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个案与短篇

体外受精-胚胎移植术后重度卵巢过度刺激综合征、双胎、胎儿畸形引产1例

李 敏,俞炽阳,李玉艳,刘永刚,李明舵,何 畏 (400038 重庆,第三军医大学西南医院妇产科,生殖医学中心)

[**关键词**] 辅助生殖技术;肺结核;卵巢过度刺激综合征;多胎妊娠;胎儿畸形
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辅助生殖技术(assisted reproductive technology, ART)临床应用至今30余年,其安全性近年来越来越受到生殖医学界关注,卵巢过度刺激综合征、多胎妊娠都是常见并发症。本研究报告1例体外受精-胚胎移植(*in vitro* fertilisation and embryo transplantation, IVF-ET)患者,术后并发重度卵巢过度刺激综合征(ovarian hyper-stimulation syndrome, OHSS)、肺结核、双胎、胎儿无羊水引产,并分析辅助生殖技术的安全性。

1 临床资料

患者,女性,28岁,BMI 19.15,因"原发不孕4年,双侧输卵管梗阻2年"于2010年8月来我院妇产科生殖医学中心行助孕治疗,既往有胸膜炎病史,常规辅助检查未发现明显禁忌证。给予GnRHa长方案,控制性超促排卵(controlled ovarian hyperstimulation, COH) 11 d,获卵9个,行常规IVF-ET,移植2个胚胎,胚胎移植术后11 d因"腹胀"住院治疗,诊断重度OHSS,予以补液、白蛋白、胶体液维持血浆胶渗压,维持电解质体液平衡,好转出院;移植术后14 d血HCG 590.48 mU/mL,继续黄体支持,胚胎移植术后33 d超声提示宫内双活胎,以后常规黄体支持至孕11周。孕20周左右无明显诱因出现发热、咳嗽、盗汗住院治疗,经院内会诊,考虑肺结核,予以异烟肼、利福霉素、乙胺丁醇抗结核治疗1个月余自行停药,孕22^{+3}周彩超提示宫内双活胎,无羊水,F2双肾实质回声增强,F1双肾未显示,行引产术,患者夫妇拒绝行胎儿脐血染色体核型检查及胎儿尸体解剖。

2 讨论

随着人类辅助生殖技术的不断发展,IVF目前的安全性受到广泛的关注,如何对IVF患者进行充分术前评估,尽量减少其并发症已成为生殖界高度重视的问题。结核是导致女性盆腔输卵管性因素不孕的重要原因,国内外已有学者报道IVF术后诱发结核病灶再活动[1],本研究报告此例IVF-ET助孕患者,术前检查胸片、血沉提示正常,其他孕前常规检查项目均未发现明显异常,临床超促排卵用药方案合理,获卵数适中,HCG用药后13 d发生重度OHSS,为晚发型,分析原因主要与妊娠后血清中高水平HCG持续刺激卵巢有关;另患者体型瘦小,也是OHSS高危因素。本例患者后继发结核活动,与妊娠时期免疫抑制,机体抵抗力降低,使机体内原有的陈旧病灶再活动有关,也可能与OHSS后大量血清白蛋白丢失,机体抵抗力降低有一定关系。

IVF是辅助生殖中最常用的技术,其子代较自然受孕出生子代暴露于更多的危险因素中,如大剂量促排卵药物的应用,体外对精子和卵子的人为操作,各种培养液对配子的影响。目前有研究认为ART出生儿不良妊娠结局增高,子代先天畸形的发生率高于自然受孕子代[2],2013年,Hansen等[3]Meta分析也认为ART子代出生缺陷率高于自然受孕子代,但也有研究认为,ART子代出生缺陷率的增高主要与亲代不孕病因本身有

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[**通信作者**] 何 畏,E-mail:anyhewei@163.com
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关,目前为止,并没有明确的证据说明ART的操作过程与出生缺陷有相关性,仍有待于更深入的研究。本例患者双胎合并胎儿畸形引产,不能排除与ART技术的相关性,也可能与辅助生殖另一重要并发症多胎妊娠有关,归因于多个胚胎的移植,据统计,经过ART技术出生的多胎妊娠率高达22.7%~31.7%,2013年,Vakrilova等[4]的研究认为,IVF子代极低体重儿畸形及生存结局与自然受孕子代没有差异,多胎妊娠是其主要原因,即使在自然妊娠中,多胎妊娠本身可能合并很多孕期和分娩的异常,如早产、低体重儿,先天畸形等。本例患者IVF术后并发OHSS、多胎,继发肺结核,口服抗结核药物治疗,异烟肼(C级)、利福霉素(C级)、乙胺丁醇(B级)等一线抗结核药物在妊娠期的应用FDA已有明确的分级,动物实验有致畸,人类尚无研究,WHO文献报道也尚未明确其对人类的致畸效应,证实其在妊娠期使用的安全性[5],但也不能完全排除抗结核药物的不良影响。

本研究提示我们,IVF治疗前、治疗中均应对患者病情充分评估,对结核复发高危患者应及早发现和干预,必要时行全胚胎冷冻,待病情稳定后行冻融胚胎移植,减少母婴孕期风险,同时尽量减少ART相关并发症,尤以OHSS和多胎妊娠,从而提高ART技术的安全性。

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