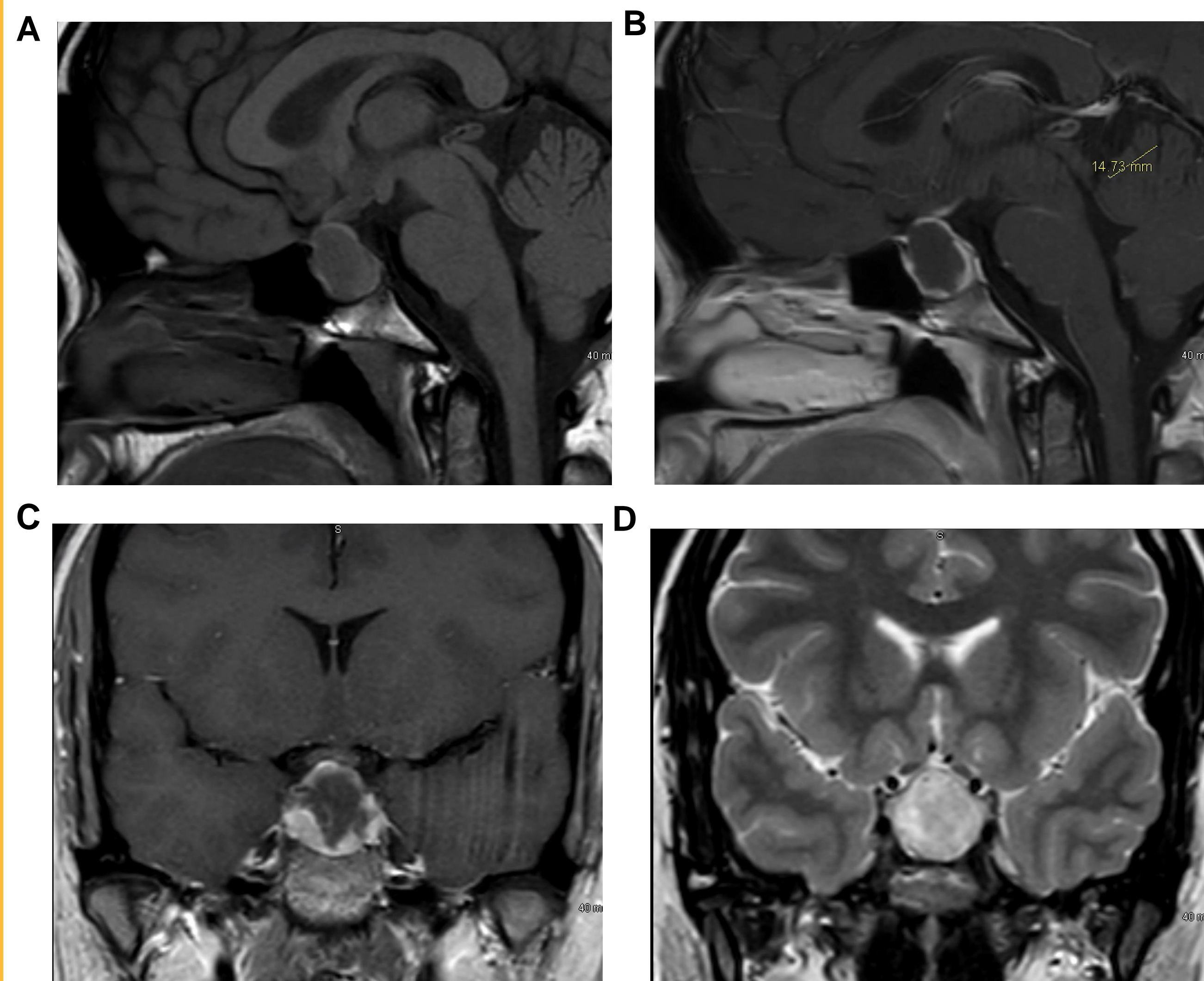


Shirin Jaggi, D.O, Richard C. Strauss, M.D.,  
Wissam Zaeeter, M.D., Vinay Palli, M.D., Helen L. Slone, M.D.

## Introduction

Pituitary adenomas are often an asymptomatic and common finding in the general population usually incidentally found on imaging. They very rarely progress to a pituitary apoplexy, which defined as an infarction or hemorrhage of the pituitary. Triggers include pregnancy, hypertension, radiation and/or surgery [1]. The most common symptom is usually severe headache associated with worsening visual defects [5]. In this case, Leuprolide, a GnRH agonist, was the rare cause of pituitary apoplexy in a patient who coincidentally had an undiagnosed pituitary adenoma undergoing fertility treatment.

## Imaging



Abnormally enlarged sella turcica with a large complex mixed cystic and solid sellar mass with extension measuring 1.5 x 2.2 x 2.1 cm. The enlarged pituitary adenoma can be visualized in (A) sagittal view of T1 weighted scan without contrast and (B) sagittal T1 weighted with contrast. The heterogeneity can further be viewed in (C) T1 weighted coronal view with contrast and (D) T2 weighted coronal image.

## Case Presentation

- A 32 year old female with no significant medical history undergoing fertility treatment with Leuprolide presented with intractable headaches and vomiting. Prior to her presentation, patient was in her usual state of health and developed these symptoms within thirty minutes of administering her first Leuprolide injection.
- Upon initial presentation, she was found to be mildly tachycardic with heart rate elevated to 110 bpm. There was no report of double vision, photophobia, diplopia, blurry vision or weakness.
- Patient had a CT head that showed a pituitary macroadenoma. It was followed by a pituitary MRI, which showed a large complex mixed cystic and solid sellar and suprasellar pituitary lesion (1.5 x 2.2 x 2.1 cm). There was also evidence of compression on the undersurface of the optic chiasm. The infundibulum was markedly compressed and displaced superiorly.
- At the time of admission, her TSH was 2.8 mIU/L (n 0.46-4.68mIU/L), Prolactin of 17.9 ng/mL (n 3.0-30.0), IGF-1 of 100 ng/mL (n 53-331ng/mL), Estradiol of 5210 pg/mL (normal in follicular phase 19-144 pg/mL), FSH of 5.3 IU/mL (normal in follicular phase 2.5-10.2 IU/mL) and LH of <0.2 IU/mL (normal in follicular phase 1.9 - 12.5 IU/mL)., She was treated at the time with IV Dexamethasone which provided minimal relief for her headache.
- Due to the worsening nature of her headache and her unusual appearance of the pituitary on MRI, there was a strong suspicion for pituitary apoplexy. She subsequently had a transsphenoidal debulking of the pituitary.
- Pathology report showed pituitary necrosis.

## Discussion

GnRH agonists such as Leuprolide have been approved for various treatments such as triggering ovulation, hormone mediated malignancies such as prostate and breast cancer, endometriosis and precocious puberty. The actual mechanism of how it triggers pituitary apoplexy continues to remain unclear. One theory is that the initial surge can have a sudden increase in vasculature of the adenoma in cases of a hemorrhage [2]. Furthermore, it is also possible that the stimulation of Leuprolide could have caused a rapid increase in metabolic activity of the adenoma and possibly induce tumor growth. The necrosis evident in our case of pituitary infarction could be a result of vessel compression due to increase in tumor size [3, 4].

There have only been fifteen reported cases of pituitary apoplexy with GnRH agonists and fourteen of which have been in adult males undergoing prostate cancer treatment [5]. To our knowledge there is only one other case of a young female undergoing fertility treatment who also clinically presented with a pituitary apoplexy after her first Leuprolide injection [3]. Although the initial presentation may be variable, all cases have presented with the initial symptom of severe headache.

We aim to make clinicians aware of this rare complication of Leuprolide. Although doing MRI scans on every person before initiating this medication is not feasible, it would still be important to do a work up with basic endocrine laboratory evaluation. It is important for clinicians to make a prompt diagnosis so that treatment initiation can be performed in those who do present with apoplexy as it can lead to change in vision, consciousness or even death.

## Summary

There have been several reported cases of the rare but important adverse effect of GnRH agonist with pituitary apoplexy with potentially life-threatening consequences. There are very few known cases with young females undergoing fertility treatment who developed pituitary apoplexy. Based on our case, we hope to caution clinicians for the risks of pituitary infarction or hemorrhage prior to initiating Leuprolide. A thorough endocrine workup should be done prior to starting treatment and imaging should be considered in anyone with abnormal laboratory findings.

## References

1. Ando S, Hoshino T, Mihara S. (1995) Pituitary apoplexy after goserelin. *Lancet*. 345:458
2. Sinnadurai M, Cherukuri RK, Moses RG, Nasser E (2010) Delayed pituitary apoplexy in-patient with advanced prostate cancer treated with gonadotropin-releasing hormone agonists. *J ClinNeuroscience* 17:1201-1203
3. Engel G, Huston M, Oshima S, Beck C, Harsh G, et al. (2003) Pituitary apoplexy after leuprolide injection for ovum donation. *J Adolesc Health* 32: 89-93.
4. Sasagawa Y, Tachibana O, Nakagawa A, Koya D, Iizuka H (2015) Pituitary apoplexy following gonadotropin-releasing hormone agonist administration with gonadotropin-secreting pituitary adenoma. *J ClinNeurosci* 22: 601-603..
5. Huang T, Lin J, Lieu A, Chen Y, Chng H, Jang M, Shen J, Wu W, Hung S, Juan Y. (2013) Pituitary apoplexy induced by Gonadotropin-releasing hormone agonists for treating prostate cancer- report of first Asian case. *World Journal of Surgical Oncology*: 11: 254