



## The Power of One Publication

McTighe T<sup>1</sup>

### Acknowledgements:

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### Abstract

A simple definition of Peer Review: A process by which a scholarly work (such as a paper or a research proposal) is checked by a group of experts in the same field to make sure it meets the necessary standards before it is published or accepted. [1] There has been considerable debate over the years as to the value of publications. This commentary is going to highlight my experience with publications and how the power of one scientific report of two cases has significantly impacted my life and the life of my family.

My career of forty-five years in the orthopaedic field with over one hundred and eight publications, 69 citations, sixteen medical device patents, membership in nine professional medical societies prepared me for one significant effort in my personal life “the discipline and experience” to spend nearly two years researching a treatment modality for lymphocytic hypophysitis.

**Conclusion:** This experience demonstrates how the power of one specific paper can influence and play a positive effective role in the direction, treatment and outcome in a rare and uncommon medical condition.

**Keywords:** peer review, publication, research, lymphocytic hypophysitis

### Introduction

Publications have a variety of value from setting you apart from hundreds, perhaps thousands of individuals in any given field, taking your curriculum vitae to a higher level and adding credibility to your career. Certainly publishing has enhanced my professional career in orthopaedics, in addition to the pleasure of collaborating with some of the worlds most acclaimed orthopaedic surgeons and scientist in the past forty-five years. All this has contributed to one of the most significant actions in my life, the ability and discipline to search for a reasonable treatment for my wife’s health care condition “lymphocytic hypophysitis”. This is a follow up to a commentary published last March “*Commentary on Grateful For Medical Advancements*”. [2]

### Background

My wife Catherine has been a significant part of my professional life and has many great friends worldwide as a result of our opportunity to travel and socialize brought about by the many activities generated by orthopaedics.

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Those close to Catherine (a retired nurse) know that she has had a significant struggle over the past two years with a rare cranial suprasellar lesion “lymphocytic hypophysitis”. This was first reported in 1962, and the condition is rare, accounting for 0.38% to 1.1% of sellar lesions excised during transsphenoidal surgery.

In February 2014 she underwent emergency endoscopic endonasal cranial surgery as a result of compression of her optic apparatus. She presented on MRI as a pituitary adenoma, which on final pathology came back as a lymphocytic infiltration without any neoplastic cells, suggestive of lymphocytic hypophysitis. Her neurosurgical team in Miami was Mohamed Samy A. Elhammady, MD, guided by Professor Roberto Heros, MD.

Surgery was very successful, Cathy’s postoperative scan showed excellent decompression of her optic apparatus and decompression of her cyst. Her visual fields completely recovered and we thought she was on her way to full recovery. However within three months the clinical symptoms of blurred vision, and disabling headaches had returned. New MRI demonstrated regrowth of the cyst (sellar and suprasellar mass). Her Miami medical team reviewed all pathology and reconfirmed diagnosis of lymphocytic hypophysitis. This is an unusual inflammatory disorder of the pituitary gland [4] with standard therapy being high-dose steroid medication. Steroid therapy has been effective in some patients however recurrent disease and morbid states have been reported. So now the medical condition was changing from a neurosurgical condition to an endocrinology situation.

Her Miami team started her on high dose prednisone (40 mg per day) and recommended she see additional endocrinology consult upon returning to Cleveland.

So appointments were made at Case Western University Hospital in Cleveland, Ohio and both the head of Neurosurgical Oncology and Bahauddin Arafah, MD saw her:

- Division Chief, Clinical and Molecular Endocrinology, UH Case Medical Center
- Program Director, Endocrinology, UH Case Medical Center
- Professor, Medicine, CWRU School of Medicine

I mention the name of her consult with the Division Chief of Endocrinology because his behavior and attitude stand out way beyond the experience Cathy and I have encountered over her treatment period or for that matter over both of our careers in medicine.

Dr. Arafah disagreed with the diagnosis from Miami of lymphocytic hypophysitis and believes she has a Rathke’s cleft cyst and prednisone treatment will not be effective. He was very insistent that only additional surgery, removing all traces of the cyst would effectively cure this prob-

lem. His only review of her medical condition was review of her MRI scans. We asked him to talk to her Miami team since they felt it was not a Rathke’s cleft cyst. He said he did not need to since he could tell by her MRI scan and he was the expert in this area.

His attitude in refusing to talk to the medical team that operated and performed the pathology on Cathy was in our opinion less than professional and was arrogant beyond an acceptable standard.

A Rathke’s cleft cyst is a benign pituitary cyst, which typically occurs in the area of the pituitary gland. It is thought to be remnants of an embryologic structure called Rathke’s pouch, hence the name. If left over after development, the cyst can slowly expand and eventually cause symptoms. Rathke’s cyst also does not respond to cortisone treatment.

Cathy decided to stay with the more conservative treatment proposed by her Miami team. Since she has begun the steroid treatment her clinical symptoms have improved and the latest MRI has demonstrated a decrease in size of the mass and resolution of the effect the mass has had on her optic chiasm (sight restored).

The high dose prednisone (40mg) was doing the job of decompression however we were very concerned with the mid to long-term effect of such high dose treatment. This also confirmed the diagnosis of lymphocytic hypophysitis versus that of Rathke’s cleft cyst. The Miami endocrinologist also suggested that Cathy see a rheumatologist and possibly receive additional chemical treatment with one of the new autoimmune drugs.

So this started out as a neurosurgical problem, then it became an endocrinology problem, and now a rheumatology problem. So she was put on to Cellcept in addition to the prednisone. Cellcept (mycophenolate mofetil) is used to prevent rejection of a kidney, liver, or heart transplant.

After almost ten months of treatment Cathy’s overall health and medical condition were getting worse. As she would reduce the dose of prednisone her clinical symptoms would resume and there appeared to be no benefit of the Cellcept medication so that was discontinued. During all this time I was reaching out to all my medical contacts on a global basis seeking any suggestions for treatment. In addition I was searching all index databases looking for any published literature on the treatment of lymphocytic hypophysitis.

I eventually found one paper on ResearchGate “Stereotactic Radiotherapy for the Treatment of Lymphocytic Hypophysitis” published in 2003 in Journal of Neurosurgery senior author by Michael T. Selch, MD. [3] The article was a report on two cases, one a 58-year-old man, the other a 75-year-old man.

The role of surgery is to decompress and for tissue diagnosis. It is typically treated medically with steroids. Resection is often incomplete due to suprasellar extension or firm adherence to adjacent Dura matter. Recurrence has been reported and validated by Cathy's recent events. Surgery may result in diabetes insipidus or worsening of the anterior pituitary function. Cathy experienced both of these conditions.

High-dose steroid therapy has been advocated in an effort to avoid invasive procedures. The clinical response to corticosteroid medications, however, may be poor or transient and symptoms frequently return after cessation of therapy. Steroid therapy treatment after many months can result in serious side effects such as Cushing syndrome, avascular necrosis, and diabetes mellitus.

Until this paper there had been no reports of radiotherapy for lymphocytic hypophysitis, although its use has proven to be successful for histopathologically similar condition elsewhere in the body. The results of this report of two cases were that stereotactic radiotherapy represents a minimally invasive treatment option for patients with lymphocytic hypophysitis.

Needless to say, this was the first research that demonstrated a potential for not just treating my wife's condition but a realistic outlook on curing her disease. Now I was faced with the prospect of finding a new experimental treatment and presenting this option to my wife without over stating, or raising expectations beyond a reasonable level. This, after all, was just a case result of two patients.

So I reached out to contact Michael Selch from UCLA only to find that he had retired and his contact information was not readily available. After about three months I was successful and Michael gave me a call. We discussed Cathy's case and Michael did feel that Cathy could possibly benefit from radiation therapy.

Since this was a new treatment modality and Michael was retired Michael suggested that we contact Dr. John Breneman, MD from Cincinnati Ohio. Michael was kind enough to reach out on our behalf and contact John.

Dr. John Breneman is a Radiation Oncologist in West Chester, Ohio and is affiliated with multiple hospitals in the area, including Christ Hospital and Cincinnati Children's Hospital Medical Center. He received his medical degree from University of Iowa Carver College of Medicine and has been in practice for 34 years.

After being contacted by Michael, John called me and we discussed Cathy's case. John requested that I send her medical files so he could review them and present them to his department at the University of Cincinnati. In the meantime we kept Cathy's neurosurgeon, Samy (Mohamed Samy A. Elhammady, MD), abreast of our discus-

sions. Samy has been our key contact since the surgery discussing every step of treatment along this challenging path. Both Cathy and I cannot express the immense respect that we have for this young gifted surgeon. He has grown into a friend making himself available day or night to help us with decisions that are very scary and experimental in nature. He has made himself available to all of Cathy's medical team even to the point of allowing us to give out his personal mobile telephone number. He made sure all of Cathy's medical files including the pathology slides were sent to John for his team to review.

John, the tumor board and the pathology department at the University of Cincinnati agreed and confirmed Miami's diagnosis of lymphocytic hypophysitis. After confirmation of the diagnosis upon meeting with John he was upfront with the fact that he and his department had no experience with treating this disease. After consultation with Michael Selch, John felt he and his team could develop a radiation therapy protocol that would benefit Cathy's condition. We were very impressed with John's open honest approach and had the confidence that we found the right man to help us at this junction.

## Treatment and Results

Radiation therapy: Definitive  
Image Guidance: Daily  
RT Dose per Fraction (Gy): 2 Gy  
RT Total Fraction Count: 15  
RT Total Dose (Gy): 30 Gy  
Elapsed Days: 20

A sixty-eight-year-old Caucasian woman completed definitive radiotherapy as instructed without unintended treatment breaks. She tolerated radiotherapy well with expected acute treatment related toxicity including fatigue. Her HA's were moderately improved during radiation.

### *RTOG Acute Radiation Morbidity Scoring Criteria*

General: grade 1 fatigue

### *Conclusion of MRI:*

MARKED IMPROVEMENT IN THE MASS IN THE PITUITARY WHEN COMPARED TO THE PREVIOUS EXAMINATION OF 5/13/2015. THE CAVERNOUS SINUSES ARE NORMAL WITH NO MASS EFFECT ON THE PITUITARY STALK (Figure 1).

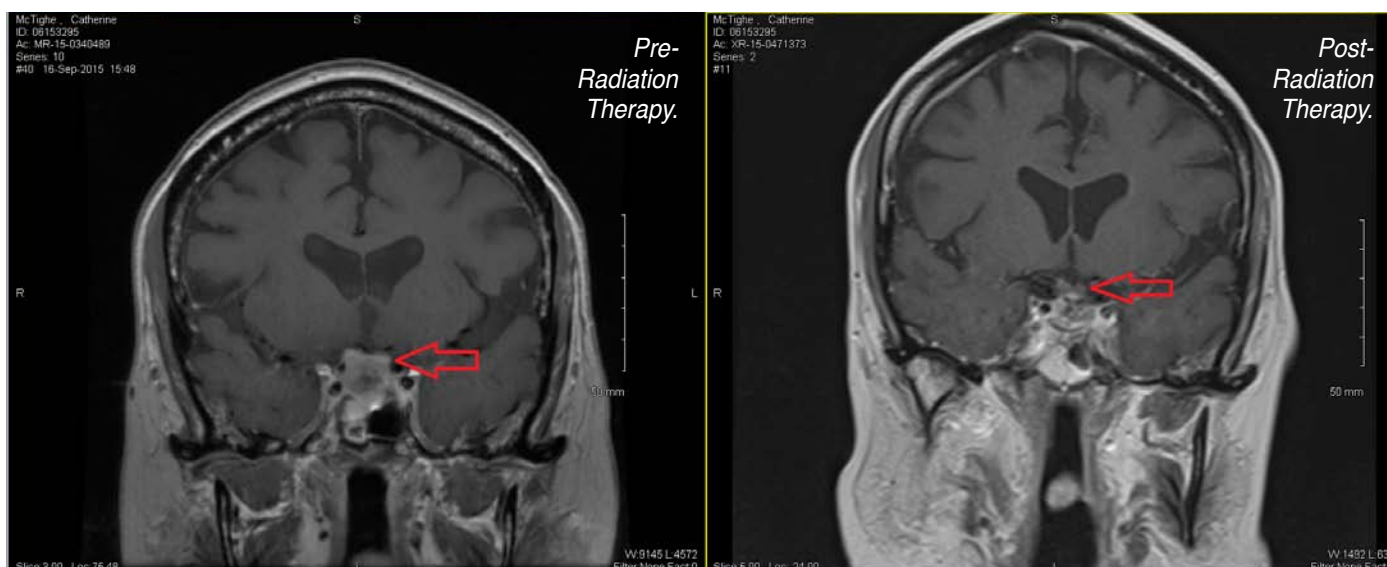


Figure 1. The new scan on the right shows a much smaller, residual area of contrast uptake in the area of the pituitary, which could represent resolving hypophysitis versus effects of radiation treatment.

## Summary

Although this is a summary of a case report on an initial neuro-surgical problem the medical situation transformed itself to a multifocal problem involving four defined medical subspecialties:

1. Neuro-surgical
2. Endocrinology
3. Rheumatology
4. Radiation Oncology

The purpose of this paper is to highlight how one publication of a case report can lead to ongoing treatment and research that has effectively improved the quality and life expectancy of one patient. In addition to the benefit of this one individual patient the improvement in the quality of life that this one patient touches: husband, children, grandchildren, friends and the real possibility of this treatment benefiting additional patients and all the people that patients touch.

I want to encourage all medical professionals to publish. Publish the good and the bad, your work is a benefit and I want to thank all, that take the time to publish their work.

In addition this experience has demonstrated that almost all the health care team Cathy and I encountered were highly professional and extremely kind. It makes you proud to be part of this profession.

### *Our team that deserves high praise :*

*Roberto Heros, MD*, Professor & Co-Chairman of Neurological Surgery, University of Miami Health System.

*Mohamed Samy A. Elhammady, MD*, Neurosurgeon, University of Miami and St. Joseph Hospital, Tampa, Florida

*Michael T. Selch, MD*, Radiation Oncologist, UCLA, Los Angeles, CA

*John Breneman, MD*, Radiation Oncologist, University of Cincinnati, OH

*Mark D. Jacobson, MD*, Interventional Radiologist, Lady Lake, FL

### *Special note of interest:*

On a personal note of interest shared by both Catherine and myself: two of Cathy's medical team are foreign born surgeons - Roberto Heros from Cuba and Mohamed Samy A. Elhammady from Egypt.

We are very grateful that these two professionals have chosen to settle in the United States and practice here. We consider them both to be friends and highly recommend them in their professions. People need to be judge based on their merit, nothing more, nothing less.

Cathy and I hope this radiation therapy protocol will benefit the increasing number of individuals that are afflicted with this disease.

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