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Perspective

The Neglected Informative Piece in the Pathogenesis of Polycystic Ovary Syndrome: Ovarian Incarceration and Progressive Strangulation

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Perspective

In 1935, Stein first described seven young women with amenorrhea and enlarged polycystic ovaries who had resumed regular menses after ovarian wedge resection **[1].** Having in mind and believing to an old saying "the first impression is the best", the initial descriptive sentence applied by Stein the Great, regarding the polycystic ovary syndrome (PCOS) was that the ovaries were characteristically large, shiny, smooth, pearly or oyster shell white, and that, cutting a wedge out of them resulted, although temporarily, in regular menses, ovulation and eventually pregnancy in tow. To approach the core concept in pathogenesis of PCOS, the very initial impression of Stein could be of utmost importance to unveil a mysterious medical entity. Based on available evidence, one could logically suggest that, there must be a powerful tissue growth factor or a cascade of synergistic growth factors ending up with the enlarged ovaries and markedly thickened sclerotic capsule. A pathologic process which could be, predictably, somehow interrupted by tearing open the sclerotic ovarian capsule. It is now fully established that, in a context of inherited insulin resistance colliding with physiologic insulin resistance of puberty and a permissive environmental trigger, the individual's serum is flooded with immense amount of insulin produced by structurally sound and functionally perfect pancreatic B-cells. This "strayed insulin**"** or better to say, "orphan signal**",** both directly, through its own receptor and indirectly, by specificity spillage over IGF-1 & 2 receptors, viciously attacks the whole cell lines of ovarian structures as a full-scale tissue growth factor and also an apoptosis demolishing substance **[2-9].** The very first outcome of this growth promoting chaos inside the ovaries is diffuse unleashed cell proliferation and disturbed cell refreshment and apoptosis. A doom and gloom pathologic event which causes a state of "cell senescence" and overt "oxidative stress", albeit, with different severity in various cell lines, defined by different rates of cell-surface insulin and IGFS receptor expression. Based on Hughesdon's pathologic descriptions of PCOS, the ovaries are characterized by average volume increase of almost 2.8 times normal and sub-cortical theca cells expansion of almost five folds, harboring large number (20-100) of growing follicles and atretic cysts as well. Contrary to the massive increase in intra-ovarian compartments, ovarian surface area is hardly doubled and the thickness of the tunica (capsule) is increased by 50 percent **[10].** Considering the above evidence, one would clearly figure out that the inner compartments of the ovaries, especially sub-cortical areas are rather more expanded compared to the surface area of the ovary. This is the neglected concept in PCOS pathogenesis; the disproportionate proliferation and expansion of ovarian compartments. Although the tunica thickness is also increased by roughly 50%, but the noble issue here to be perceived is that, it is not only enough to keep pace with unleashed ovarian growth, but also, increasingly prevents the ovarian expansion by the thick and tight ovarian capsule, with rather malformed and somehow maleficent fibrous tissue; added to this is marked edema coming out of smoldering oxidative stress and ensuing inflammatory reactions. That is why the ovaries in PCOS look smooth and pearly-white. To be exact, the pale, pearly white and faintly cyanotic appearance of ovaries in a "deep-seated" PCOS is the result of three different but related phenomena:

a) Thickened and sclerotic tunica

b) Condensation and consolidation of sub-cortical and to a lesser extent inner layers of ovarian tissues

c) Decreased overall ovarian circulation, particularly at the microcirculation level due to less extensible capsule, causing a state of poor tissue oxygenation and tissue pallor

The net effect of reduced ovarian surface area in conjunction with pathologically thick, poorly distensible tunica is to prevent the ovary from proper expansion in response to insulin-driven massive proliferation of inner compartments. This would understandably result in a progressive state of ovarian entrapment, incarceration and slow but progressive strangulation. Increased intra ovarian pressure insensibly impedes the ambient blood circulation and tissue oxygenation. The true picture or better to say the fully-featured PCOS is displayed at this stage of disease process. In response to this oxidative stress, a wide variety of hypoxia-inducible growth factor genes are also expressed; a grave vicious cycle of cell-proliferation and tissue expansion culminating in further restriction and progressive suffocation of the ovaries. The different phenotypes of PCOS, meaningfully defined by Azziz, are in fact, the above mentioned developmental stages of the disorder with respect to the degree of ovarian incarceration. Markedly deviated intra-ovarian signal-receptor interactions gives rise to a state of ovarian testiculization with massive in-situ androgen production and anti-mullerian hormone (AMH) gene expression. This might be the noble philosophy behind the high serum concentration of AMH; a serum marker that might be considered as an excellent indicator of PCOS gravity.

Contemplating the presented idea, one would be able to clearly

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explain why wedge resection or laser drilling of ovaries came out as the first and probably foremost method for management of ovulation induction and infertility in sever PCOS, and also explain the philosophy behind the furious and ferocious nature of the ovaries in response to ovulation induction with FSH or even clomiphene citrate; the well-known medical emergency coined as ovarian hyper stimulation syndrome. For years, it was erroneously believed that thick and sclerotic ovarian capsule acts as a mechanical barrier to successful ovulation, but, what I am trying to address is that the thickened tunica entraps, incarcerates and finally strangulates the growing ovaries. As a matter of fact, wedge resection or laser drilling, temporarily depressurizes the suffocating ovaries and aborts the doomed downhill pathologic process culminating in short-lived amelioration of ovarian function.

Considering the proposed hypothesis, one might suggest a major break- through in management of infertility in PCOS, that is, medical nutritional therapy, increased physical activity plus long-term and full-doses of insulin sensitizers accompanied, at the end, by "laparoscopic topography-assisted laser peeling" of the ovaries; a procedure that involves bilateral extensive laser-assisted ovarian tunicamileusis similar to "LASIK" technique being applied by ophthalmologists for correction of refractory defects of the cornea.

References

1. Stein IF. Leventhal NL. Amenorrhea associated with bilateral poly cystic ovaries. AM J Obstet Gynecol. 1935; 29: 181.
2. Dunaif A. Insulin resistance and poly cystic ovary syndrome: mechanism and implications for Pathogenesis. Endocr Rev. 1997; 18: 774-800.
3. Burghea GA, Givens JR, Ketabchi AE. Correlation of hyperandrogenism and hyperinsulinemia in poly cystic ovarian disease. J clin Endocrino Metab. 1980; 50: 113-116.
4. Devgarte CM, Bartolucci AA, Azziz R. Prevalence of insulin resistance in the poly cystic ovary syndrome using the homeostasis model assessment. Fert steril. 2005; 83: 1454-1460.
5. Velazquez EM, Mendosa S. Hamer T, Sosa F, Glueck CJ. Metformin therapy in poly cystic ovary syndrome reduces hyperinsulinemia, insulin resistance, Hyperandrogenemia, and systolic blood pressure, while facilitating normal menses and pregnancy. Metabolism. 1994; 43: 647-654.
6. Kwintkiewicz J, Giudice LC. The interplay of insulin-like growth factors, gonadotropins, and endocrine disruptors in ovarian follicular developmental function. Semin Reprod Med. 2009; 27: 43-51.
7. Adashi EY, Resnick CE, D'Ercole AJ, Svoboda ME, Van Wyk JJ, et al. Insulin-like growth factor as intraovarian regulator of granulose cell growth and function. Endocr Rev.1985; 6: 400-420.
8. Tavakolian Arjmand A, Nouri M, Tavakolian Arjmand S. Surprisingly low infertility rate in married type2 diabetes women: a rather curious paradox to the current opinion of insulin resistance as the joint pathogenesis of poly cystic ovary syndrome and type 2 diabetes mellitus. Diabetes Metab Syndr. 2015; 9: 201-214.
9. Duleba AJ, Spaczynski RZ, Olive DL. Insulin and insulin-like growth factor-1 stimulate the proliferation of human theca-interstitial cell. Fertil Steril. 1998; 69: 335-340.
10. Hughesdon PE. Morphology and morphogenesis of the Stein-Leventhal ovary and of so-called hyperthecosis. Obstet Gynecol Survey. 1982; 37: 59-77.

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