Acta Scientific Women's Health (ISSN: 2582-3205)

Volume 2 Issue 2 February 2020

Case Report

Successful Live Birth in a Couple with Poor Ovarian Reserve and Severe Teratozoospermia (Acephalic Spermatozoa Syndrome) with ICSI and MACS Technique

Mona Shroff*, Akshay Jani, Chaitali Patel and Mamta Jani

Nova IVF Fertility, Surat, Gujarat, India

***Corresponding Author:** Mona Shroff, Nova IVF Fertility, Surat, Gujarat, India.

DOI: 10.31080/ASWH.2020.02.0079

Received: December 02, 2019

Published: January 10, 2020

Abstract

We report a case of primary infertility with successful pregnancy outcome in a couple with poor ovarian reserve and severe teratozoospermia (acephalic spermatozoa syndrome).

Couple presented with primary infertility of 12 years' duration. Evaluation of female partner revealed poor ovarian reserve with AFC of 2/3 and AMH of 1.4 ng/mL. Semen analysis revealed 100% morphologically abnormal sperms with 99% pinhead sperms. In spite of counselling for poor prognosis, couple wanted to go for ICSI with self sperms. Patient was stimulated as per antagonist protocol -5 oocytes were retrieved, out of which 4 were metaphase II. Semen sample revealed 99% pinhead sperms with very few bent neck sperms. Density gradient (DG) was carried out followed by Magnetic Activated Cell Sorting (MACS) on post DG semen sample. ICSI was done with bent neck sperms with normal head. 3 oocytes were fertilized (Fertilization rate was 75%). Two cleavage stage embryos were transferred resulting in singleton pregnancy with successful live birth at full term.

Pinhead sperm is a variant of microcephalic sperm with no or minimal DNA content. Even in cases of acephalic spermatozoa syndrome, a good fertilization rate and successful pregnancy outcome can be achieved by isolating sperms with abnormally implanted head and using MACS to separate DNA fragmented apoptotic sperms from healthy sperms. Very few successful cases has been reported in literature and this could be the first to use MACS.

Keywords: Acephalic Spermatozoa; Genetic Origin; Infertility; Pin Heads; Sperm Pathology; MACS; Teratozoospermia; ICSI; Diminished Ovarian Reserve

Introduction

Infertility affects approximately 15% of couples worldwide, and nearly half of the infertility cases are attributed to the male [1]. Numerous cases of male infertility are caused by morphological defects of the spermatozoa, which hamper the fertilization process and is termed teratozoospermia. Acephalic spermatozoa syndrome is a rare but severe type of teratozoospermia that is characterized by the predominance of headless spermatozoa in the ejaculate [2,3].

In some individuals with acephalic spermatozoa, the syndrome has been identified to be familial, strongly suggesting that this syndrome has a genetic origin like defects in SUN5 or homozygous mutation in PMFBP1 (polyamine modulated factor 1 binding protein) [4-6]. No medical treatment have been proven to be successful so far for these cases.

Case Report

We report a case of primary infertility with successful pregnancy outcome in a couple with poor ovarian reserve and severe teratozoospermia (acephalic spermatozoa syndrome).

Couple (wife aged 32 years, Husband 35yrs) presented with primary infertility of 12 years' duration. Multiple cycle of ovulation induction with planned intercourse were done previously. Seven cycles of IUI done outside, with normal semen analysis reported.

Evaluation of female partner revealed poor ovarian reserve with Antral Follicle Count of 2 and 3 and AMH of 1.4 ng/mL.

Semen analysis at Nova revealed 100% morphologically abnormal sperms (teratozoospermia) with 99% pinhead/acehalic sperms. Most spermatozoa showed small globular cephalic thick-

enings not corresponding to sperm heads but displayed active movements, Less than 1% consisted of spermatozoa with heads abnormally implanted in the middle piece. The heads attached either to the tip or to the sides of the middle piece without a linear alignment with the sperm axis. The angles between heads and tails were up to 90–180°.This morphological entity was missed in previous analysis reports. In spite of counselling for poor prognosis outcome, couple wanted to go for ICSI with self sperms.Two semen samples were frozen before starting ICSI stimulation. Patient was stimulated as per antagonist protocol with Rfsh 225 and HMG 225 -5 oocytes were retrieved, out of which 4 were metaphase II. Semen sample revealed 99% pinhead sperms with very few bent neck sperms. Density gradient (DG) was carried out followed by Magnetic Activated Cell Sorting (MACS) on post DG semen sample. ICSI was done with bent neck sperms with normal head. 3 oocytes were fertilized (Fertilization rate was 75%). Two cleavage stage embryos were transferred resulting in βhCG positive (511.93 IU) after 2 weeks and singleton pregnancy with successful live birth at full term.

Figure 1

Discussion

Assessment of sperm morphology is associated with a number of difficulties related to lack of objectivity, variation in interpretation or poor performance in external quality-control assessments. Teratozoospermia has been frequently reported as the main abnormality responsible for fertility issues in males and very often subjectively overlooked. However, this diagnosis is a poorly understood seminal condition defined solely on the basis of the alterations observed in sperm shape, and does not provide a clear understanding of the pathophysiological mechanisms responsible for lower fertility, depending on the type of anomalies, in these patients. Defective spermatogenesis and some epididymal pathologies are commonly associated with an increased percentage of spermatozoa with morphological defects which are usually mixed variety.

Two main types of teratozoospermia have been identified. In the first and most frequent variety, morphological examination have non-specific and variable defects in different sperm components. This heterogeneous pattern shows no common defect and results from random alterations in sperm organelles. The second variety shows a very homogeneous microscopic pattern with a systematic sperm abnormality present in most spermatozoa. To this variety belong “globozoospermia”, round head acrosomeless spermatozoa [7,8], the ‘miniacrosome sperm defect' [9], the ‘dysplasia of the fibrous sheath or stump tail defect' [10], and the dynein deficient axonemes of the `immotile cilia syndrome' [11], alterations in the head–neck attachment “acephalic spermatozoa”. This defect has been referred to as ‘pin heads’ [12], a misnomer that implies that the heads are very small, when they are in fact absent. Pinhead sperm”, or “acephalic sperm”, refers to the condition in which ejaculate contains mostly sperm flagella without heads, a variant of microcephalic sperm with no or minimal DNA content [13].

Acephalic spermatozoa in men are of testicular origin and result from a failure of the tail anlage to establish a proper attachment to the caudal pole of the spermatid nucleus during spermiogenesis [14]. So it is basically a pathology of sperm neck [15] due to defect in formation of the connecting piece of spermatozoa during late spermiogenesis.

Testosterone propionate treatment was attempted in earlier studies, to achieve spermatogenic regression in an attempt to promote the expansion of the clone of normal spermatozoa during the rebound phenomenon that follows testosterone-induced oligo-azoospermia. No significant changes were found in sperm morphology along the course of spermatogenic regression or after recovery, and the percentage of normal spermatozoa remained very low and unchanged hence no medical treatment was possible [16].

Pin head/acephalic	Bent neck
Headless	Head attached laterally
No/minimal DNA	DNA preserved
Centriole-centrosomal malfunction	? Normal centriole-centrosome
Not used for ICSI	? Can be used for ICSI

Figure 2

Initial few studies with studies with abnormal head-tail sperm reported successful ICSI but all degenerated zygotes and no pregnancy [16-18].

Later a few successful pregnancies by microinjection of rigorously selected spermatozoa have been reported [19-21].

Only three case reports till date have demonstrated successful pregnancies with acephalic sperms.

These dissimilar results indicate variations in the degree of abnormalities of the head-neck junction, some of them compatible with normal centrosomal function.

Morphological anomalies have been associated with abnormal DNA and increased DNA fragmentation [22], an increased incidence of structural chromosomal aberrations [23], immature chromatin [24] and aneuploidy [25,26].

MACS technique is a sperm preparation technique that enables the immune magnetic separation of healthy spermatozoa from apoptotic and DNA fragmented spermatozoa which have less possibilities of survival. This technique is based on the use of magnetic microspheres Annexine –V (Diameter 50 nm) that have specific antibodies attached which are able to detect several markers located on the sperm membrane. The antibodies which are attached to the microspheres detect this marker when the spermatozoa are exposed to a magnetic field and retain only the damaged sperm (those with the marker).

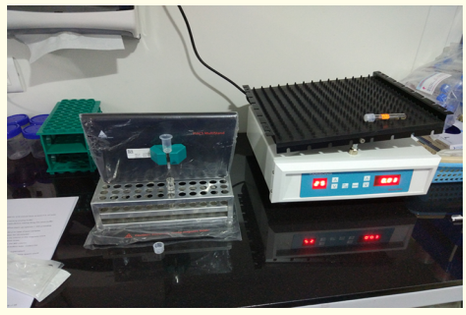

Figure 3

MACS appears to be a safe and efficient method to select functional sperm with consistently good results. This technique may improve pregnancy rates when used to complement standard sperm selection methods in ART especially in sperms with high DFI (DNA Fragmentation Index), with improved sperm quality and functionality and positive effects on motility and morphology [27].

Conclusion

Males with teratozoospermia have lower fertilization potential depending on degree and type of abnomality. Careful morphological evaluation of sperms is vital before initiating fertility treatment. Pinhead sperm", or "acephalic sperm", refers to the condition in which ejaculate contains mostly sperm flagella without heads, a variant of microcephalic sperm with no or minimal DNA content. Centrosomal function variation are possible in case of acephalic sperms where sperms with few abnormally implanted head can be looked for, which can result in successful outcome with ICSI. Addition of MACS technique is a promising option to separate out apoptotic and fragmented DNA sperm for a better outcome in such cases.

Bibliography

1. MC Inhorn P. "Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century". *Human Reproduction Update* 21 (2015): 411-426.

2. Perotti ME., *et al*. "Ultrastructural study of the decapitated sperm defect in an infertile man". *Journal of reproduction and fertility* 63 (1981): 543-549.

3. Rondanino C., *et al*. "Evaluation of sperm nuclear integrity in patients with different percentages of decapitated sperm in ejaculates". *Reproductive Bio Medicine Online* 31 (2015): 89-99.

4. Zhu F., *et al*. "Biallelic SUN5 Mutations Cause Autosomal-Recessive acephalic spermatozoa syndrome". *American Journal of Human Genetics* 99 (2016): 942-949.

5. PF Ray., *et al*. "Genetic abnormalities leading to qualitative defects of sperm morphology or function". *Clinical Genetics* 91 (2017): 217-232.

6. Fuxi Zhu. "Mutations in PMFBP1 Cause Acephalic Spermatozoa Syndrome". *The American Journal of Human Genetics* 103.2 (2018): 188-199.

7. Holstein AF., *et al*. "Human spermatids and spermatozoa lacking acrosomes". *Journal of reproduction and fertility* 35 (1973): 489-491.

8. Nistal M., *et al*. "Teratozoospermia absoluta de presentación familiar: espermatozoides microcéfalos irregulares sin acrosoma andrologia". 10 (1978): 234-240.

9. Baccetti B., *et al*. "A `miniacrosome' sperm defect causing infertility in two brothers". *Journal of Andrology* 12 (1991): 104-111.

10. Chemes HE., *et al*. "Dysplasia of the fibrous sheath: an ultrastructural defect of human spermatozoa associated with sperm immotility and primary sterility". *Fertility and Sterility* 48 (1987a): 664-669.

11. Afzelius BA., *et al*. "Lack of dynein arms in immotile human spermatozoa". *Journal of Cell Biology* 66 (1975): 225-232.

12. Zaneveld LJD and Polakoski KL. "Collection and physical examination of the ejaculate". In Hafez, E.S.E. (ed.), Techniques of Human Andrology". Elsevier/North-Holland Biomedical Press, Amsterdam (1977): 147-172.

13. Yuan S., *et al*. "SPATA6 is required for normal assembly of the sperm connecting piece and tight head-tail conjunction". *Proceedings of the National Academy of Sciences of the United States of America* 112.5 (2015): E430-439.

14. Perotti ME and Gioria M. "Fine structure and morphogenesis of `headless' human spermatozoa associated with infertility". *Cell Biology International Reports* 5 (1981): 113.

15. Chemes HE and Alvarez Sedo C. "Tales of the tail and sperm head aches: changing concepts on the prognostic significance of sperm pathologies affecting the head, neck and tail". *Asian Journal of Andrology* 14.1 (2011): 14-23.

16. HE Chemes ET., *et al*. "Acephalic spermatozoa and abnormal development of the head-neck attachment: a human syndrome of genetic origin". *Human Reproduction* 14.7 (1999): 1811-1818.

17. Rawe VY., *et al*. "A pathology of the sperm centriole responsible for defective sperm aster formation, syngamy and cleavage". *Human Reproduction* 17 (2002): 2344-2349.

18. Saias-Magnan J., *et al*. "Failure of pregnancy after intracytoplasmic sperm injection with decapitated spermatozoa: case report". *Human Reproduction* 14 (1999): 1989-1992.

19. Porcu G., *et al*. "Pregnancies after ICSI using sperm with abnormal head-tail junction from two brothers: case report". *Human Reproduction* 18 (2003): 562-567.

20. Emery BR., *et al*. "Pregnancy from intracytoplasmic sperm injection of a sperm head ad detached tail". *Fertility and Sterility* 81 (2004): 686-688.

21. Gambera L., *et al*. "Intracytoplasmic sperm injection and pregnancy with decapitated sperm". *Fertility and Sterility* 93 (2010): 1347.

22. Gandini L., *et al*. "Study of apoptotic DNA fragmentation in human spermatozoa". *Human Reproduction* 15 (2000): 830-839.

23. Lee JD., *et al*. "Analysis of chromosome constitution of human spermatozoa with normal and aberrant head morphologies after injection into mouse oocytes". *Human Reproduction* 11 (1996): 1942-1946.

24. Dadoune., JP *et al*. "Correlation between defects in chromatin condensation of human spermatozoa stained by aniline blue and semen characteristics" andrologia 20 (1988): 211-217.

25. Devillard., F *et al*. "Polyploidy in large-headed sperm: FISH study of three cases". *Human Reproduction* 17 (2002): 1292-1298.

26. Martin RH., *et al*. "A comparison of the frequency of sperm chromosome abnormalities in men with mild, moderate, and severe oligozoospermia". *Biology of Reproduction* 69 (2003): 535-539.

27. Gil M., *et al*. "Sperm selection using magnetic activated cell sorting (MACS) in assisted reproduction: a systematic review and meta-analysis". *Journal of Assisted Reproduction and Genetics* 30 (2013): 479.