Hypopituitarism Secondary to Unruptured Intrasellar Aneurysm Misdiagnosed as Pituitary Adenoma: A Case Report

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Abstract
Background: Hypopituitarism secondary to intrasellar aneurysms is not extremely common. Most of the clinical manifestations are secondary to apoplexy or rupture of the aneurysm. Hypopituitarism and hyperprolactinemia are common endocrinopathies encountered with ruptured intrasellar aneurysms.

Case: A 37 year-old female presented for management of secondary infertility with past medical history significant for long standing amenorrhea and a pituitary mass, not requiring treatment. She was taken to surgery for surgical excision of pituitary mass but on day of surgery was diagnosed to have an intrasellar aneurysm instead. Fortunately the patient never experienced complications of aneurysm rupture and currently stable under management for hypopituitarism.

Conclusion: Diagnosing an intrasellar aneurysm as a cause of hypopituitarism is of critical importance and a team approach is essential with consultants in radiology, endocrinology and neurosurgery.

Introduction
Intrasellar aneurysms that mimic pituitary tumors with are rare with few previous reports [1-4]. 10% of such aneurysms can cause parasellar syndromes and 1.4-5% of such cases managed by neurosurgeons have been found to extend into the sella turcica [5]. They may present with symptoms of mechanical compression or endocrinopathies. Though absence of endocrine symptoms may distinguish an aneurysm from a pituitary adenoma in most cases, mass effect from an enlarged aneurysm may prove the opposite in rare cases [6]. Interestingly, most pituitary lesions may or may not present with typical compression symptoms depending on the size of the lesion. Most symptoms of hypopituitarism secondary to intra or parasellar aneurysms have been reported from the effect of rupture or apoplexy [5,7,8].

Hypopituitarism secondary to pituitary or sellar masses may have a variety of manifestations such as headaches, visual disturbances from optic nerve compression, amenorrhea with or without galactorrhea, infertility from hypogonadism and symptoms of hyperprolactinemia [5]. Diagnosing a pituitary lesion requires contrast Computed Tomography Scan (CT) or Magnetic Resonance Imaging (MRI) once the clinical suspicion is established based on a detailed history and physical exam. The MRI has proven to be advantageous over CAT scan and does not expose the patient to ionizing radiation. MRI is the investigation of choice for evaluation of sellar and juxta sellar structures. Though the MRI is a very sensitive test, its interpretation needs to be carried out by an expert in the field of neuroradiology. A wrong diagnosis may delay the management of a patient and lead to unwarranted complications such as intracerebral hemorrhage and even death. A similar misdiagnosis of an intrasellar aneurysm as a pituitary adenoma was made in a patient described in the case below.

Case
A 37 year-old G1P1 female presented at our infertility clinic for consultation regarding secondary infertility of long and interrupted duration. She desired a second child with her husband who was 46 years old with a history of vasectomy and had two prior children from a past relationship. She had a full term normal vaginal delivery after a natural conception in 1992. At the age of 23, she started having new onset headaches and stopped having regular menstrual cycles. She was evaluated for such manifestations and was diagnosed with Premature Ovarian Failure (POF) with a small pituitary lesion (<1 cm per patient’s description as no report was available). Prolactin level was drawn and was within normal limits during this first investigation. Therefore, other than a diagnosis of POF; no other endocrinopathy was detected. Hormone replacement therapy was recommended; however, the patient declined.

Apart from presenting with infertility, review of systems yielded recent fatigue, weight loss, cold intolerance and excessive dryness of skin. The patient did not report any current headaches, vision changes or any history of hospitalization other than her term delivery.

Pertinent history obtained revealed that she underwent menarche at the age of 12 with normal pubertal development. She had 25-pack year history of smoking along with occasional alcohol intake. She denied any sexually transmitted infections, abnormal PAP smears, bone pain or history of osteopenia or osteoporosis. She was not on any medications other than over the counter vitamins.

A complete physical exam with an office pelvic ultrasound was performed. Physical exam was unremarkable with BMI- 28, normal blood pressure and normal gynecological exam. The office pelvic ultrasound revealed a small uterus (5.31×1.87×3.08 cm), endometrial stripe of 0.34 cm, right ovary measuring 1.41×0.7 cm, left ovary-1.21×0.7 cm with right ovary containing 1 follicle and the left ovary with 2 follicles. The patient was recommended to consult an endocrinologist and a neurosurgeon for additional management. Laboratory evaluation

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of serum Follicle Stimulating Hormone (FSH), Thyroid Stimulating Hormone (TSH) with free T4, Anti Mullerian Hormone (AMH), Estradiol (E2), Prolactin (PRL), vitamin D, fasting early morning Cortisol and Insulin like Growth Factor 1 (IGF1) were ordered along with a brain MRI to reevaluate the pituitary lesion.

Our initial evaluation indicated hypogonadotrophic hypogonadism in contrast to the initial diagnosis of premature ovarian failure. Laboratory results showed low cortisol, low free T4 and vitamin D. The results are as follows- FSH- 1.0 m IU/mL, AMH- 1.6 ng/mL, TSH- 0.819 µIU/L, FT4- 0.6 ng/dL, PRL- 3.5 ng/mL, E2- <12 pg/mL, Cortisol- 7.4 µg/dL, Vitamin D- 14 ng/mL, and IGF-1- 142 ng/mL. The brain MRI revealed a 1.7×1.8×2.8 cm sellar mass extending to suprasellar cistern and laterally over superior aspect of internal carotid artery bilaterally (Figure 1). The mass touched the optic chiasm and cisternal portion of optic nerve bilaterally. Unfortunately there was no prior record for comparison since the last brain imaging was performed more than 20 years ago.

Recommendations by endocrinologist were to repeat the thyroid profile, conduct an ACTH challenge test, and start vitamin D supplementation with smoking cessation. The hormonal evaluation revealed that the morning 8 AM cortisol and ACTH baseline were markedly reduced (1.8 mcg/dL, ACTH- <5 pg/mL respectively) with suboptimal response to the ACTH challenge test revealing severe ACTH deficiency (maximum cortisol level at 60 min was 17.2 mcg/dL). Based on lab results and findings in MRI, the endocrinologist recommended initiation of cortisol supplementation and an evaluation by a neurosurgeon.

The patient was evaluated by a neurosurgeon that performed a complete neurologic examination with visual field testing which was within normal limits. The plan included continuation of the hydrocortisone and thyroid supplementation with preparation for a transphenoidal resection of the pituitary mass. The pituitary mass described by the neurosurgeon was a possible pituitary adenoma with hemorrhage around its periphery. On the day of the surgery before commencement of the procedure, a carotid angiogram was ordered by the neurosurgeon to rule out aneurysm in the pituitary region. This intervention was critical which avoided a major catastrophe. Bilateral carotid angiography demonstrated a 1.8×1.7 mm cavernous Left Internal Carotid Artery (LICA) aneurysm pointing medially which likely represented the remaining patent portion of a larger thrombosed aneurysm (3 x 1.7 mm) with calcification (Figure 2). The surgery was cancelled and the patient was advised to continue hormonal supplementation as recommended.

Our current recommendation for management of infertility mainly concerns the existence of the intrasellar aneurysm. Though estrogen and progesterone supplementation for constructing a uterine environment suitable for pregnancy and utilizing gonadotropin for controlled ovarian stimulation may assist in achieving pregnancy, the health of the patient is of primary importance. The patient was counseled about...

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**Figure 1:** MRI brain showing intrasellar lesion with hypo density in the center occupying the pituitary fossa (arrows).

**Figure 2:** Carotid angiogram showing aneurysms of the left internal carotid artery (arrows).
risks of intracranial aneurysms and increased morbidity and mortality in pregnancy. The patient had decided to defer her wishes of conceiving although the general endocrinologist and the neurosurgeon had issued clearances for management of infertility.

**Discussion**

An intrasellar aneurysm is a rare case of hypopituitarism. It accounts for 0.17% of all cases of hypopituitarism. Though rare, it is quite possible to encounter a patient in the fertility or gynecology clinic with symptoms of hypopituitarism such as irregular periods or infertility. Presentations related to adrenal, thyroid and gonadal deficiencies are most commonly observed [3] with visual impairment being one of the most common presenting symptoms [3]. Most cases of intrasellar aneurysms are diagnosed either at the time of surgical exploration or via imaging, typically MR [9]. Rupture of an intrasellar aneurysm is the most severe complication, which leads to intrasellar bleeding followed by subarachnoid extension. These aneurysms typically mimic pituitary tumors and potentially may have catastrophic outcomes if not appropriately recognized and managed [5].

While some patients present with aneurysmal rupture, the most common symptoms in order of decreasing frequency include headache, visual field cuts, decreased visual acuity, endocrinopathies, symptomatic hypotension and rarely cranial nerve paresis [5]. The most common endocrinopathies are typically hyperprolactinemia and hypogonadism [3]. Our patient presented with hyperprolactinemia instead, possibly because the size was not large enough to compress the pituitary stalk. Her prolactin had been within normal limits at her first evaluation; therefore, the lesion had potentially grown in size thus causing the decreased value. It is also probable that the aneurysm had replaced the pituitary tissue to an extent leading to features of hypopituitarism. While very rare, it is important to recognize that up to 20% of intrasellar aneurysms may present in conjunction with pituitary adenomas [5,10,11]. Hence it is important for such coexistence to be ruled out if surgical management of the pituitary tumor is considered to prevent potentially life threatening complications. Often patients with long standing amenorrhea also have decreased bone mineral density. That was not the case with our patient despite an extended smoking history, and these findings are in contrast to what is expected. We are unable to explain this finding, and suffice it to say that although decreased bone mineral density was expected there are other factors, for example genetic, which affect the multifactorial pathogenesis of this condition.

There are 2 primary anatomical subtypes of intrasellar aneurysms. The first type is infradiaphragmatic (cavernous/clinoide segment of internal carotid artery) aneurysms with medial extension into the sella. The second type is supradiaphragmatic, which are suprasellar aneurysms originating from the ophthalmic segment of the ICA or the anterior communicating artery [5]. Infradiaphragmatic intrasellar aneurysms are much more likely to present with endocrinopathies, while supradiaphragmatic are more likely to present with visual changes [5]. It is thus important to establish a proper diagnosis prior to management. Extensive use of MRI or CT scan can assist in differentiating the two types of intrasellar masses. Characteristic radiological findings with proper delineation of origin of the aneurysms can be established with MR angiography. Hence consulting with an expert in neuro- radiology should be sought in cases where intrasellar aneurysm may mimic an adenoma prior to management. Interventions are usually reserved for symptomatic lesions or for those with extension into the subarachnoid space. Management options of these lesions depend on their subtype. Infradiaphragmatic lesions, typically require endovascular techniques or surgical trapping and for supradiaphragmatic lesions surgical clipping is the most often treatment of choice [5].

**Conclusion**

While rare, intrasellar aneurysms should be ruled out in patients presenting with pituitary masses. The presentations are typically identical to pituitary adenomas as well as the associated symptoms, which arise from the mass effect of the aneurysm much like other pituitary masses. Misdiagnosis can be catastrophic in cases of ruptured aneurysms, and in cases of attempted surgical excision in an otherwise misdiagnosed aneurysm for pituitary adenoma.

**References**