Cabergoline Induced Psychosis During Medical Therapy of Macroprolactinoma

Samuel L Dengler, MD[1], Alan R Turtz, MD[2] , Warren Goldman, MD[2] ,
Thomas Holdbrook, MD[1] , Gregory Kubicek, MD[2] , and Farah Hena Morgan, MD,[1]
(1) Cooper University Hospital, Camden, NJ, (2) MD Anderson Cancer Center at Cooper, Camden, NJ

Introduction

Dopamine agonist (DA) treatment is the mainstay of therapy for prolactinomas, and in many tumors can result in significant decreases in tumor size. DA therapy is not without its risks however, with some patients reporting adverse effects such as nausea, lightheadedness, and rarely increased impulsivity or even psychosis.
Here we present a case involving a patient with macroprolactinoma on DA therapy with cabergoline (CBG) who developed psychosis requiring discontinuation of CBG, and eventually transsphenoidal surgery (TPS) as well as stereotactic radiotherapy (STRT) to diminish the effects of his giant prolactinoma.

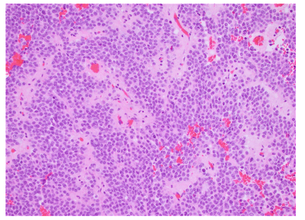
Case Presentation

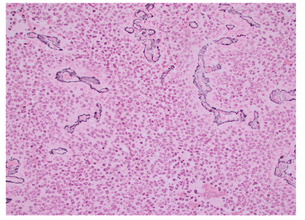
A 43 yo man with a history of hypercholesterolemia and oligospermia (diagnosed in s/o infertility work up) with no psychiatric history who initially presented with worsening visual field cuts over several months. He was referred to ophthalmology who diagnosed his syndrome as bitemporal hemianopsia, prompting an ER visit in March 2018, with an urgent pituitary MRI revealing a macroadenoma measuring 6 x 3.29 x 3.77 cm, and a serum prolactin level of > 3,707 ng/mL. The patient was seen by endocrinology and started on CBG 0.25 mg twice weekly, which was increased to 0.5 mg twice weekly on week 2.
The patient experienced anxiety and trouble sleeping, which progressed over the next 24 hours to paranoia and frank psychosis, prompting hospital admission and psychiatric evaluation. CBG was stopped during his hospital stay, and he underwent TPS to reduce tumor burden.
Given the inability to receive DA therapy post-operatively, the decision was made to pursue STRT, and the patient underwent cyberknife radiotherapy. The patient had panhypopituitarism after the initial surgery, requiring hormonal replacement for central adrenal insufficiency, central hypothyroidism, central hypogonadism, and partial central diabetes insipidus. There has been a steady decline in his prolactin levels, stabilizing around 262 ng/mL.

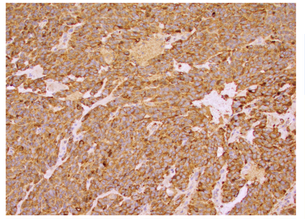
Figure 1. Top:
Pituitary adenoma (prolactinoma)- The tumor shows sheets of monomorphic cells with eosinophilic cytoplasm and round nuclei with prominent nucleoli (H&E, X200).

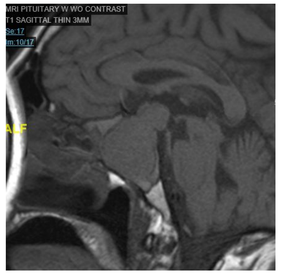
Figure 2. Middle:
Pituitary adenoma (prolactinoma)- A reticulin histochemical stain shows loss of the normal acinar architecture. There is absent staining within the adenoma (except for the blood vessels) (reticulin, X200).

Figure 3. Bottom:
Pituitary adenoma (prolactinoma)- Diffuse strong immunoreactivity for prolactin throughout section. (prolactin IHC, X200).



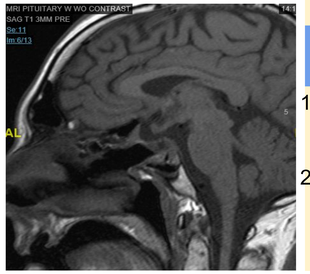






LEFT-
Preoperative MRI Pituitary demonstrating mass

RIGHT-
Postoperative MRI pituitary- significant reduction in mass



Discussion

DA therapy is the mainstay of medical treatment of prolactinoma and hyperprolactinemia. It has myriad benefits in this setting, including restoration of gonadal function, decreased galactorrhea, lower prolactin levels and decreased tumor size. Treatment is long term in many patients, and therefore consideration of adverse effects is of prime importance.
The most common side effects of DA therapy are nausea, headaches, dizziness, and orthostatic hypotension. Less commonly, patients can develop symptoms related to an impulse-control disorder. Manifestations include pathological gambling, hypersexuality, binge eating, compulsive shopping, compulsive medication use, obsessive hobbying and punding.
Even more rarely, patients on DA therapy can develop severe psychiatric disturbances, including severe depression, mania, psychosis, and even catatonia. These events have been reported in patients in the absence of significant psychiatric history.
While severe psychiatric disturbances are uncommon with DA therapy, it is prudent to discuss these rare but serious side-effects with patients prior to initiating DA therapy, and to routinely discuss adverse behavioral changes at each follow up.

Conclusion

We present a patient with macroprolactinoma causing visual defect as well as significant pituitary hormonal compromise who developed psychosis in the setting of cabergoline therapy, but was subsequently treated successfully with a combination of TPS, stereotactic radiotherapy, and hormonal replacement with serial monitoring.

References

1. Psychological effects of dopamine agonist treatment in patients with hyperprolactinemia and prolactin-secreting adenomas. European Journal of Endocrinology. (2019) 180, 31–40.
2. Diagnosis and Treatment of Hyperprolactinemia: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinology Metabolism. (2011) 96(2): 273-288.