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Complete Asthenospermia: To Diagnose or Not to Diagnose?

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At times, the presentation of a patient poses not only interesting clinical questions regarding his care, but also much larger questions regarding the role that a physician plays in treating male reproductive dysfunction in diagnosis and therapy. Such is the case of a patient with complete asthenospermia that was related by Dennis Matt:

> We have a patient who has presented twice with normal semen parameters, except for completely immotile sperm that, nonetheless, have more than 75% viability. Efforts to induce motility by washing and incubating the sperm with pentoxyphilin have not worked. I suspect that this patient has primary ciliary dyskinesia (PCD), but this has yet to be determined. If the patient has situs inversus, then I guess the answer is yes. If not, does anyone have an easy way to diagnose this, or does anyone know of a laboratory that perform the appropriate tests?
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> More importantly, this couple wishes to go through in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI). There is one report (Westlander et al, 2003), to my knowledge, that has found that testicular sperm yields a better outcome than ejaculated sperm in Kartagener patients when using the hypo-osmotic shock treatment (HOST) method. Does anyone have any experience or opinions regarding this issue?

Ibrahim Fahmy addresses the latter question regarding the preference of ejaculated vs testicular sperm when using ICSI:

> In response to the e-mail posted by Dr Dennis Matt, the use of testicular sperm for ICSI in patients suffering from immotile cilia syndrome depends on the viability of the sperm in the ejaculate and the number of retrieved oocytes on the day of ICSI. The viability of sperm in testicular tissue is usually above 90%. Therefore, if the viability in the ejaculate is low and the number of oocytes is small, it is better to use testicular sperm to avoid a failure of fertilization and cancellation of the cycle.

Kerem Dirican writes about techniques that can be used when selecting sperm from such patients for use in ICSI and comments on the necessity of a complete diagnosis for the asthenospermic condition:

If the following observations are made, a diagnosis of PCD is supported: 1) totally immotile spermatozoa before and after preparation 2) no morphologic neck, midpiece, or tail abnormalities; 3) more than 60% vitality by eosin Y and more than 50% tail swelling by HOST; and 4) clinical findings supporting a genetic ciliary defect (chronic sinusitis, etc), and situs inversus in some cases (not necessary for all cases). Of course, the only way to verify the diagnosis is to have an experienced cytologist perform a transmission electron microscopy examination of the spermatozoa, but this is not necessary.

There appears to be nothing in the literature that addresses the issue of whether a patient with PCD who has been selected for ICSI by HOST will present an outcome that is comparable with the use of regular asthenozoospermic samples. But it is logical to expect good fertilization, embryo development, and implantation rates with HOST in PCD cases. My experience also reflects this premise. In all cases, I have had enough HOST-positive spermatozoa, normal fertilization rates (same as regular asthenozoospermic cases), good embryo development, and comparable implantation rates, and I have never performed testicular sperm extraction to improve the outcome because it was not necessary and seems to be an unnecessary overtreatment for the male.

David Karabinus notes that, because conditions leading to complete asthenospermia may be inherited, the couple ought to be informed of the possibility of the transmission of this condition to their offspring:

It may be prudent for the clinician to counsel the couple regarding the inheritance aspects. Although it is generally believed that PCD is autosomal recessive, a quick MEDLINE review suggests that an X-linked or autosomal-dominant inheritance is also involved.

Arnold Belker also notes the significance of germ line transmission of the asthenospermic condition:

I wish to echo the concerns of David Karabinus about the hereditary aspects of performing IVF/ICSI using sperm from men with immotile cilia syndrome, often termed dysplasia of the fibrous sheath, and its variants. The couple contemplating IVF/ICSI using such sperm must be made aware of the potential hereditary medical consequences, such as respiratory disease. The exact hereditary mechanism has yet to be resolved, but the potential transmission of medical, as well as of reproductive, abnormalities must be explained to patients in this situation.

Deborah O'Brien writes that more than one transmissible condition may lead to asthenospermia:

There are other potential genetic causes of sperm motility defects besides the axonemal defects found in PCD. Our recent studies indicate that glycolysis and the sperm-specific enzymes in this pathway are essential for sperm motility. When we eliminated the sperm-specific enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDS) by gene targeting, we generated mice with male infertility and a complete lack of progressive sperm motility. Like Dr Matt's patient with immotile sperm, these mice produce normal numbers of viable sperm (PNAS 101:16501, 2004).

To my knowledge, human mutations in GAPDS have not yet been identified. However, we expect mutations that eliminate the activity of GAPDS or other sperm-specific glycolytic enzymes to cause severe defects in sperm motility without major changes in sperm number,

> morphology, or other semen parameters. Screening efforts to identify genetic causes of infertility should consider these enzymes, particularly when the only obvious defect lies in sperm motility.

Finally, Hector Chemes argues persuasively for a complete diagnosis of the patient's asthenospermic condition, including electron microscopy:

> The case of total asthenozoospermia presented by Dr Matt merits special attention because, among other issues, it brings to focus the question: Should andrologists go ahead with assisted reproduction (particularly ICSI) without a proper diagnosis of the patient's pathology? Is the role of the andrologist just to provide a "technological solution" for the couple?
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> Even though, with the details provided, it seems that a likely diagnosis is PCD, it cannot be confirmed unless an electron microscopic evaluation of the spermatozoa is conducted (or nasal epithelium if the patient has respiratory symptoms).
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> Although they occur rarely, there are cases of complete immotility not due to PCD when there is not a genetic background for the defect. There are also PCD patients without respiratory symptoms.
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> I agree about the need of genetic counseling, but what counseling can be performed without a diagnosis?
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> Maybe electron microscopy is not an "easy procedure" to perform, but it is what this patient needs.
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> We have published a review (*Hum Reprod Update.* 2003; 9:405–428), where this topic is discussed. The pdf file of the article is available for whomever may be interested.

To physicians treating infertility, ICSI provides a tool by which dysfunctional, even dead, sperm may be used to fertilize an ovum. Providers of this powerful technology may ask the question, Why does one need a complete diagnosis if the therapy is highly effective regardless of etiology, especially if that diagnosis involves sophisticated laboratory methods that may not be available at even the most up-to-date centers? Regarding this particular form of medical therapy, as reproduction involves germ line transmission, accurate diagnosis translates directly into a prediction of the probability of disease in the offspring. We look forward to the time when molecular genetic tools are widely available to directly and accurately diagnose patients seeking reproductive care.

Footnotes

Note: Postings to *Androlog* have been lightly edited before publication.