Spontaneous Pregnancy and Unexplained Infertility: A Gift With Many Whys

Dear Editor,

Infertility is defined as the inability to conceive after 12 months of unprotected sexual intercourse. The dualism between the so-called "Psychogenic hypothesis" and the hypothesis of "Psychological consequences of infertility" has been solved with the proposal of an interactive and bidirectional relationship between infertility and psychosocial diseases.[1] Infertility itself can cause severe stress on both partners and start a vicious cycle resulting in the decreasing likelihood of pregnancy and even of treatment success. The infertility treatment could be responsible for a major impairment of the sex life because it frequently digs into the intimacy of the couple. Moreover the "emotional rollercoaster" related to the treatment is felt, especially by the women, to be extremely mentally stressful. Sexual intercourse can lose its spontaneity because it is aimed at "baby-making" and it is strictly restricted to "fertile" days. Sexuality can be therefore deprived of its recreative and erotic value and subordinated to the direct goal of pregnancy. Furthermore, sexual intercourse may be increasingly associated with a sense of failure, affecting even the patient's image of his/her own body. According to a recent meta-analysis, sexual disorders - depending on both infertility itself and infertility diagnosis and treatment - are common in infertile couples, with women more affected than men.[2]

Little is known about spontaneous pregnancy after infertility therapy either successful or failed. Couples dealing with long-term involuntary childlessness usually consider *in-vitro* fertilization (IVF) treatments as a final option but a relative high incidence of treatment-independent pregnancies especially in couples with unexplained infertility is frequently reported. Hennely *et al.*, analyzed the spontaneous conception rate after a successful IVF cycle. In this retrospective study 106 of 513 (20.7%) couples obtained a spontaneous pregnancy two years after Assisted Reproductive Technology (ART) birth success.^[3] The likelihood of spontaneous conception was higher in younger women and was strongly connected to the duration of infertility. Indeed, women who have been

infertile for a shorter period more likely achieved a spontaneous pregnancy. In a recent study, [4] 2134 couples were retrospectively analyzed in order to estimate the frequency of spontaneous pregnancies among couples previously treated by IVF. The spontaneous pregnancy rate was 17% among couples who previously achieved pregnancy through ART and 24% among couples who conceived spontaneously after unsuccessful medical treatment. Among both groups, almost 60% of the spontaneous pregnancies occurred two to three years after the last IVF transfer. The proportion of spontaneous pregnancies was higher in couples with unexplained infertility, suggesting a better fertility prognosis compared with couples whose infertility is of known origin. Spontaneous conception in couples with unexplained infertility could be related either to the stress relief after the decision to abandon the therapy or to the placebo effect after being placed in the waiting list before starting the treatment. Treatment-independent pregnancies occur sometimes after a successful ART procedure or after adoption, suggesting the important impact of psychological factors on fertility.

Nevertheless spontaneous pregnancy in couples diagnosed with unexplained infertility remains nowadays a mysterious event. Many questions are still unanswered. Is spontaneous conception connected to a previous ovarian stimulation, necessary in some IVF cycles? Could the previous pregnancy be responsible for endocrine changes that increase the reproductive potential? Or is it mainly related to the stress relief that undoubtedly occurs after achieving parenthood? A lot of work in that direction needs to be done. It remains however important to remind to every couple starting an infertility treatment that spontaneous conception before, during or after ART-procedures has to be taken into account!

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