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A case of problems in supporting a patient after Y-chromosome long arm microdeletion testing at a Japanese general hospital

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ABSTRACT

There are only few reports on the problems faced post-Y-chromosome microdeletion tests that decide the use of micro testicular sperm extraction. We report a case wherein we faced issues in supporting a patient post-testing. One patient with azoospermia factor c (*AZFc*) deletion gave birth to a baby boy, who could have inherited the *AZFc* deletion; however, we could not inform the young patient. Therefore, it is necessary to establish a post-testing support system for patients and infants.

1. Introduction

In male patients with infertility, microdeletions are concentrated in three regions located on the long arm of the Y chromosome.[1] These three regions form the azoospermia factor (*AZF*) locus; they have three sub-regions, *AZFa*, *AZFb*, and *AZFc*. Micro testicular sperm extraction (TESE) is not indicated in patients with microdeletions in the *AZFa*, *AZFb*, or AZFb + *c* regions, because they lack spermatogenesis. The European Molecular Genetics Quality Network in 2004 recommended micro-TESE as an essential test for male patients with infertility. However, Y chromosome microdeletion testing in Japan became widespread in 2015 after the development of a test kit that could detect polymorphisms in the Japanese population.[2] Few studies have reported the challenges faced by clinicians and patients after being informed about the results of chromosome microdeletion testing in Japanese clinical settings.

In this study, we report the issues faced after the results of a Y chromosome microdeletion testing were reported to a Japanese male patient with infertility at our clinic.

2. Case presentation

We performed Y chromosome microdeletion testing on patients diagnosed with azoospermia or severe oligozoospermia at our hospital between January 2016 and December 2020. The medical records of these patients were retrospectively analyzed. The Y chromosome microdeletion tests were performed using the Y Chromosome Deletion Detection System, Version 2.0 (Promega, WI, USA). This study was approved by the Clinical Research Review Committee of our hospital.

A 29-year-old male, who was diagnosed as harboring an *AZFc* deletion with the expectation of sperm recovery, underwent intracytoplasmic sperm injection (ICSI) using sperm recovered via micro-TESE and had a baby.

We explained to the parents that the boy would inherit the *AZFc* deletion from his father and suggested testing; however, they did not wish to test their child for the deletion. We could not formulate a policy on how and when to communicate the details about the condition to the child when he grew up.

3. Discussion

The long arm of the Y chromosome harbors genes that regulate spermatogenesis. In ~10% of the patients diagnosed with azoospermia or severe oligozoospermia, microdeletions are observed in the *AZFa*, *AZFb*, and *AZFc* regions.[1]

In patients with deletions in either of the *AZFa* or *AZFb* regions, sperm retrieval is not possible, because spermatogenesis is completely absent; therefore, TESE is not indicated. However, in patients with an *AZFc* deletion—the most common deletion accounting for infertility in 60–80% of patients—various phenotypes ranging from severe oligozoospermia to azoospermia is observed, and micro-TESE is indicated if sperm retrieval is feasible.[1]

Y chromosome microdeletion tests are performed to identify the cause of male infertility and are useful in determining whether micro-TESE is indicated. However, a challenge was observed concerning patient support.The *AZFc* deletion is inherited by male children from their fathers; therefore, it is important to explain the implications of the

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genotype to the parents and follow up with the baby after its birth.[2] We explained the implications to the parents; however, they did not want to perform genetic testing for their child. We advised that the test could be performed at our hospital; however, we could not decide on a policy on how and when to inform the child in the future. This is an important issue because as the child grows, he will need to be informed and supported. There is a tendency to encourage disclosure in cases of artificial insemination by donors (AID).[3] Male children born with *AZFc* deletions should be counseled and informed at an early age so that their sperm can be collected via TESE and stored for the future.[4] A Y chromosome microdeletion test result that reveals the absence of spermatogenesis can seriously impact a couple's relationship.[5] Therefore, continued support should ideally be provided to patients after the results of Y chromosome microdeletion analysis are made available to them. However, under the current medical system in Japan, patients with an *AZF* deletion typically end up using infertility treatment without continued support.

Based on the present findings, we propose that primary and higher medical institutions in our region should collaborate to track and support patients lacking spermatogenesis.

4. Conclusion

The chromosome and Y chromosome microdeletion tests are useful in deciding whether to use micro-TESE. However, in the future, it is necessary to establish a continuous support system for patients and their infants after the genetic testing results are made available to them.

Consent

Informed consent was obtained after a written explanation was provided to the patients.

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Declaration of competing interest

There are no conflicts of interest to declare.

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