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Cancer Prone Disease Section

Mini Review

Peutz-Jeghers syndrome

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Identity

Note
Syndrome associating mucocutaneous melanotic pigmentation, intestinal polyposis, and an increased risk of cancers

Inheritance
Autosomal dominant with a high penetrance; frequency is about $3.5/10^5$ newborns; 1/3 to 1/2 of cases are new mutations.

Clinics

Phenotype and clinics

Skin numerous brown or bleuish mucocutaneous macules (melanin spots), especially around the orifices (mouth, including the buccal mucosa, eyes, nostrils, anus, genitalia), on the hands...; they tend to deseapear with age; (at puberty or in adulthood); Note: in patients with isolated mucocutaneous melanotic pigmentation (without polyps), the cancer risk is lower, and the genetic defect looks different.
Gastrointestinal tract (GI tract): polyps of amartomatous origin (with a characteristic arborization of nonstriated muscles) may be found in any portion of the GI tract with varying frequencies: from 95% to 15%: in the small bowel, jejunum, ileum, large intestin, rectum,stomach, and the duodenum; risk of intussusception, which may be cause of death; onset for symptoms occurs from the firstyear of life to elderness (median age10-25 years, somewhat earlier in male patients); polyps of other organs can occur.

Neoplastic risk

Tumors develop, with a relative risk of 10-20, and a cumulative risk of more than 90% between ages 15 and 64; mean interval between the diagnosis of Peutz-Jeghers syndrome and the diagnosis of cancer is about 20 yrs..Cancers at risk are:
- small intestin: 500 fold increase,
- stomach:200 fold,
- pancreas: 100,
- colon: 85,
- esophagus: 60,
- ovary: 30, and the benign sex cord tumor with annular tubules,
- uterus, breast, lung: 15 to 20.

Treatment

Surveillance with endoscopic (GI tract) and gynecologic regular screenings, surgery when necessary.

Genes involved and proteins

STK11

Location
19p13.3

Note
Mutations in STK11 is found in about 70 % of cases of Peutz-Jeghers syndrome; there is genetic heterogeneity, and yet undiscovered gene(s) may also be responsible for the disease.

DNA/RNA
Description: 10 exons

Protein
Function: Serine/threonine protein kinase.

Mutations
Germinal: Most mutations in Peutz-Jeghers syndrome are null alleles; they are dispersed through the entire gene.
Somatic: Many of the polyps that develop in Peutz-Jeghers syndrome show loss of heterozygosity.

References

Hemminki A, Markie D, Tomlinson I, Avizienyte E, Roth S, Loukola A, Bignell G, Warren W, Aminoff M, Höglund P, Järvinen H, Kristo P, Pelin K, Ridanpää M, Salovaara R, Toro T, Bodmer W, Olschwang S, Olsen AS, Stratton MR, de la Chapelle A, Aaltonen LA. A serine/threonine kinase gene defective in Peutz-Jeghers syndrome. Nature. 1998 Jan 8;391(6663):184-7

Jenne DE, Reimann H, Nezu J, Friedel W, Loff S, Jeschke R, Müller O, Back W, Zimmer M. Peutz-Jeghers syndrome is caused by mutations in a novel serine threonine kinase. Nat Genet. 1998 Jan;18(1):38-43

Jiang CY, Esufali S, Berk T, Gallinger S, Cohen Z, Tobi M, Redston M, Bapat B. STK11/LKB1 germline mutations are not identified in most Peutz-Jeghers syndrome patients. Clin Genet. 1999 Aug;56(2):136-41

Boardman LA, Pittelkow MR, Couch FJ, Schaid DJ, McDonnell SK, Burgart LJ, Ahlquist DA, Carney JA, Schwartz DI, Thibodeau SN, Hartmann LC. Association of Peutz-Jeghers-like mucocutaneous pigmentation with breast and gynecologic carcinomas in women. Medicine (Baltimore). 2000 Sep;79(5):293-8

Giardiello FM, Brensinger JD, Tersmette AC, Goodman SN, Petersen GM, Booker SV, Cruz-Correa M, Offerhaus JA. Very high risk of cancer in familial Peutz-Jeghers syndrome. Gastroenterology. 2000 Dec;119(6):1447-53

Sapkota GP, Kieloch A, Lizcano JM, Lain S, Arthur JS, Williams MR, Morrice N, Deak M, Alessi DR. Phosphorylation of the protein kinase mutated in Peutz-Jeghers cancer syndrome, LKB1/STK11, at Ser431 by p90(RSK) and cAMP-dependent protein kinase, but not its farnesylation at Cys(433), is essential for LKB1 to suppress cell vrowth. J Biol Chem. 2001 Jun 1;276(22):19469-82

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