Y Chromosome Microdeletions

Indications for Ordering

- Determine the cause of infertility in men with
  - Nonobstructive azoospermia
  - Moderate or severe oligospermia
- Help predict effectiveness of assisted reproductive technologies in men with specific Y chromosome microdeletions

Test Description

Multiplex polymerase chain reaction followed by gel electrophoresis

Tests to Consider

Primary test

Y Chromosome Microdeletion 2001778

- Aid in determining cause of azoospermia or oligospermia
- Predict effectiveness of assisted reproductive technologies

Related test

Chromosome Analysis, Peripheral Blood 2002289

- Detect chromosome rearrangements causing oligospermia or azoospermia

Disease Overview

Prevalence

Y chromosome deletions and microdeletions – 1/2,000-3,000 males

Diagnostic issues

- Infertility affects 10% of couples of reproductive age
  - Male-factor infertility is responsible for one-half of cases
- Genetic testing in men with azoospermia or oligospermia when other causes of infertility have been eliminated
  - Chromosomal abnormalities in 5-10% of men
  - Microdeletions detected in 5-13% of men
- Y chromosome microdeletions are most commonly detected in men with
  - Azoospermia (absence of sperm)
  - Severe oligospermia (< 1million sperm/mL semen)
- Y chromosome deletions may be detected in men with sperm counts 1-5 million sperm/mL semen
- Identification of deleted azoospermia factor (AZF) region has implications for assisted reproductive technologies
  - Testicular sperm retrieval is ineffective for males with Sertoli cell-only syndrome (SCOS)
    - Exception is men with AZFc deletion
- Y chromosome microdeletions are transmitted to all male offspring if assisted reproductive techniques are used
  - Male offspring are at high risk for infertility
  - Female offspring have no increased risk for infertility

Genetics

Inheritance – Y linked

Penetrance – near 100%

De novo mutations – most Y chromosome microdeletions are de novo

Mutations

- Microdeletions frequently involve one or more of three AZF regions
  - AZFa – 5% of cases
  - AZFb – 10% of cases
  - AZFc – 70% of cases
  - AZFbc – 13% of cases
  - AZFabc – 2% of cases

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity – ~5-10% for men with nonobstructive azoospermia or severe oligospermia
- Analytical sensitivity/specificity – 99%

Results

- Positive
  - AZFa deletion – spermatogenic failure (SCOS) resulting in azoospermia
  - AZFb deletion – azoospermia/spermatogenetic arrest
  - AZFbc deletion – SCOS/spermatogenic arrest
  - AZFc deletion – variable phenotype ranging from mild oligospermia to azoospermia and SCOS
    - Only AZFc microdeletion appears to be associated with successful assisted reproduction technology
  - 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

Limitations

- Breakpoints of identified microdeletions will not be determined
- Mutations within individual genes included in the AZF regions will not be detected
- Rare diagnostic errors may occur due to primer-site mutations
- Male infertility due to causes other than the common Y chromosome microdeletions tested will not be detected