots, bleeding and irregular, long cycles. She had occasional midcycle pain with PMS and breast tenderness for 2 to 3 days per month. At age 24 she began treatment with herbs and acupuncture, and she improved. Her periods became unremarkable until May, 2001, when she experienced her first alteration in menstruation with a scanty cycle, after which she had no period for the next several months.

Other: She experienced difficulty both falling asleep and waking too early. She had a history of chronic constipation alternating with loose stool. Her appetite was often poor, but diet was moderate to good. She had chronic low level vaginal yeast infections which were not helped by natural methods. Treatment with Diflucan temporarily helped. The patient experienced intermittent pain from abdominal adhesions and scarring.

Medical findings: In December, 2001, she had an MRI, which was positive for a pituitary macroadenoma (1 cm x 1.2 cm). The MRI was interpreted as a prolactin-secreting adenoma—the cause of her high prolactin and amenorrhea. The tumor was “abutting the optic chiasm without any definite compression.”

Medical concerns: This patient’s tumor was already abutting the optic chiasm. Second, excess prolactin (PRL) inhibits the reproductive cycle at every level—hypothalamic, pituitary, and ovarian. This means that ovulation and periods cease to occur, resulting in infertility and other effects of lowered estrogen levels (i.e., bone loss, decreased libido, and hirsuitism). Galactorrhea is usually seen as well. There is a risk for endometrial hyperplasia due to unopposed (even if reduced) estrogen stimulation.

Medical treatment: A dopamine agonist was prescribed as a potentially long term, open-ended therapy to control PRL levels and limit tumor size. Side effects of these medications include nausea, vomiting, and postural hypotension in about 25% of people. Other common side effects include constipation, nasalsuffiness, dry mouth, vertigo, insomnia and nightmares. These may be ameliorated at lower doses. More serious side effects of auditory hallucinations, delusions, cardiac and hematological problems occur rarely. In this case, Cabergoline, a newer dopamine agonist more likely to work in the case of a macroadenoma, was prescribed. Surgery may be recommended if PRL levels do not come down sufficiently or if the patient cannot tolerate the medication.

OM Treatment Summary with Results

The patient presented with chronic constipation, nasal congestion, and headaches, as well as high anxiety levels which disrupted her mood and sleep. She consulted a neurologist and an endocrinologist, both of whom agreed that several months of watchful waiting would be safe so long as her PRL levels were closely monitored. Therefore, treatment commenced as noted above.

November 20, 2001: Symptoms included breast itching and discharge, constipation, headaches and sense of “spaciness,” amenorrhea and anovulation, galactorrhea, anxiety, insomnia, frequent rash, frequent yeast infections, frequent right lower quadrant pain at site of surgical adhesions, and scarring. PRL: 78.2 mcg/L (Reference Range: 10-29 mcg/L).

Pulse: 72 BPM

General quality: weak and tight.

Notable qualities: L side more forceful than R

Chi: especially weak and tight on L, slippery on R.

Guan: R=tight, L=weak

Tongue: Pale-purple, scalloped and swollen

Upper jiao area reddish and peeled

Lower jiao area medium greasy yellow tongue coat

Eyes: Kidney area dark and slightly puffy

Expression: fearful and anxious, but ok.

Acupuncture: Points are selected to calm the nervous system, bring energy into the reproductive system, and stimulate ovulation. Treatment is weekly, except for a few missed appointments.

Internal treatment: Vitex agnus-castus (standardized extract) 1 BID,

B vitamin complex with antioxidants, extra B6 – 100mg, magnesium – 600-800 mg (to tolerance), progesterone cream: days 14-28.

Chinese herbal medicine taken as a liquid decoction: Shu di, shan yao, shu di, shan yao, huang jing, bu gu zhi, yin yang huo, chao zhi zi, mu
dan pi, qing pi, hu ji tian, xian mao, gan cao, da zao, rou gui and Sheng mai ya.11

Patient is asked to begin a basal body temperature (BBT) chart to monitor fluctuation in hormone levels and whether there is any “attempt” at a luteal surge.

Analysis: Chinese medicine formula to tonify the kidney yin and yang, and clear heat. Sheng mai ya (Hordeum vulgare) in high doses to inhibit lactation.12 Vitex agnus castus inhibits prolactin, promotes ovulation. B vitamins & magnesium together to nourish and calm nervous system, support clearance of excess hormones, and support adrenal function. Magnesium to reduce constipation, calm and help sleep, replenish this mineral after loss during period of high stress.

Progesterone cream used during time of anovulation to provide progesterone, encourage ovulation, and as a ying hormone to check excessive yin of prolactin and unopposed estrogen. It is used during presumptive luteal phase only to preserve cycle parameters, even without menstruation.

In mid December, 2001, after no period for several months, Provera was given to induce a light period. On December 26, 2001, the Chinese herbal formula was increased as well as Vitex. The Sheng mai ya was made as a freeze dried powder for ease of administration.13 Her next period came on day 26 (01/02/02).

The temperature chart showed a rise on 1/08/02, accompanied by breast tenderness and irritability for one week. Then the temperature dropped and, beginning on 1/18/02, she had a light to moderate period with cramps, headaches, and clotting. Ovulation occurred with a shortened luteal phase of 10-11 days. Frequent frontal headaches made worse with reading occurred as well as difficulty concentrating.

02/14/02: Endocrinologist suggests her tumor may not be a prolactinoma and refers her to a surgeon. The surgeon also agreed to watchful waiting, so OM treatment continues.

02/26/02: Menses come on day 26, (2/15/08) after a drop in temperature, with right lower quadrant pain and some premenstrual acne. Bleeding lasted 6 days. PRL level dropped from 78.2 to 62 mcg/L. Other blood abnormalities noted: thyroid peroxidase slightly high @ 2.8 (reference range 0.0 – 2.0). Other symptoms included very severe breast itching during period and around mid-cycle. Headaches and fogginess are not as severe, but frequent.

Analysis: This is a second cycle with ovulation, luteal phase, and period. The period is significantly heavier, showing more estrogen and blood production. Prolactin levels are being affected by the treatment, so we are on the right track.

Changes and Analysis in Treatment Strategy

The Chinese herbal formula was revised to shu di, shan yao, huang jing, bu gu zhi, yin yang huo, chuan bei mu, e zhu, san leng, bai jie zi, chao zhi zi, zhi gan cao, da zao, shi chang pu, rou gui, lu rong.15

Explanation: After two doctors’ analysis that this was not a simple prolactinoma, we changed the formula strategy. Rather than rely only on reducing PRL (dampness) to shrink the tumor, we included blood cracking herbs to treat the tumor itself (blood stasis). Shi chang pu16 was also added for the headaches and fogginess and to penetrate through the dampness. Lu rong and rou gui17 were added to warm kidney yang (and thereby dispel damp-cold). Zhi zi18 was added to treat itching.
3/06/02: Neurologist provides second opinion and recommends 2-6 months of dopamine agonist medication. Due to the size and type of tumor, he thought there was a 15% chance the tumor would shrink and that she was a good candidate for surgery based on the size and position of the tumor. She declined surgery at this time.

3/06/02: Menses came on day 31 (March 16). Overall she felt well with no PMS symptoms, but the bleeding was scanty and of some concern.

Treatment change: Increase mai ya to 1 tsp to further inhibit prolactin. Increase Vitex dosage to 2 BID to further promote ovulation, progesterone and inhibit PRL.

4/01/02: Day 16 with some headaches and foginess. Breast itching began around day 11 or 12 with some clear discharge.

4/16/02: Reports headaches and foginess, depression and upset. Noted that she was at the end of both her cycle and her school semester. No changes made until after next menses.

5/15/02: Symptoms recurred post vacation with fatigue, depression, heavy-headed with low energy and constipation.

CM treatment change: Formula now includes nü zhen zi. Some of the warming herbs were removed and put into a second formula to take 3 grams BID only: shi chang pu, wu wei zi, ren shen, bai jie zi, rou gui, chuan jiao, lai fu zi.

Analysis: I felt the formula was trying to do too many things, and each strategy was getting short shrift. By reducing ingredients in the main formula, its action to support kidney and treat blood stasis was strengthened. The warm, penetrating herbs were added separately thus allowing for better adjustment of dosages for each strategy as needed.

6/02/02: Very light and scanty menses on 5/15/02. Symptoms returned after two weeks.

CM treatment change:
Shao yao gan cao tang (20gm), yin yang huo, xian mao, shu di huang, chai hu, dang gui, chuan xiong, xu jin, gui zhi, hai zhi, xi xin, qiang huo, jiang feng.

Treatment change: New references were found showing that shao yao gan cao tang could be used to lower prolactin. The cycle had become much more regular but with scanty bleeding; goal is to increase the blood nourishing aspect of treatment. Sinus pain and congestion were more pronounced, and included in treatment as wind-damp invasion due to the blood deficiency (admitting wind) and yang deficiency (admitting cold/damp).

6/18/02: Menses on day 20 with a moderate, better flow. Her spirits and symptoms fluctuate.

7/18/02: Menses came on day 39 with pain and some clots but with a good flow. For the first time, there was no premenstrual breast itching.

8/15/02: Prolactin is down to 43 mcg/L. The high end of normal is 30mcg – she feels better! She has a 28 day cycle with a very good BBT chart. She has a normal, moderate flow and almost no breast itching except when herbs were missed. She did have a two day migraine. Mental clarity is poor as she feels “cobwebs in the head.” Constipation persists.

8/26/02: MRI ordered to track the tumor growth.

8/27/02: The patient called from the doctor’s office. The interpretation was as follows: no mass is present. The tumor is gone. Much rejoicing.

9/11/02: She contracted chicken pox, was treated with Valtrex, and took herbs to stop the itching.

9/24/02: She is mostly recovered. Today is day 16 with temperature rising to 98.1, sticky cervical discharge, no breast itching. Headaches are worse in damp weather.

10/10/02: Her period came on day 28 with excellent biphasic chart. She felt well during the luteal phase with only one day of PMS. Flow was better and the blood color was good with minor clots. She had slight breast itching during the period. A headache occurred during the first day of PMS and lasted through the period. In general, she reports less anxiety and some return of libido.

For the next several months, cycles are regular between 28 and 32 days. PMS is minor, occasional breast itching, headaches are less frequent, and there is recurrent constipation.

4/21/03: Prolactin level is normal at 28.9! OM treatment was scaled back. Sheng mai ya and Shaoyang Gancao Tang removed, and Vitex reduced to a maintenance dose of one per day. Her prolactin levels were checked periodically and continued to decline. In April, 2006, she became pregnant, and after an uneventful pregnancy, she gave birth to a healthy baby girl in December, 2006.

1. A macroadenoma measures > 1 cm.
2. Harrison’s p 2087
3. Harrison’s p 2087
5. It was not possible to know for certain whether the levels were low or simply the action on the pituitary insufficient.
7. Harrison’s p 2087
8. Harrison’s p 2087
9. Vitanica Vitex extract plus Chaste Tree Berry. 1 capsule contains 215 mg contains Vitex agnus castus extract 0.6% aucubin
10. 25 mg vitex agnus castus
11. Emerita Progest cream: 1/4 tsp BID = 15 -20 mg of USP progesterone BID
15. 5 gns BID of 5.1 granules. This is approximately equivalent to 50gm of the raw herb per day. The amount used in reports on lowering PRL was higher, 100-200gm per day; but this was just not realistic for her in a granulated form. In addition, we were relying on the synergistic effect of the other parts of treatment to support the PRL-reducing effects.
17. Cervus, cinnamomum bark.
18. Gardenia.
19. Ligustrum.
20. Acorus, schizandra, panax ginseng, brassica, cinnamomum bark, zanthoxylum, raphanus seed.
21. Peony & Licorice combination (20gm), epimedium, curculigo, prepared rehmannia, bupleurum, angelfica root, cinnidium, curcuma, cinnamomum twig, atracyloides, asarum, notopterygium, siler.