



Correspondence

The vanishing follicle in women aged over forty: Premature, mechanical, LH-independent luteinization may reflect oocyte–follicle low quality?

Healthy ovulation in a natural cycle is triggered by a sharp rise in LH (LH surge). In ART cycle, hCG is used as an LH-surrogate. In order to prevent premature LH surge (and cycle cancellation), GnRH analogs (agonists or antagonists) are used. Indeed, LH surge is reliably prevented, setting the ground for precise ovulation timing with hCG. However, clinical experience indicates that premature luteinization does occur, even when frequent LH measurements rule out an endogenous LH surge. The population mostly affected by this phenomenon is patients in their 40s. A typical scenario is of a 40+ year old patient with 2–3 mature follicles (>17 mm in diameter), and compatible hormonal profile (normal LH levels), who is given a bolus of hCG as trigger the same day. However, on day of oocyte retrieval, some, or all of the follicles disappear, with concomitant appearance of free fluid in the Douglas pouch. Detailed review of hormonal records and patient compliance typically yields no apparent mistakes. Alternatively, during oocyte pick-up, a follicle bursts due to a moderate pressure on the abdominal wall in an effort to bring the ovary closer to the ultrasound transducer.

To the best of my knowledge, ‘‘vanishing follicles’’ have not been described in the medical literature; therefore, the mechanism remains speculative. It is well established that oocyte quality deteriorates with age, especially as a woman enters her fifth decade of life. It would seem surprising that other components of the follicu-

lar–oocyte unit would retain their young age quality. More likely, granulosa and theca cell layers, show signs of ageing in parallel to diminished oocyte quality. For the basement membrane, ageing may manifest as yielding to surrounding tissue pressure as the follicle grows, resulting in mechanical, LH or hCG-independent rupture of the follicle. Such rupture leads to follicular partial luteinization, and of course, will not produce a fertilizable oocyte. Clinically, the growing follicles disappear without apparent rise in endogenous LH, while progesterone levels increase, albeit not to the same degree as expected following healthy luteinization. In the following cycle, it would seem wise to trigger ovulation before the follicles reach their spontaneous rupture diameter, though, based on personal experience, the chance for healthy pregnancy is very low.

In summary, patients over 40 years of age represent about 25% of ART activity in many centers. The ‘‘vanishing follicles’’ phenomenon is not rare in that population, probably reflecting diminished quality and ageing of the growing follicles.

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