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Peutz–Jeghers Syndrome

Peutz-Jeghers syndrome (PJS) is a rare genetic condition that leads to the growth of non-cancerous polyps in the gastrointestinal (GI) tract and dark spots (pigmented macules) on the skin and mucous membranes. Although it usually starts in childhood, it can be diagnosed at any age. PJS is caused by mutations in the STK11 gene (also known as LKB1) on chromosome 19, and it follows an autosomal dominant pattern, meaning that a person with the mutation has a 50% chance of passing it on to their children. This condition increases the risk of developing both benign and cancerous tumors, particularly in the GI tract, breasts, and reproductive organs.

Genetic Basis and Inheritance

Peutz-Jeghers syndrome is caused by changes (mutations) in the STK11 gene, which plays a role in controlling cell growth and metabolism. When this gene is mutated, its ability to prevent tumor growth is impaired, leading to the development of polyps and a higher risk of cancer. The condition follows an autosomal dominant inheritance pattern, which means that having just one copy of the mutated gene is enough to develop the disorder. As a result, close family members of someone with the syndrome have a 50% chance of inheriting it.

Clinical Manifestations

- **Pigmented Macules**

  One of the main signs of Peutz-Jeghers syndrome is the appearance of dark brown to bluish-black spots on the skin and mucous membranes. These pigmented macules are usually found on the lips, inside the mouth, nose, hands, feet, and around the genitals. The spots are typically small (a few millimeters in size) and appear by age two, with oral lesions often being the first to show up. These marks are harmless and usually do not need treatment, but they are important for diagnosing Peutz-Jeghers syndrome. While the spots can persist throughout life, they may fade or become less noticeable as a person gets older.

- **Hamartomatous Polyps**

  Peutz-Jeghers syndrome is also known for causing benign growths called hamartomatous polyps, which commonly develop in the gastrointestinal (GI) tract. Although these polyps are generally non-cancerous, they can cause problems in adulthood, including abdominal pain, blood in the stool, or even intussusception, a condition where part of the intestine slides into another, causing a blockage. Polyps may also form in other organs such as the

lungs, breasts, pancreas, and reproductive organs, which can increase the risk of certain cancers.

Malignancy Risk

Peutz-Jeghers syndrome increases the risk of developing several types of cancer due to the genetic mutation in the STK11 gene, which affects how cells grow and function. The cancers most commonly linked to Peutz-Jeghers syndrome include:

- *Gastrointestinal malignancies:* There is a significantly higher risk for cancers of the stomach, small intestine, and colon. Polyps in the GI tract can sometimes develop into cancer, although the exact cause is not fully understood.
- *Pancreatic cancer:* People with Peutz-Jeghers syndrome are at increased risk of pancreatic cancer. This type of cancer is difficult to detect early because it often doesn't show noticeable symptoms.
- *Breast and ovarian cancer:* Women with Peutz-Jeghers syndrome are at a higher risk of developing breast and ovarian cancer, often at younger ages than the general population.
- *Testicular cancer:* Men with this condition are at a greater risk for testicular cancer, particularly a type called Sertoli cell tumors.

Because of the increased risk of cancer, regular screenings and early detection are essential for managing and addressing potential issues as early as possible.

Diagnosis

Peutz-Jeghers syndrome is primarily diagnosed based on its characteristic features, such as the pigmented spots (macules) on the skin and mucous membranes, along with a family history of the condition. To confirm the diagnosis, genetic testing for mutations in the STK11 gene is often recommended, especially in cases where the symptoms are less obvious or when the typical signs are not present.

Endoscopic tests are important for detecting polyps in the gastrointestinal tract, particularly for individuals with a family history of Peutz-Jeghers syndrome. Due to the increased risk of cancer associated with the condition, routine screenings for various cancers are advised to catch any potential issues early.

Management and Treatment

There is no cure for Peutz-Jeghers syndrome, but management focuses on monitoring and reducing the risks associated with polyps and the increased chances of developing cancer. Key aspects of management involve cancer screening. Early and regular screenings are essential to detect cancers before they become more advanced. These screenings include:

- ***Colonoscopy****:* Begin screenings at age 8, with follow-up every 3 years. If polyps are found, they may need to be removed to lower the risk of developing cancer.
- ***Upper GI Endoscopy****:* Annual endoscopies are recommended to check for gastric and intestinal cancers in individuals with GI polyps.
- ***Breast cancer screening****:* Women should start annual mammograms at age 25, along with regular breast self-exams. They should also have annual gynecological exams, including pelvic ultrasound and Pap smears to screen for ovarian and cervical cancers.
- ***Testicular cancer surveillance****:* Men should have annual testicular exams and discuss with their healthcare provider whether additional imaging is needed for monitoring.

Surgical Management of Polyps

For individuals with Peutz-Jeghers syndrome who experience symptoms from their polyps, such as blockages or twisting of the intestines (intussusception), surgery may be needed. If a polyp is large or causing problems, it might be removed through a procedure called polypectomy. In cases where there are many polyps or there is a concern about cancer, part of the intestine may need to be removed through a surgery called intestinal resection. These treatments help manage symptoms and reduce potential complications.

Genetic Counseling

Since Peutz-Jeghers syndrome is inherited in an autosomal dominant manner, it is important for affected individuals and their families to receive genetic counseling. Genetic testing for close relatives is recommended to detect the condition early and provide timely treatment. Families with a known history of Peutz-Jeghers syndrome may also consider prenatal testing to assess the risk for future children.

Supportive Care

Peutz-Jeghers syndrome affects multiple parts of the body, so it is important for individuals with the condition to receive care from a team of specialists, including gastroenterologists, oncologists, and genetic counselors. The focus of care is on managing symptoms, such as abdominal pain, and preventing complications from polyps or cancer.

Prognosis

The outlook for individuals with Peutz-Jeghers syndrome depends on factors like the severity of polyps, the presence of cancer, and how well early interventions are managed. While people with PJS may have a slightly shorter life expectancy due to a higher risk of cancer, many can live into adulthood with proper monitoring and treatment. Ongoing management of polyps and cancer risks is key to maintaining health.

Conclusion

Peutz-Jeghers syndrome is a rare inherited condition characterized by pigmented spots on the skin and polyps in the gastrointestinal tract, which can increase the risk of certain cancers, including in the gastrointestinal area, breasts, ovaries, and testes. Early diagnosis, genetic testing, and regular check-ups are essential for managing the condition and improving long-term health. While the condition is lifelong, with proper care and monitoring, individuals with Peutz-Jeghers syndrome can lead productive lives with a lower risk of cancer-related health issues.

References

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