Diagnostic Evidence of Two Distinct Polycystic Ovarian Morphologies

To the Editor: Ultrasound evidence of polycystic ovarian morphology (PCOM) is of great importance to the field of reproductive medicine, as it is a key diagnostic marker in the evaluation of adult polycystic ovary syndrome (PCOS).[1] With the development of more sensitive sonographs, the observation of PCOM has become an established tool for assessing ovarian structure and function, allowing clinicians to discern distinctive patterns associated with reproductive disturbances. Originally observed during the 18th century,[2] the inclusion of PCOM within PCOS was laid out during the joint European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASMR) consensus meeting held in Rotterdam in 2003, and PCOM became one of the diagnostic criteria for PCOS diagnosis along with hyperandrogenism and the presence of an irregular menstrual cycle.[3] As at least 2 of these clinical signs must be present as per the Rotterdam criteria, which identified 4 PCOS phenotypes, 3 of which (A, B, and C) are hyperandrogenic and 1, phenotype D, which is normoandrogenic. This specific difference has led several authors to question whether normoandrogenic subjects should fall under the umbrella of PCOS,[4] with recent research focusing on unveiling the distinctive characteristics of the different phenotypes. However, how ultrasound aspects differ between phenotypes has never been investigated in detail. To date, studies have considered only quantitative aspects, such as ovarian volume and the number of follicles, finding no difference between PCOS phenotypes.

Discussion

Flashback to 1981—Swanson et al, describing the sonographic appearance of polycystic ovaries, concluded that: "it is not clear why some patients had uniformly sized cysts arranged in the periphery of the ovary, whereas others had cysts of varying size spread throughout the parenchyma of the ovary," thus observing an unexplained difference in the ovarian morphology among patients with PCOS.[5] Such information has fallen by the wayside, and the scientific community has progressively lost interest in investigating the sonographic features of different PCOS phenotypes.[6]

It is only recently that we stumbled upon a fascinating historical text, which reported 2 separate morphologies of PCOM taken from deceased PCOS patients.[7] In the upper image from 1956, we see the traditional "string of pearls" morphology, with ovarian cysts arranged peripherally in the ovarian cortex, while in the lower image from 1956 we see a random distribution of ovarian cysts within the stroma. Even though the authors were unable to pinpoint the cause for such difference, they observed that only the former was associated with signs of virilization in the subject.

These 2 pieces of evidence from the past are in concordance with the more recent stance of the EGOI-PCOS society that normoandrogenic and hyperandrogenic PCOS are 2 separate conditions, with a different pathological onset.[8] The basis of this theory is the metabolic involvement characterized by insulin resistance, hyperinsulinemia, or metabolic syndrome, which is routinely seen in hyperandrogenic patients but rarely in normoandrogenic PCOS patients. Excessive insulin levels can trigger androgen production, thus becoming the causative factor for the hyperandrogenism observed in PCOS patients. We theorized whether the presence or lack of hyperandrogenism may explain the difference in ovarian morphology, rather than influencing ovarian volume and the number of follicles. Support for this hypothesis exists within the literature. A 1991 study investigated the ovarian characteristics of female-to-male transexuals, observing arrested follicles arranged around the periphery of the ovary.[9] These patients had gone through androgen therapy, and it is possible these heightened levels of testosterone could be responsible for the observed morphological disturbances. Although not directly transferable to PCOS patients, this work provides a good model that may facilitate understanding of morphological changes of ovaries subjected to excess androgen levels.

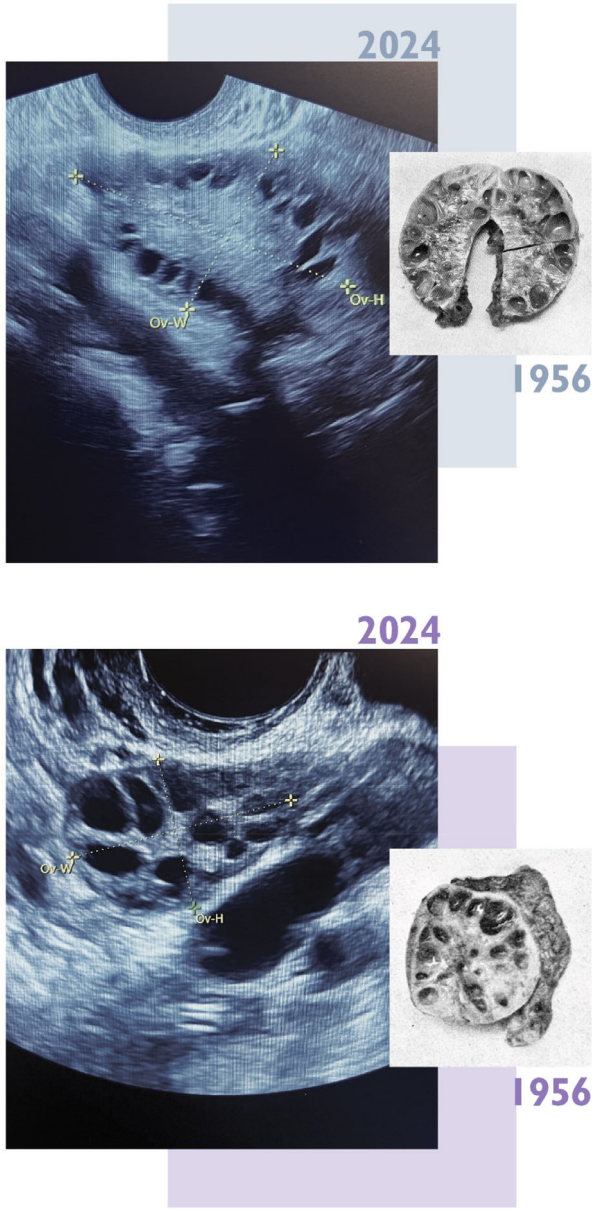
To explore this theory further, we retrospectively investigated ultrasounds taken from hyperandrogenic and normoandrogenic patients from our clinical practice. To our surprise, ovarian morphology differed between hyperandrogenic and normoandrogenic patients, and an exemplary representation for both groups is shown in Figure 1. Ultrasonography analysis of hyperandrogenic patients revealed the presence of

multiple small follicles (< 10 mm in size), arranged peripherally in the ovarian cortex with the typical "string of pearls" appearance (upper image 2024), in addition to a hyperechoic stroma at the center of the ovary.

Interestingly, the ultrasonographic analysis of the normoandrogenic revealed an altered ovarian appearance (lower image 2024). Notably while the cysts had a similar size to the hyperandrogenic group (<10 mm) they were not arranged at the edge of the ovary, and instead were randomly distributed in the stroma, which had an altered appearance. Moreover, the appearance of the stroma changed from hyperechoic to hypoechoic.

It is of our humble opinion that, when compared to the historical oophorectomies of J. Botella Llusia, the ultrasounds taken from our clinical practice demonstrate similar morphologies. While further study is clearly required, the presence of hyperandrogenism may give a plausible rationale as to why to the differences in patient morphologies. It is the intention of the authors to present these images in order to stimulate discussion within the community and encourage further research.

Figure 1. A comparison of historical oophorectomies of J. Botella Llusia (1956) and modern ultrasounds (2024), both of which demonstrate two distinct morphological patterns. The ovarian morphologies in the upper images show a classic string of pearls morphology with cysts arranged peripherally in the ovarian cortex. The ovarian morphologies in the lower images show a random distribution of ovarian cysts within the stroma.



Consent to Publish

The authors affirm that human research participants provided informed consent for publication of the images in Figure 1.

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