Ectopic pregnancy without therapy despite previous failure with in vitro fertilization and a male partner with an extremely low hypoosmotic swelling test score: Case report

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Summary

Purpose: To record an ectopic pregnancy achieved through natural intercourse despite previous implantation failure following in vitro fertilization-embryo transfer (IVF-ET) with a male partner who had an extremely low hypoosmotic swelling test (HOST) score.

Methods: A hypoosmotic swelling test was performed for the first time on the semen of a male partner who was advised previously that his sperm specimen was perfectly normal.

Results: The standard semen parameters except normal morphology with strict criteria were normal. The HOST score was 33%.

Conclusions: The HOST score of 33% was the lowest level recorded in anyone achieving a pregnancy. The fact that it resulted in an ectopic pregnancy in a woman with apparently normal tubes and failure to achieve an intrauterine pregnancy despite transfer of 13 embryos with good morphology may suggest that the low HOST score inhibits the blastocyst from implanting in the uterus rather than from failure to develop a blastocyst from a multi-cell embryo.

Key words: Implantation defect; Male factor; Tubal pregnancy.

Introduction

The hypoosmotic swelling test (HOST) is a measurement of the functional integrity of the sperm membrane [1]. The HOST, when subnormal, has proven to be a much better predictor of the subnormal male than either motile density or strict morphology [2]. In the aforementioned study there were no pregnancies in the wives of 14 males with HOST scores < 50% who were undergoing in vitro fertilization-embryo transfer (IVF-ET) [2].

In one matched control study there was only one live pregnancy in 27 IVF-ET cycles (3.7%) with low HOST scores [3]. There were no live pregnancies after 22 IVF-ET cycles in a study comparing IVF outcome in women sharing oocytes where one male partner had a normal HOST score and the other male partner a subnormal one [4]. Interestingly, 11 of 22 achieved a pregnancy when the HOST was normal [4]. An in vivo study found no pregnancies in 13 couples where the HOST score was < 50% despite eight months of apparently completely normal cycles [5].

The case presented here is the first ectopic pregnancy to date reported when the male partner's HOST score was < 50%.

Case report

A-43-year old woman recently remarried a 39-year-old man and they attempted to have a child together. The female partner had one previous pregnancy at age 19 with her first husband but used oral contraceptives thereafter. The male partner had had been previously married but he and his former wife failed to conceive over a 3-year period of time. The previous physicians thought the problem was a female factor since the male partner's sperm evaluation was considered perfectly normal.

When they failed to conceive after several months they were evaluated by a reproductive endocrinologist who suggested IVF-ET because of the age of the female partner. A hysterosalpingogram showed bilateral tubal patency and a normal uterine cavity. She failed to conceive following her first IVF-ET cycle at age 42 despite the transfer of six embryos on day 3 with good morphology including three 8-cell embryos. A similar IVF attempt also failed when she just turned age 43 where seven embryos were transferred including three 7-cell and one 8-cell embryo. The oocytes had been fertilized by conventional insemination and not intracytoplasmic sperm injection (ICSI). The fertilization rates were over 75% in both cycles.

Four months after her last unsuccessful IVF attempt she conceived naturally but unfortunately the pregnancy was ectopic and a right salpingectomy was performed. The left tube looked perfectly normal as did the right tube with the exception of the ectopic pregnancy.

She came to the Cooper Center for IVF three months following the ectopic pregnancy for another opinion. A repeat semen analysis showed a volume of 5.7 ml, the sperm concentration of 43.2 x 10^6/ml with 55% motility. However, only 5.5% showed rapid linear motion. The normal morphology using strict criteria was only 4%. Antisperm antibody levels were normal (5% IgG, and 15% IgA). However, the HOST score was very subnormal at 33%.

Discussion

Previous studies showed that the fertilization of oocytes with sperm with HOST scores < 50% does not have an adverse affect on fertilization [2-8]. Thus it was not surprising that the fertilization rates were so normal nor, based on previous studies, was it surprising that the embryo morphology was so good [4].

However it was not surprising that the patient failed to conceive despite the transfer of 13 embryos (the equiva-

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lent of 4 IVF-ET cycles in most IVF centers) since the HOST defect seems to cause embryo implantation abnormalities without fertilization impairment or embryo development at least up to 72 hours [9].

What is surprising was that the patient did conceive naturally with a HOST score not only < 50% but as low as 33%. In the case where the one pregnancy occurred [3] the HOST score was 47%. This leads to at least the question as to whether the subnormal HOST may prevent uterine implantation but not inhibit implanting into a tube.

Sperm cells bear specific antigen moleties that are incorporated into the zygote at the time of fertilization. Sperm surface antigens remain on the surface of the zygote during the first divisions and are internalized and/or degraded [10]. Interestingly, some studies have found that poor quality sperm may result in normal fertilization rates if adjustments are made to increase concentration of sperm; however pregnancy rates were still poor [11, 12]. Other studies have found that poor quality sperm could impair the development of the blastocyst despite attaining multi-cell embryos [13]. Other data do not agree that poor morphology using strict criteria have much of a predictive value for poor pregnancy outcome even in vivo [14, 15]. Thus, based on our own experience, we would suggest that the low HOST score of 33% rather than the morphology score of 4% was responsible for the subfertility [1-4, 13, 14].

The possibility exists that abnormal sperm proteins, similar to antisperm antibodies, may cause a development block just before genomic activation [16]. The adverse effect could be on cleavage signal proteins. Thus, the possibility exists that the HOST score defect impairs blastocyst formation. However, the case described here of an ectopic pregnancy that did progress has to make one reconsider the possibility that the defect prevents blastocysts from implanting into the uterine cavity but does not prevent attaching to the fallopian tube.

It would seem relatively easy to determine whether sperm with HOST score abnormalities inhibit blastocyst formation or blastocyst implantation by simply attempting to develop embryos formed by conventional insemination to blastocyst stage and to see if those with low HOST scores do not attain blastocyst formation effectively. However, consistent with the theory of toxicity of the supernumerary sperm that attach to the zona pellucida [9], bypassing zona pellucida contact by performing ICSI results in a normal pregnancy rate [17]. The Cooper Center for IVF started to use ICSI for low HOST scores prior to the popularization of blastocyst transfer and thus performing the aforementioned study above would not be possible.

It is hoped that some IVF centers not familiar with the HOST for male factor and who perform blastocyst transfer will be encouraged to measure the HOST score subsequent to previous IVF cycles to try to determine if subnormal HOST scores inhibit blastocyst formation or prevent blastocyst implantation. The study may even show that allowing the embryo to develop to blastocyst stage before transfer could overcome the low HOST score. The HOST once subnormal seems to remain stable over time, and thus the test performed at a later date could be assumed to have probably been subnormal when the last IVF-ET cycle was performed [18].

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