Hyperprolactinemia and Polycystic Ovary Syndrome: The Debate Continues

Dear Editor,

We read with interest the recent review article on the "Rational approach to the evaluation and management of patients with hyperprolactinemia" by Aldahmani *et al.*^[1] The review was comprehensive with several important points for practicing physicians. However, we noted that the authors have listed polycystic ovarian syndrome (PCOS) among the pathological causes of hyperprolactinemia. As PCOS is a condition commonly encountered by various practitioners in our region of the Middle East and North Africa, we felt that a comment is worthy to clarify a couple of controversial issues of practical importance.

A quick search of the PubMed Online database on June 30, 2020, using the search term ([PCOS OR "Polycystic Ovary Syndrome"] AND [Hyperprolactinemia OR hyperprolactinemia]) between 1978 to date retrieved 239 articles. In many of those studies, the authors have explored multiple plausible theories including GnRH pulsatility, decreased dopaminergic tone, hyperestrogenemia, increased angiogenesis, and pituitary growth factors, but no hypothesis proposed so far could ever be confirmed in large studies. Furthermore, PCOS and hyperprolactinemia are frequent endocrine diseases and a fortuitous association cannot be excluded.

Hyperprolactinemia and PCOS are the two most common endocrine etiologies of anovulation in women. The link between hyperprolactinemia and PCOS comes from old studies in which PCOS was diagnosed according to nonconsensual criteria and in which hyperprolactinemia was insufficiently explored in the light of recent knowledge. The gradual improvement of MRI techniques has allowed the detection of smaller adenoma. Interestingly, the Endocrine Society guidelines recommended to screen for causes of hyperprolactinemia and consider pituitary MRI in

cases of PCOS. In addition, data from the literature suggest that there is no hyperprolactinemia related to PCOS once hyperprolactinemia was rigorously explored in these women and other causes such as prolactinoma, drug-induced hyperprolactinemia, pregnancy, hypothyroidism, chronic renal failure, cirrhosis, chest wall lesions, and breast stimulation have been explored. Moreover, a recent study demonstrates that the elevation of prolactin linked to the presence of a macroprolactin is not uncommon in PCOS women and that it is therefore essential to be screened for.^[2] It is, therefore, essential to limit the misdiagnosis and thus avoid the unnecessary prescription of a pituitary MRI or even dopaminergic agonist treatment, as already pointed out by another study years ago.[3] Filho in 2007 clearly demonstrated that when the etiological investigation of hyperprolactinemia was rigorous, there was no hyperprolactinemia related to PCOS.[4]

In conclusion, it is prudent to infer that the link between hyperprolactinemia and PCOS is that of association rather than causation, until proven otherwise. The data from the literature are still insufficient to be conclusive on the subject, and a rigorous study on a larger cohort of PCOS women at different age categories is needed to confirm the relationship of both conditions.

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Compliance with ethical principles

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