

## Unnecessary life threatening complications after IVF in mixed connective tissue disease

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I have read with great interest the recent demonstrative case report by Sioulas & Gracia on ovarian stimulation and embryo banking for fertility preservation in a woman with severe mixed connective tissue disease [MCTD] [1], and congratulate the authors for their integrity and self criticism. The authors correctly emphasize the life threatening complications associated with pulmonary hypertension and IVF in MCTD, as dramatically demonstrated by their case report.

However, one important point has been overlooked by the authors and should be mentioned. Gonadotropin releasing hormone agonists [GnRH-a] may possibly provide ovarian protection against the gonadotoxic effect of chemotherapy either by ovarian suppression and/or by decreasing ovarian perfusion as it simulates a reversible prepubertal hypoestrogenic hormonal milieu, or by possible other mechanisms [2]. We have preliminarily reported, 10 years ago, 5 cases of POF in 9 SLE patients in the control group, while none of the 8 patients treated with GnRH-a suffered POF (3). Similarly, in another study, Somers and coworkers (4) described that only one woman among 20 SLE female patients in the GnRH-a group developed POF compared with 6/20 (30 %) among the controls ( $P < 0.05$ ). In a larger group of SLE patients we have found that GnRH-a decreases cyclophosphamide-

associated gonadotoxicity and POF in young women with systemic lupus erythematosus and other autoimmune diseases. Manger and coworkers [3] started a RCT (the PREGO study) a few years ago, and we are all looking forward to its results. Therefore this treatment should be considered and recommended to every young woman before gonadotoxic chemotherapy. The authors [1] mention the possibility "...that GnRH may exacerbate autoimmune diseases, an association that merits further research". The answer to their raised question has been supplied by others and by us [2, 4, 5]. None of our SLE or MCTD patients [2, 4] treated with GnRH-a developed any exacerbation, similar to the experience of others [5]. It may be concluded that in high risk MCTD or SLE patients, especially those with pulmonary hypertension, fertility preservation before cyclophosphamide pulses could be offered with GnRH-a and not ovarian hyperstimulation for IVF.

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