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Alterations in pituitary gland volume in polycystic ovary syndrome: a structural magnetic resonance imaging study

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ABSTRACT

The purpose of this prospectively designed cross-sectional observational study was to evaluate the effect of polycystic ovary syndrome (PCOS) on pituitary gland volume (PGV) under the hypothesis that endocrinologic changes may lead to morphologic changes of the pituitary gland. Twenty-six PCOS patients and 31 control subjects underwent magnetic resonance imaging (MRI) of the pituitary. Informed consent was obtained from all subjects. PGV was significantly larger in PCOS patients than in control subjects. Luteinizing hormone/follicle-stimulating hormone ratio was the only predictor of PGV. The association between pituitary gland enlargement and PCOS should be kept in mind when pituitary hypertrophy is detected on MRI.

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common female endocrinopathy, affecting 4–10% of the female population in their reproductive years [1]. It is a diverse and complex endocrine disorder with regard to clinical presentation and laboratory manifestations. The underlying defect in polycystic ovaries still remains unknown; however, there is a growing consensus that the key features are hyperandrogenism, hyperinsulinemia, and abnormal excessive serum luteinizing hormone (LH) concentrations [2].

PCOS is characterized by increased LH pulse amplitude and exaggerated LH responses to exogenous gonadotropin-releasing hormone (GnRH), whereas plasma follicle-stimulating hormone (FSH) levels are relatively low and the reason for hypersecretion of LH from the pituitary gland is not exactly known [1].

The pituitary gland is known to produce hormones such as LH and FSH, which control the activity of other endocrine glands. Moreover, based on previous magnetic resonance imaging (MRI) studies, the pituitary gland is a dynamic organ that changes in response to different influencing factors, such as age or stress. Its volume increases in puberty, in pregnancy, or with the administration of exogenous estrogens [3–5].

MRI is currently the technique best suited to examine the pituitary gland because of its high spatial and contrast resolution [6–8]. In healthy adults, the normal size of the pituitary gland is approximately 5–10 mm in height, 10 mm in length, and 10–15 mm in width [9].

It is well established that dysfunctions, such as major depressive disorder [10,11], psychosis [4], or primary hypothyroidism [5] leading to elevated adrenocorticotrophic hormone (ACTH) or thyroid-stimulating hormone (TSH) levels, are associated with an increased volume of the pituitary gland.

This study was initiated after we noted that some patients who had pituitary enlargement on their MRI scans had increased LH/FSH ratio. In the current study, we aimed to assess the impact of PCOS on pituitary gland volume (PGV) as measured by MRI under the hypothesis that the endocrinologic changes in PCOS can lead to morphologic changes, namely, hypertrophy of the pituitary gland. Also we aimed to investigate the associations among pituitary volume, mean ovarian volume, age, and hormonal parameters. To the best of our knowledge, this is the first study examining PGV in patients with PCOS.

2. Methods and materials

2.1. Patients

This prospectively designed cross-sectional observational study was carried out between January 2014 and May 2014 at our university hospital. Informed consent was obtained from all included subjects, and the study protocol was approved by the local Ethical Committee. All women

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with PCOS were recruited from among those who visited the Department of Obstetrics and Gynecology of our university hospital. The diagnosis was based on the Rotterdam criteria [12].

The patient group consisted of 26 normal-weight women with PCOS and 31 age-matched and body mass index (BMI)-matched normal-weight female volunteers with normal ovulating cycles (28±2 days, blood progesterone levels of >10 ng/ml in two consecutive cycles), no signs of hyperandrogenism, and normal ultrasonographic appearance of the ovaries.

BMI (kg/m^2) was calculated by dividing weight in kilograms (kg) by height in meters, squared (m^2) to assess obesity. The subjects with normal weight were included in the study because of the possible effect of obesity on hypothalamic–pituitary–adrenal axis [13]. None of the women studied had any systematic disease that could possibly affect their reproductive physiology. Also, all the study population had a normal brain MRI as evaluated by a clinical neuroradiologist. Exclusion criteria for both groups were as follows: age of <16 or >35 years, BMI of <18.5 kg/m^2 or >25 kg/m^2, galactorrhea, causes of increased pituitary volume such as pregnancy, administration of exogenous estrogens, hypothalamic and pituitary tumors, primary hypothyroidism, Addison's disease, psychosis, and severe major depression.

2.2. MRI data acquisition

All subjects were scanned with a 1.5-T Philips Intera MR unit (Philips Medical Systems, Amsterdam, The Netherlands) using a three-dimensional (3D) spoiled gradient echo sequence (T1-FFE) on the second to the fifth day of their menstrual cycle. T1-weighted images were obtained in the coronal plane with 1.5-mm contiguous sections. Image parameters were as follows: matrix size, 574×574; field of view, 20 cm, time to echo, 4,5 ms; time to repetition, 25 ms; flip angle, 12°. Additionally, a dual-spin echo sequence was used to obtain T2-weighted images in the axial plane to determine unexpected structural lesions.

2.3. Image analysis

Pituitary glands were manually traced on structural T1 sequence MRIs by one rater (EK) who was blinded to any identifying information such as the presence/absence of PCOS. Each pituitary gland was initially identified on the sagittal plane where anterior and posterior borders were marked and used to define the number of coronal slices containing the gland. Then, pituitary glands were traced in all coronal slices, where the pituitary gland could be visualized following clearly defined anatomical boundaries, i.e., diaphragma sellae, superiorly; the sphenoid sinus, inferiorly; and the cavernous sinuses, bilaterally (Fig. 1) [4,5,10,11]. An average of 7.08±1.05 slices was used. The infundibular stalk was excluded from the tracings, but the posterior pituitary was included [4,5,10,11].

Anatomical volume measurements of the pituitary gland were conducted on a DELL Precision Workstation. A segmentation process was performed in order to use images for 3D reconstruction. Collection of data and the segmentation process were performed using Mimics 10.1 software (Materialise, Leuven, Belgium). The segmentation process was converted to a 3D mesh model using an adapted marching cubes algorithm and the volume value was obtained (Fig. 1) [14]. Intracranial volumes were also computed. Measurements were performed by two radiologists with segmentation experience (EU and MBA). The overall Pearson correlation for inter-observer reliability, assessed on 10 randomly selected images, was 0.95 and the intrarater reliability based on 10 scans measured twice by the same rater (EU) was 0.97. All these values are well within acceptable limits.

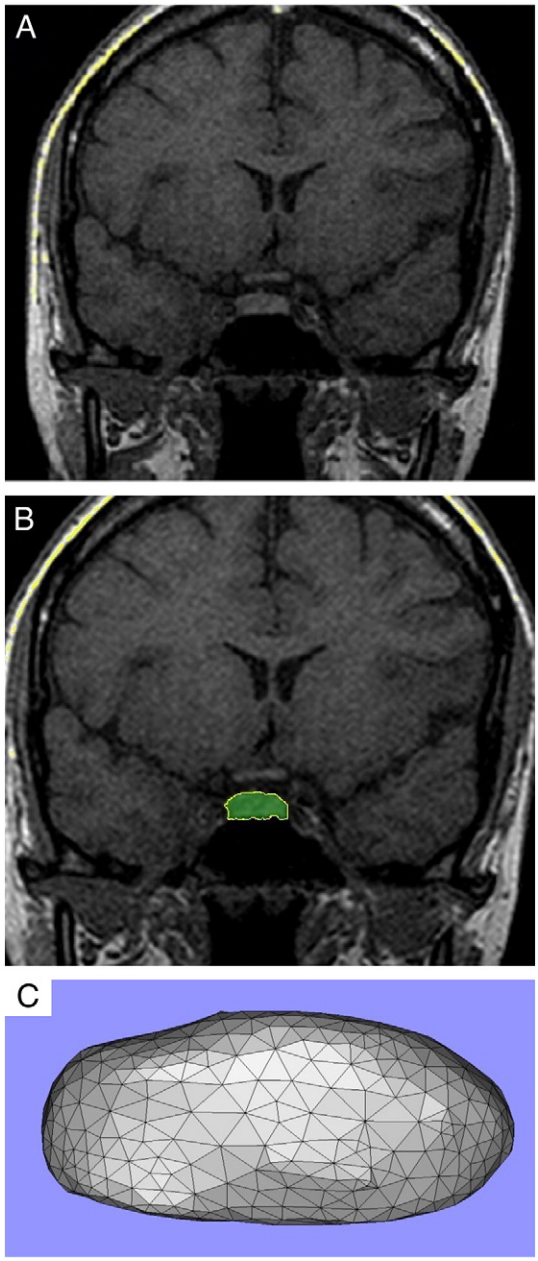

Fig. 1. (A) Each pituitary was manually traced on coronal slice of T1 sequence MRI. (B) A segmentation process was performed in order to use images for 3D reconstruction and was converted to a 3D mesh model using an adapted marching cubes algorithm.

2.4. Serum hormone level measurements

Fasting blood samples were collected for measurements of serum levels of estradiol, FSH, LH, prolactin, free testosterone (Ftest) and total testosterone (Ttest), and dehydroepiandrosterone sulfate (DHEAS) on days 2–5 (early follicular phase) of the spontaneous menstrual cycle.

2.5. Transvaginal/pelvic ultrasonography

Transvaginal/pelvic ultrasonography was also performed on the same day and the volume of each ovary and the number of follicles in each ovary were determined. Polycystic ovaries were diagnosed when ≥12 follicles with a diameter of 2–9 mm were present in one or both ovaries and/or when the ovarian volume was >10 cm^3. Each ovary was measured in three dimensions and the volumes were calculated