Ataxia-Telangiectasia Testing

Introduction

Ataxia-telangiectasia (A-T) testing is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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What is Ataxia-telangiectasia

Definition

Ataxia-telangiectasia (A-T) is a progressive neurological disorder that is caused by mutations in the ATM gene.

Prevalence

The prevalence of A-T is approximately 1 in 40,000 to 1 in 100,000 live US births. It is the most common cause of childhood progressive cerebellar ataxia in most countries.

Symptoms

Signs and symptoms of A-T include

- truncal and gait ataxia
- ocular apraxia
- slurred speech
- head tilting, after the age of 6 months
- conjunctival telangiectasias
- immunodeficiencies
Onset

The onset for A-T is typically between the ages of 1 and 4 years.

Related conditions

ATM heterozygotes (carriers) may be at an increased risk for breast cancer, especially women with a strong family history of breast cancer.\textsuperscript{4-7} Epidemiological data has also suggested an increased risk for cardiovascular disease in carriers.\textsuperscript{6,7} Therefore, carriers of ATM mutant alleles may need to be screened for breast cancer and cardiovascular disease.

Inheritance

A-T is inherited in an autosomal recessive inheritance pattern. Males and females are equally likely to be affected. If both parents are carriers of A-T, the risk for a pregnancy to be affected is 1 in 4, or 25%. Preimplantation and prenatal diagnosis are available for couples known to be at-risk.

Prognosis

Although individuals with A-T live to adulthood, they are at an increased risk for early death. Currently, most individuals live beyond 25 years, with some surviving into their 50s. Cause of death is associated with A-T associated cancers, infection, and pulmonary failure.\textsuperscript{1}

Test information

Introduction

Testing for Ataxia-telangiectasia may include sequence analysis, deletion/duplication analysis, or known familial mutation analysis.

Sequence analysis

Sequence analysis of the ATM gene can identify 90-95% of A-T mutations in affected individuals.\textsuperscript{1}

Deletion and duplication analysis

Deletion and duplication analysis of the ATM gene can identify another 1-2% of mutations.\textsuperscript{1}
Known familial mutation analysis

Once a deleterious mutation has been identified, relatives of affected individuals can undergo tests. Detection of carriers impacts medical management in the case of breast cancer screening and cardiovascular disease screening.

Prenatal testing is available to individuals with a known family mutation. Genetic testing can be performed on amniocytes obtained through amniocentesis or chorionic villi obtained through a chorionic villus sampling.

Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to Ataxia-telangiectasia testing.

International Workshop on A-T

The Eighth International Workshop on Ataxia-telangiectasia (A-T) was convened in 1999. The workshop described ATM mutations and cancer risk in heterozygotes, and potential therapeutic approaches. Genetic testing strategies were not described. ⁸

Criteria

Introduction

Requests for Ataxia-telangiectasia testing are reviewed using these criteria.

ATM known familial mutation analysis

• Genetic Counseling:
  o Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND
• Previous Genetic Testing:
  o No previous genetic testing of ATM, AND
• Carrier Screening Individuals:
  o Known family mutation in ATM in 1st, 2nd, or 3rd degree biologic relative(s), OR
• Prenatal Testing for At-Risk Pregnancies:
  o ATM mutations identified in both biologic parents.
ATM sequencing

• Genetic Counseling:
  o Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND

• Previous Genetic Testing:
  o No previous ATM gene sequencing, and
  o No known ATM mutation in family, AND

• Diagnostic Testing for Symptomatic Individuals:
  o Elevated Alpha-fetoprotein (AFP) levels, or
  o Decreased ATM protein detected by immunoblotting, and
  o Progressive cerebellar ataxia, or
  o Truncal and gait ataxia, or
  o Oculomotor apraxia, OR

• Diagnostic Testing for Carriers:
  o One mutation detected by targeted mutation analysis, and
  o Elevated Alpha-fetoprotein (AFP) levels, or
  o Decreased ATM protein detected by immunoblotting, OR

• Testing for Individuals with Family History or Partners of Carriers:
  o 1st, 2nd, or 3rd, degree relative diagnosed with Ataxia-Telangiectasia clinical diagnosis, family mutation unknown, and testing unavailable, or
  o Partner is monoallelic or biallelic for ATM mutation, and
  o Has living children with this partner, or
  o Has the potential and intention to reproduce

ATM duplication and deletion analysis

• Genetic Counseling:
  o Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND

• Previous Genetic Testing:
  o No previous deletion/duplication analysis of ATM, and
o No mutations detected in full sequencing, or
o Heterozygous for mutation and individual is expected to be affected (eg, elevated alpha-fetoprotein levels, decreased ATM protein detected by immunoblotting (if performed), other features of disorder are present).

References

Introduction

These references are cited in this guideline.


2. National Organization for Rare Disorders. Ataxia Telangiectasia. Available at: https://rarediseases.org/rare-diseases/ataxia-telangiectasia/


