Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer)

Lynch syndrome, or hereditary nonpolyposis colorectal cancer (HNPCC), is a hereditary cancer syndrome inherited in an autosomal dominant manner. It leads to defective DNA mismatch repair, causing a predisposition to cancer growth via microsatellite instability. Patients with lynch syndrome have an 80% likelihood of developing colon cancer. These typically affect the proximal colon, and different presentations of Lynch syndrome can involve endometrial, ovarian and skin cancers. Clinical suspician can warrant genetic testing through the 3-2-1 rule, or Amsterdam criteria. Treatment for Lynch syndrome includes frequent screening and eventually, colectomy.

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Characteristics

Autosomal Dominant
Domino
Lynch syndrome is inherited in an autosomal dominant manner. It is sometimes referred to as a "cancer syndrome."

Defective DNA Mismatch Repair
Broken Mismatched DNA Repair-man
Lynch syndrome is associated with the instability of short tandem DNA repeats (micro-satellites) due to germ-line mutations in DNA mismatch repair genes (e.g., MLH1, MSH2, and MSH6). DNA mismatch repair is a mechanism for recognizing and repairing erroneous DNA base insertion during replication or tissue damage. This is a type of "cancer syndrome" leading to a predisposition for tumor formation.

80% Risk of Colon Cancer Development
(80) Eating with Colon Tumors
There is a reported 80% incidence of colon cancer development in patients with Lynch syndrome.

Proximal (Right) Colon
P-proximal Colon
Colorectal cancers from Lynch syndrome almost always involve the proximal, or right, colon. Lynch Syndrome I (HNPCC I) only involves the right colon, while Lynch Syndrome II (HNPCC II) involves the right colon along with other manifestations (endometrium, ovaries, skin).

Type II associated with Endometrial, Ovarian and Skin Cancers
Inner-layer of Uterus, Ovaries, and Skin-suit with Tumors
Lynch Syndrome II (HNPCC II) involves the right colon along with other manifestations (typically endometrium, ovaries, or skin). Patients who are tested to have this genetic variation should be tested for carcinoma of the ovary, endometrium, small bowel, stomach, and pancreas.

3-2-1 Rule

3 Relatives with Colon Cancer
3 Relatives with Tumors
The first part of the 3-2-1 rule, or Amsterdam criteria, is that there is a high suspicion of Lynch syndrome if the patient has 3 relatives with colon cancer.

Occurs Across 2 Generations
2 Generations (Father and Son)
The second part of the 3-2-1 rule, or Amsterdam criteria, is there is a high suspicion of this syndrome if the patient's relatives who have colon cancer show it occuring across two generations.

1 Relative Diagnosed < 50 Years Old

1 Relative Under (50) Cent

The third part of the 3-2-1 rule, or Amsterdam criteria, is that there is a high suspicion of Lynch syndrome if the patient one relative who was diagnosed with colon cancer under the age of 50 years old.

Treatment

Frequent Screening

Frequent-clock with Screen-doors

After meeting the 3-2-1 criteria, genetic screening is done to confirm the existence of Lynch syndrome. Once diagnosed with Lynch syndrome, frequent screening is important to prevent progressed, untreated colon cancer. Patients should have a colonoscopy every 6 months after reaching the age of 25 years old. Females will need regular endometrial and ovarian screening.

Colectomy

Colon removed by scalpel

Surgery is the mainstay of treatment. Colectomy can be done electively to prevent cancer formation, or after tumors are found.
There is controversy about medical treatment, but aspirin has been studied in preventing colorectal cancer presentation in these patients.