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Case Report

A Case of Exaggerated Pituitary Hyperplasia in a Pregnant Woman

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Abstract

Pituitary hyperplasia occurs as a result of an increase in pituitary cell subtypes. It can be a consequence of either a physiological or pathological condition. In our case, a 31-year-old pregnant woman at 16 weeks gestation presented with headaches and vision changes. Visual field testing demonstrated bitemporal hemianopsia, and magnetic resonance imaging (MRI) brain showed enlargement of the pituitary with compression of the optic chiasm. She was treated with cabergoline and steroids, and her symptoms improved. In a subsequent pregnancy, the patient developed similar symptoms, and with cabergoline treatment, her symptoms resolved. A postpartum MRI of her brain revealed a decrease in pituitary size back to baseline with normal pituitary hormone levels. This patient's likely diagnosis was physiologic pituitary hyperplasia. Pituitary hyperplasia can be difficult to diagnose since there are no explicit guidelines. Through deduction of imaging findings and hormonal levels, diagnosis of pituitary hyperplasia becomes a more manageable task.

Key Words: pituitary hyperplasia, pregnancy, prolactin

Abbreviations: IGF-1, insulin-like growth factor-1; MRI, magnetic resonance imaging.

During pregnancy, there are numerous physiologic and anatomic changes that affect the pituitary gland. The weight of the pituitary can increase by about one-third, and its volume can increase to up to 136% during pregnancy [1, 2]. This occurs as a result of lactotroph hyperplasia, where the percentage of lactotrophs can increase to up to 40% due to increased maternal estrogen [3]. This increase in the number of lactotrophs leads to elevated prolactin levels [4]. Progesterone is another hormone that stimulates production of prolactin. Higher prolactin during pregnancy is essential to prepare breast tissue for lactation. In addition, normal pregnancy is associated with higher activity levels of the hypothalamic-pituitary-adrenal axis, which includes almost a three-fold increase in cortisol by the third trimester. Although some degree of pituitary enlargement is a normal physiologic response in pregnancy, it is critical to consider other pathologies in the differential diagnoses of pituitary enlargement during pregnancy. Examples include a pituitary adenoma, pituitary apoplexy, and lymphocytic hypophysitis [4]. The most common pituitary adenomas that are encountered during pregnancy are prolactinomas [3]. Therefore, if a patient develops headaches or vision changes while pregnant, it is important to initiate testing with magnetic resonance imaging (MRI) scanning and visual field tests [5]. The following case demonstrates a very marked hyperplasia of the pituitary in response to pregnancy.

Case Presentation

A 31-year-old woman with no significant past medical history, at 16 weeks' gestation, initially presented with a 2-week duration of vision changes and headaches. Vision changes were more prominent in the left eye. The headaches occurred almost daily and were gradually worsening in intensity. She saw an ophthalmologist and was found to have bitemporal hemianopsia. An MRI brain scan without contrast was obtained and showed enlargement of the pituitary gland, measured at $1.8 \times 1.3 \times 1.1$ cm, possibly compatible with a macroadenoma, with slight compression of the optic chiasm. Initial laboratory values showed an elevated prolactin to 467.3 ng/mL (467.3 mcg/L) (normal range, typically 50-270 ng/mL [50-270 mcg/L] during pregnancy) and total thyroxine (T4) of 7.3 mcg/dL (93.95 nmol/L) (normal range, 8.9-17.4 mcg/dL [114.56-223.97 nmol/L] during second trimester of pregnancy). Other pertinent laboratory values included thyrotropin (TSH) of 0.38 uIU/mL (0.38 mIU/L), cortisol of 26 µg/dL (717.24 nmol/L), and insulin-like growth factor 1 (IGF-1) of 238 ng/mL (31.1 nmol/L). Due to vision loss and concern for worsening vision, the patient was started on treatment with cabergoline 0.5 mg twice per week. In addition, levothyroxine 50 mcg daily was started. Due to worsening headaches and vision changes, she consulted with a neurosurgeon who recommended a dexamethasone taper, which she started 2 weeks after the start of cabergoline treatment. After several weeks of Decadron and cabergoline, the patient's symptoms improved, with normalization of visual field testing and diminished headaches. Repeat MRI of the brain without contrast showed a decrease in size of the pituitary. However, she delivered her baby prematurely at 25

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weeks. The infant died several weeks later. Postpartum, her headaches and vision changes had completely resolved. Cabergoline and levothyroxine were discontinued 1 week after delivery. One month postpartum her prolactin level was 16.2 ng/mL (16.2 mcg/L), and 6 months postpartum, prolactin was 27.0 ng/mL (27.0 mcg/L) (Table 1). Given 2 normal postpartum prolactin levels while off cabergoline, a prolactinoma was effectively ruled out.

Subsequently, the patient returned for follow-up 6 months later at 11 weeks' gestation. She began to have headaches again without vision changes. Her initial visual field testing at 7 weeks' gestation was normal. MRI of the brain without contrast showed an increase in pituitary size to $1.3 \times 2.3 \times 0.7$ cm (Table 2). The patient was hesitant to restart medications due to the outcome of her last pregnancy. Nonetheless, her visual field testing gradually worsened, which necessitated adding cabergoline to her medication regimen. She was not treated with steroids as was the case in her first pregnancy. After 3 weeks of cabergoline 0.5 mg twice weekly, visual field testing was normal, and her symptoms had improved significantly. By the third trimester of pregnancy, the patient requested to stop cabergoline so that she would be able to breastfeed after delivery. She carried the baby to term without any complications.

A year and a half later, the patient presented for follow-up. She was being considered for pituitary surgery after her last pregnancy but repeat MRI had shown significant interval decrease in size of the pituitary. Consequently, surgical intervention was not pursued. She did not have any recurring symptoms since delivery of her child. An MRI brain performed at 16 months postpartum showed a 4 mm adenoma, and pituitary function remained normal, with normal cortisol and IGF-1 levels. Prolactin was initially slightly elevated at 42.3 ng/mL (42.3 mcg/L), which may have been in the setting of breastfeeding. Repeat prolactin 3 weeks later was normal at 25.5 ng/mL (25.5 mcg/L). The patient is now considering another pregnancy and is agreeable to restart cabergoline at that time if needed.

Discussion

The pituitary is expected to enlarge during pregnancy, with a progressive increase in height of about 0.08 mm for every gestational week [2]. This expected enlargement is a direct result of estrogen-mediated hypertrophy of lactotrophs. Progesterone is another essential hormone involved in increased prolactin production by lactotrophs. In the nonpregnant state, lactotroph cells encompass 20% of anterior pituitary cells, which increases to 60% by the third trimester of pregnancy [6]. Hyperplasia typically leads to symmetric enlargement of the pituitary; thus, pituitary pathology should be considered in pregnancy among those with asymmetrical growth of the pituitary, increase in pituitary height larger than expected, deviation of the stalk, or symptoms consistent with a possible tumor. Examples of diagnoses to consider include pituitary adenomas, lymphocytic hypophysitis, suprasellar meningiomas, pituitary apoplexy, and pituitary hyperplasia.

Prolactinomas are the most common pituitary tumor and account for 40% to 50% of functioning adenomas [1]. Women of childbearing age with an untreated prolactinoma may have infertility due to decreased follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion secondary to elevated prolactin levels [2]. Lymphocytic hypophysitis is an autoimmune disorder characterized by infiltration of the pituitary by lymphocytes, macrophages, and neutrophils [2]. Lymphocytic hypophysitis typically occurs as a sellar lesion that can cause signs of hypopituitarism, visual disturbances, or headaches [1]. Suprasellar meningiomas form near the skull base by the pituitary gland and optic nerve can also lead to potential visual deficits and pituitary dysfunction.

Pituitary hyperplasia is defined as an absolute increase in one or more distinct pituitary cell subtypes. It is typically attributed to either a physiologic or pathologic process. Physiologic pituitary hyperplasia can occur during youth, pregnancy, or menopause. Meanwhile, physiologic pituitary hyperplasia can be a consequence of gonadal insufficiency or primary hypothyroidism [7]. One research study examined pituitary enlargement in 7 female patients between the ages of 15 and 27 and determined that a pituitary gland greater than 9 mm should be classified as normal physiologic pituitary hypertrophy when hormone levels and MRI findings are unremarkable [8]. In most cases, surgical management is not indicated, and therefore the diagnosis of pituitary hyperplasia necessitates a combined radiologic, hormonal, and clinical approach.

In the scenario where surgery is needed in a non-pregnant patient, a biopsy may be obtained. The classic histologic findings of pituitary hyperplasia involve a hypercellular, polymorphic population of cells with an enlarged, intact acinar network [9]. However, the findings from a biopsy may sometimes be limited due to regional variation in cell subtypes and inadequate localization of the specimen. Immunohistochemistry for pituitary hormones can also be performed if there is high suspicion based on hormone levels. From a radiologic perspective, typical features of pituitary hyperplasia on MRI include symmetrical and diffuse pituitary enlargement, homogenous gadolinium uptake, and similar intensity to gray matter [9]. Even with all of these features, diagnosis of pituitary hyperplasia can still be challenging since there are no well-defined guidelines.

Table 1. Timeline of patient's prolactin levels

Date	Prolactin level (ng/mL) (mcg/L)
First pregnancy: 16 weeks	467.3 (assay reference range, 10-209 ng/mL)
1 month postpartum: first pregnancy	16.2 (assay reference range, 3-30 ng/mL)
6 months postpartum: first pregnancy	27.0
16 months postpartum: second pregnancy	42.3
17 months postpartum: second pregnancy	25.5

Table 2. Timeline of patient's adenoma size on MRI brain

Date	Pituitary Adenoma Size
First pregnancy: 16 weeks	$1.8 \times 1.3 \times 1.1$ cm
2 months postpartum: first pregnancy	$2.0 \times 0.8 \times 1.0$ cm
Second pregnancy: 11 weeks	$1.3 \times 2.3 \times 0.7$ cm
Second pregnancy: 13 weeks	$1.3 \times 2.5 \times 1.3$ cm
16 months postpartum: second pregnancy	0.4 cm

Inoue et al discussed a case report of a pregnant woman presenting with blurry vision in her left eye during her thirtieth week of pregnancy [10]. Further testing revealed a prolactin level of 331.8 ng/mL (331.8 mcg/L), and MRI of the brain showed pituitary enlargement to $12 \times 10 \times 11$ mm with compression of the anterior optic chiasm. Sixteen weeks after delivery of her child, the patient's symptoms had completely resolved. Visual field testing was normal and repeat MRI brain demonstrated a normal sized pituitary with no compression of the optic chiasm. This particular case parallels the patient presented in our case, where her pituitary function and clinical symptoms resolved post-pregnancy.

The differential diagnosis of pituitary enlargement in pregnancy can be complex, considering MRI imaging is not specific enough to distinguish between each condition. In the example of our patient, it can be ascertained that pituitary hyperplasia was the most probable diagnosis. The patient did not have any hormonal deficits, and thus lymphocytic hypophysitis would be less likely. Furthermore, lymphocytic hypophysitis is typically associated with autoimmune diseases, which the patient did not have [10]. Even though prolactinomas are the most common reason for pituitary enlargement in pregnancy, an adenoma is less likely in this patient's case given the resolution of her symptoms and MRI findings after delivery. One would not expect a pituitary adenoma or a suprasellar meningioma to resolve postpartum if no intervention was pursued. Through exclusion of these disease processes, a diagnosis of physiologic pituitary hyperplasia was made in this patient. Although a pituitary biopsy through a neurosurgical procedure would be needed to make a definitive diagnosis [10], it was not necessary in this case as the patient symptomatically improved after delivery. Ultimately, it can be concluded that the diagnosis of pituitary hyperplasia requires an approach that integrates radiographic and clinical findings.

Learning Points

- Pregnant patients who present with vision changes and headaches should undergo visual field testing, evaluation of pituitary function, and MRI brain without contrast for further evaluation.
- Differential diagnoses of pituitary enlargement in pregnancy include pituitary hyperplasia, pituitary adenoma, and lymphocytic hypophysitis.
- Diagnosing pituitary hyperplasia involves an integration of radiologic, hormonal, and clinical findings.

Contributors

All authors made individual contributions to authorship. M.C.: involved in diagnosis and management of this patient and manuscript submission. R.M.: manuscript submission. All authors reviewed and approved the final draft

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Informed Patient Consent for Publication

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Data Availability Statement

Original data generated and analyzed during this study are included in this published article.

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