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# “Heart-Breaking” Assisted Reproductive Technology: Successful Pregnancy After an Intracytoplasmic Sperm Injection Procedure Complicated by Acute Myocardial Infarction of the Male Partner

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## ABSTRACT

Sometimes even conditions that could be prologue to tragedy may turn out to have a happy ending. The couple we had in care was composed by a 36 years old woman in general good health and a 42 years old man in good conditions despite being an average smoker and having arterial hypertension. Since first level Assisted Reproductive Technology (ART) was unsuccessful, we proceeded to Intracytoplasmic Sperm Injection (ICSI) with the indication of mild male factor infertility. On day 9 of the second ICSI cycle, the male partner complained typical myocardial pain. The patient was hospitalized for a myocardial infarction and underwent a percutaneous trans-luminal coronary angioplasty during which three stents were placed. We deemed relevant reporting this case: despite the male partner of this couple experienced the misfortune of a myocardial infarction during a cycle of ART, he still successfully accomplished to collect his semen for oocytes fecundation. The cycle was therefore happily brought to an end with the implantation and the on-going progression of a dichorionic diamniotic twin pregnancy.

**Keywords:** Assisted reproductive technology; Plasmic sperm injection; Acute myocardial infarction

## Introduction

In high-income countries, approximately 15% of heterosexual couples experience difficulties conceiving when pregnancy is desired, and in up to half of these couples, infertility is attributable to the male partner [1]. Medical science still has problems to determine when and whether a male problem is the primary or contributing cause in fertility. Thus any factor that may affect sperm quality is relevant for any attempt at pregnancy. Furthermore, it is impossible not to consider also

male sexual difficulties when dealing with a couple with problems in conceiving naturally. Results from the National Health and Social Life Survey indicate that 10.4% of men aged 18–59 years report to have had trouble in achieving or maintaining an erection over the past 12 months [2]. In this prospective, the bio-psychosocial model is the current gold standard for assessing and treating sexual dysfunction in men and women. In brief, this model proposes an integrative look at the medical and non-medical (psychological and social) factors contributing to sexual problems as well as an integrative strategy for treatment. Medical contributions to sexual dysfunction within this model may be either specific diseases or conditions (such as diabetes) that have a direct pathophysiologic effect on sexual functioning, or the indirect medical factors such as chronic pain or chronic obstructive pulmonary disease, which may also adversely impact on sexual functioning. The non-medical factors within this model are either individual factors (personality, sexual history, and comorbid mental health problems), or relationship/partnership factors (quality of partnership as well as partner’s sexual and mental health concerns), or environmental factors (conditions under which sex occurs) [3]. Psychology is so interconnected with male sexuality that according to many studies, not only obvious mental diseases like substance abuse, depression, general anxiety disorder, obsessive compulsive disorders and post-traumatic stress disorders can cause sexual dysfunction; but also certain personality styles seem to increase a man’s vulnerability to such issues [2]. Furthermore a 2011 meta-analysis of 57 cross-sectional multinational studies (including 29914 patients) showed that psychological stress could lower sperm density and sperm progressive motility and increase abnormal sperm, linking psychology not only to erectile dysfunctions, but also to the wider field of infertility in general [4]. Such findings are explained by the fact that circulating levels of glucocorticoids increase stress and affect gonadal function at multiple levels in the hypo-thalamo-pituitary-gonadal axis, by decreasing the synthesis and release of gonadotropin-releasing hormone

(GnRH) in the hypothalamus, by inhibiting synthesis and release of LH and FSH in the pituitary gland, and by directly modulating steroidogenesis and/or gametogenesis in the testes or ovaries [4,5].

A change in chronic stress conditions and the motivation to reach a certain goal could be relevant, (although still debated) in the treatment of many disease states. Such findings not only apply to reproductive medicine, but also to cardiovascular medicine and oncology [5-9].

In the light of such background, we want to report the case of an infertile couple in which what seemed to be a normal case of mild male factor infertility, was indeed complicated by the myocardial infarction of the male spouse. Nevertheless, the high quality standard cares and the motivation of this man allowed him to not only get through this acute fatal event, but also to successfully conceive a couple of twins.

## Case Description

The male partner was 42 years old and the female partner was 36. They came all the way through Italy, to receive the cares of Fertility Centre of tertiary care hospital humanities Research Hospital, because of a problem of idiopathic infertility with a suspect of a mild male factor. The couple had been searching a pregnancy since 2012.

The female partner was of normal weight, non-smoker and in general good health. She also showed good ovarian reserve indexes: 24 antral follicles, FSH 5.5 IU/mL and AMH 5.1 ng/mL. Before the start of the stimulation cycle she was cured for a mild hypothyroidism (TSH 3.5 mIU/L) with Levothyroxine 50 mcg/die and underwent a hysteroscopy polypectomy in the past.

The male partner was overweight (BMI 28) and showed no systemic pathology and the beginning of the cycle, despite being an average smoker (around 20 pack years) and having a mild arterial hypertension still untreated.

After three cycles of unsuccessful IUI, ICSI was chosen. In July 2015 they underwent an ICSI procedure from which three blastocysts were cry conserved and then transferred, resulting in an abortion at the 8<sup>th</sup> week and in a biochemical pregnancy (bHCG maximum value was 42). On July 2015 his sperm analysis, collected for the first ICSI procedure was of borderline quality, with a total progressive motility count (TPMC) of 6.500.000 (basal spermatozoa count of 13.000.000/mL, basal progressive motility 25% and normal forms 2%).

In March 2016 a second ICSI procedure was started and the couple was staying close to our centre for follicle monitoring. The woman received oral oestrogen-progestin and, after checking for proper suppression, controlled ovarian stimulation was initiated with recombinant FSH (rFSH) (Gonal F; Serono Inc.) at a dose of 125 IU daily the first 9 days and then 150 IU until the 12<sup>th</sup> day of the cycle. A GnRH antagonist (Orgalutran, MSD) was started on day 6 at a dose of 250 IU daily.

After 12 days of induction she had 14 follicles of more than 12 mm in diameter and average level of estradiol (1673 pg/mL) and progesterone level (1.8 ng/mL). In order to reduce the Ovarian

Hyper stimulation Syndrome (OHSS) risk, the ovulation was induced with a GnRH agonist (Decapeptyl 0.2 mg in single administration) 32 hours before oocyte retrieval.

Although the cycle was going well on the female side, on day 9 of follicle study, the male partner complained typical myocardial pain and an ECG recorded at the emergency room of our hospital showed an ST elevation in inferior myocardial location. At the coronary angiography was found a focal eccentric severe 90% stenosis in medial-proximal segment of the anterior inter-ventricular branch at the bifurcation with II diagonal branch, a focal 70% stenosis of the marginal branch of the left coronary artery and a pre-occlusive 95% stenosis in proximal location of right coronary artery. The patient then underwent a percutaneous trans-luminal coronary angioplasty during which three stents were placed in proximal right coronary artery (Ultimaster 4.0/18 mm and spot stent Ultimaster 4.0/9 mm), medial-proximal anterior inter-ventricular (Xience Alpine 3.0/18 mm) and circumflex-marginal coronary artery (Xience Alpine 3.5/18 mm).

After the reperfusion procedure an ECG was recorded still showing small q waves in inferior location with minimal persistence of ST elevation. An echocardiogram performed 5 days later showed a globally conserved systolic function (FE>55%) a mild hypertrophy of the inter-ventricular septum (11-12 mm) and hypokinesia of the inferior myocardial wall (the basal segment was found to be a kinetic), of the medial-distal portion of the posterior wall and of basal segment of the posterior septum. A carotid ultrasound imaging and Doppler ultrasound of the lower limbs were performed and both the exams were negative.

At discharge the patient therapy consisted in Prasugrel 10 mg/die, Acetylsalicylic acid 100 mg/die, Omeprazole 20 mg/die, Alprazolam 0.25 mg/die, Metoprolol 50 mg/die, Atrovastatine 80 mg/die and Enalapril 10 mg/die.

Even if such event could have stopped the ART cycle due to the impossibility of male semen production, it didn't stop the male partner of our couple. On the second last day of his hospitalization, and day 14 of the ICSI cycle, the man collected his semen for oocyte fertilization. The seminogram resulted of similar quality to that generated the year before: with a TPMC of 10.000.000. Under deep sedation 14 oocytes were retrieved and we decided for a rescue therapy with active luteal phase support (HCG 1500 UI single dose, Estradiol 4 mg and Progesterone 400 mg daily). 9 oocytes were fertilized of which 5 didn't evolve, 2 embryos were transferred in day 3 and 2 blastocysts were frozen. Thirteen days later bHCG monitoring showed a successful level of 668 and 4 days later a promising rise to 3560. Four weeks after embryo transfer, trans-vaginal scan showed a dichorionic diamniotic twin pregnancy with 2 viable embryos. At the 20<sup>th</sup> week of pregnancy DNA fetal test, fetal translucence test had already been performed both with negative result. Hoping for an uneventful and at term delivery we continue to follow the pregnancy evolution.

## Discussion

More and more patients come at humanities Fertility Centre showing similar features to those of our male patient. Being more than 40 years old, chronic stress and comorbidities are now part of the general anamnesis of an increasing number of patients asking for assisted reproductive technology (ART). Postponement of attempts to conceive not only affects fertility because of direct age related effects, but also through age related comorbidities. Delayed parenthood reduces the chance that both parents will survive until their children reach adulthood, marry or become parents themselves, and this counteract to some extent the effects of longer life, which increased the number of generations surviving at any one point in time [10].

Furthermore chronic psychological stress conditions, so common in nowadays society, not only affects fertility itself but may also participate to the genesis of many chronic diseases that today affect ageing population [4,5,11].

Despite the hints to negative sides of modern society, our case also shows the positive results of technological and organizational advancements in nowadays health care.

In particular the advancement in therapeutic techniques and the gathering of high level integrated health services in humanities Research Hospital (a highly specialized hospital, research and teaching centre humanities University), assures to its patients the best possible medical cares.

Built around centres for the prevention and treatment of cancer, cardiovascular, neurological and orthopaedic disease together with an Ophthalmic Centre and Fertility Centre humanities also operates a highly specialized Emergency Department. In addition to these humanities is also the first Italian hospital quality certified by Joint Commission International and is accredited by the National Health Care System.

In conclusion, the reproductive medicine physician takes care of couples who may show health problems others than those related to fertility at when they attempt conception, thus we must address such patients to the most appropriate care centres for comorbidities as soon they show up. In this sense is crucial for fertility centres to be part of structures, like humanities, that offer many high level specialities gathered all together.

What in fact actually saved our patient was the possibility to have access to specialized cares in a highly integrated centre. Indeed, besides being able to provide him life-saving cares promptly and appropriately, such tertiary care hospital was also able to fulfil the greatest wish of this couple: to build a family.

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