Article title: Review of Hereditary non-polyposis colorectal cancer
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Review of Hereditary non-polyposis colorectal cancer

Introduction.
Hereditary non-polyposis colorectal cancer is also known as Lynch syndrome. It is autosomal dominant and is one of the most common causes of inherited colon cancer (1,2). A family history of colorectal cancer in first-degree relatives in two generations, and one case before the age of 50 is seen with Lynch syndrome (3).

Abstract

The purpose of this paper is to provide a review of hereditary non-polyposis colorectal cancer. This paper covers the causes, epidemiology, pathophysiology, histology, diagnosis, and treatment for the disease.

Body.

Cause
The cause of Lynch syndrome is a germline mutation in DNA mismatch repair. This leads to defective repair of DNA causing abnormal cell growth and tumor formation (4).

Epidemiology
The epidemiology of Lynch syndrome is as follows: it has a prevalence of about 1% of 6% in the white race population. Colorectal cancer is usually found about 10 to 15 years earlier than the general population and there is no variation in diagnosis between men and women (1).

Pathophysiology
The following is the pathophysiology of Lynch syndrome. In Lynch Syndrome, there is defective DNA mismatch repair. This can result in a base substitution from an insertion or deletion in a newly formed strand of DNA. Normal DNA mismatch repair identifies the mismatch and repairs it. However, mutations with the mismatch repair genes can lead to inadequate DNA repair causing malignant transformation. Mutations in the following genes lead to defective mismatch repair:

- hMLH1 on chromosome 3p22
- hMSH2 and hMSH6 on chromosome 2p16
- hPMS1 on chromosome 2q32 and hPMS2 on chromosome 7p22
- hMSH3 on chromosome 5q14.1
- EXO1 on chromosome 1q43.

Approximately 75 to 80% of Lynch syndrome is caused by mutations in hMLH1, hMSH2, and hMSH6 genes (1,5)

Histology
The histology of Lynch syndrome is characterized by mucus poorly differentiated signet ring cells. There is a lymphocytic infiltrate with a germinal center (6).

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Diagnosis
Mutations in any one of hMLH1, hMSH2, and hMSH6 genes establishes the diagnosis of lynch syndrome.

The Amsterdam II criteria is used to diagnose patients with Lynch syndrome. The criteria are listed below:

1. Three or more relatives with histology showing Lynch syndrome cancers such as colorectal cancer, endometrial cancers, small bowel cancers or kidney cancers. One individual must be a first degree relative and the other two must have familial adenomatous polyposis ruled out.
2. At least two generations with Lynch syndrome cancers

3. At least one cancer diagnosed before age 50 (1,7).

The Bethesda criteria guidelines are used to identify individuals who requires tumor testing for microsatellite instability testing. Patient with the following should undergo genetic testing for microsatellite instability:

1. Colorectal cancer in individuals less than 50 years old
2. Lynch syndrome associated tumors
3. Colorectal cancer in individuals less than 60 years old, along with microsatellite instability histology.
4. At least one first degree relative with the Lynch syndrome, tumor such as colorectal, endometrial, stomach, small bowel, ovarian or Billary.
5. Colorectal cancer in two or more first-degree relatives with Lynch syndrome tumors (1,7).

Clinical features of Lynch syndrome include the following: constipation, diarrhea, abdominal pain, bloating, blood in the stool, iron deficiency anemia, unexplained weight loss or generalized fatigue (1).

Treatment

Treatment for colorectal cancer is usually done with a total abdominal colectomy along with an iliorectal anastomosis. This is followed by annual endoscopies for rectal surveillance (8).

A segmental colectomy can be done for individuals who are not candidates for total colectomy. A prophylactic hysterectomy with bilateral salpingo-oophorectomy can be done for women undergoing colectomy (8).

Immune therapy targeting programmed death receptor – 1 has shown to be helpful with patients with metastatic colorectal cancer (1).

Cancer prevention strategies include prophylactic hysterectomy and bilateral salpingo-oophorectomy surgery, and oral contraceptives (1,9).

Conclusion.

Hereditary non-polyposis colorectal cancer, also known as Lynch syndrome, is caused by mutations in the genes for DNA mismatch repair. This is due to microsatellite instability. Diagnosis is made with genetic testing revealing mutations in MLH1, MSH2, MSH6, and PMS2) or EPCAM genes. Amsterdam II criteria can be used for diagnosis. Treatment is with total abdominal colectomy (1).

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