Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome (PJS) is characterized by the development of noncancerous growths called hamartomatous polyps in the gastrointestinal tract (particularly the stomach and intestines) and an increased risk of developing certain types of cancer. Malignant tumors are most commonly found in the gastrointestinal tract, pancreas, cervix, ovary, and breast; management guidelines have been published by the National Comprehensive Cancer Network (NCCN).[1] Polyps may also result in associated noncancerous health problems, including recurrent bowel obstructions, chronic bleeding, and abdominal pain. Children with PJS may also develop dark colored spots (hyperpigmentation) on face and body, which may fade with age.[2]

Disease Overview

Prevalence

1/25,000-280,000[3]

Symptoms

- GI polyposis, including hamartomatous PJS-type polyps, resulting in[4]:
  - Chronic bleeding, anemia, recurrent obstruction, intussusception
  - Adenomatous polyps in colon, small intestine, stomach, large bowel, nasal passages
- Hyperpigmentation presenting as dark blue to brown macules around mouth, eyes, nostrils, perianal area, buccal mucosa, fingers[4]
- Increased risk for intestinal and extraintestinal malignancies: colorectal, gastric, pancreatic, breast, sex cord tumors in ovary or testes, adenoma malignum of cervix, uterine, and lung[4]
- Lifetime risk for any cancer varies between 37-93%[5]

Age of Onset

- Hyperpigmented macules most pronounced before age 5; not usually present at birth[4]
- Median age for gastrointestinal (GI) symptoms is 10 years[6]

Genetics

Gene

STK11[4]

Inheritance

Autosomal dominant[4]

Penetrance

100%[4]

Tests to Consider

Peutz-Jeghers Syndrome (STK11) Sequencing and Deletion/Duplication 2008398

Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

- Preferred test to confirm diagnosis of PJS in symptomatic individual
- Use for disease prediction in presymptomatic individual with family history of PJS

Familial Mutation, Targeted Sequencing 2001961

Method: Polymerase Chain Reaction/Sequencing

Recommended test for a known familial sequence variant previously identified in a family member

- A copy of the family member's test result documenting the familial variant is required
- Consultation with a genetic counselor is advised.

Deletion/Duplication Analysis by MLPA 3003144

Method: Multiplex Ligation-dependent Probe Amplification

Use to assess for large deletion/duplication previously identified in a family member

- A copy of a relative's lab report is required
- Consultation with a genetic counselor is advised

See Related Tests

De novo Variant(s)

Approximately 45% of affected individuals have no family history of PJS; however, the exact proportion of de novo variants is unknown[4]

Test Interpretation

Sensitivity/Specificity

Clinical sensitivity

- PJS (*STK11*) sequencing and deletion/duplication
  - ~87-99% sensitivity in individuals with family history of PJS[7]
  - ~91-98% in individuals without a family history[7]

Analytical sensitivity/specificity: 99%

Results

- Positive: diagnosis confirmed
- Negative: diagnosis of PJS is less likely but not excluded
- Uncertain: gene variant detected, but whether the variant is benign or pathogenic is unclear

Limitations

- Regulatory region and deep intronic variants will not be detected
- Large deletion/duplication breakpoints will not be determined
- Diagnostic errors can occur due to rare sequence variations
- This assay is not designed to detect somatic variants associated with malignancy
- Interpretation of this test result may be impacted if the patient has had an allogeneic stem cell transplantation

References

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6. Amos CI, Keitheri-Cheteri MB, Sabripour M, et al. Genotype-phenotype correlations in Peutz-Jeghers syndrome. J Med Genet. 2004;41(5):327-333. PubMed

7. Resta N, Pierannunzio D, Lenato GM, et al. Cancer risk associated with STK11/LKB1 germline mutations in Peutz-Jeghers syndrome patients: results of an Italian multicenter study. Dig Liver Dis. 2013;45(7):606-611. PubMed

Related Tests

Hereditary Breast and Ovarian Cancer Panel, Sequencing and Deletion/Duplication 2012026

Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray

Hereditary Gastrointestinal Cancer Panel, Sequencing and Deletion/Duplication 2013449

Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray/Sequencing/Multiplex Ligation-dependent Probe Amplification

Hereditary Cancer Panel, Sequencing and Deletion/Duplication 2012032

Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray

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