Y Chromosome Microdeletions

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Infertility affects 15-20% of couples of reproductive age, with male-factor infertility accounting for one-half of cases. Y chromosome microdeletions are typically characterized by azoospermia (absence of sperm), severe to moderate oligospermia, or abnormal sperm morphology/motility, depending on the size and location of the deletion. Identification of deleted azoospermia factor (AZF) region has implications for assisted reproductive technologies. Men with AZFc deletion have a positive prognosis for finding sperm sufficient for assisted reproduction. However, assisted reproductive techniques are contraindicated for men carrying AZFa, AZFb, AZFbc or AZFabc microdeletions, which are classically associated with spermatogenic failure. When assisted reproduction is successful, Y chromosome microdeletions are transmitted to all male offspring, making them at high risk for infertility. Female offspring have no increased risk for infertility.

Genetics

Variants

Microdeletions involve one or more of three AZF regions. Among individuals with Y chromosome microdeletions, the frequency of the deletion type is:

- AZFa: 5% of cases
- AZFb: 10% of cases
- AZFc: 70% of cases
- AZFbc: 13% of cases
- AZFabc: 2% of cases

Etiology

The prevalence of Y chromosome deletions and microdeletions is approximately 1/2,000-3,000 males.

Inheritance

Y-linked

Penetrance

Approaches 100 percent in males; variable expression may result in intrafamilial variation of fertility in men with an identical microdeletion.

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity: Approximately 5-10% for men with nonobstructive azoospermia or severe oligospermia
- Analytic sensitivity/specificity: 99%

Featured ARUP Testing

Y Chromosome Microdeletion 2001778

Method: Polymerase Chain Reaction (PCR)/Electrophoresis

- Use to determine the cause of infertility in men with nonobstructive azoospermia or moderate or severe oligospermia
- Aids in predicting effectiveness of assisted reproductive technologies in men with specific Y chromosome microdeletions
### Results

<table>
<thead>
<tr>
<th>Result</th>
<th>Deletion Detected</th>
<th>Clinical Significance</th>
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<tbody>
<tr>
<td>Positive</td>
<td>AZFa deletion</td>
<td>Spermatogenic failure (SCOS) resulting in azoospermia</td>
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<tr>
<td></td>
<td>AZFb deletion</td>
<td>Azoospermia/spermatogenetic arrest</td>
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<tr>
<td></td>
<td>AZFbc deletion</td>
<td>SCOS/spermatogenetic arrest</td>
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</tbody>
</table>
| | AZFc deletion | Variable phenotype ranging from mild oligospermia to azoospermia and SCOS  
Males with AZFc microdeletion have a high likelihood of finding sperm sufficient for successful ICSI for assisted reproduction |
| | AZFabc deletion | SCOS associated with azoospermia |

**Negative**

| Lack of detection of AZF microdeletion | Greatly reduces the possibility of Y chromosome deletion as the cause of azoospermia or oligospermia |

ICSI, intracytoplasmic sperm injection; SCOS, Sertoli cell-only syndrome

### Limitations

- Diagnostic errors can occur due to rare sequence variations.
- Breakpoints of identified microdeletions will not be determined.
- Variants within individual genes included in the AZF regions will not be detected.
- Male infertility due to causes other than the Y chromosome microdeletions tested will not be detected.

### References


### Related Information

**Evaluation of Infertility**