7-25-2018

Lynch Syndrome

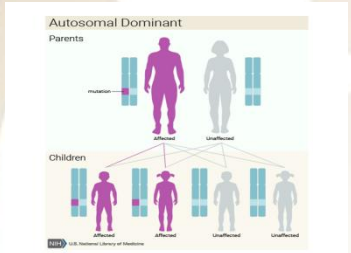
Raejeanne B. Nutter
Otterbein University, raejeannep@hotmail.com

Lynch Syndrome

Raejeanne B. Nutter, BSN, RN, CCRN
Otterbein University, Westerville, Ohio

Introduction

- Lynch syndrome (LS) runs in families as an autosomal dominant disease. This means that if one parent carries a mutated Lynch syndrome gene, there is a 50 percent chance that the mutation will be passed on to each child. (8) This topic was chosen because I have Lynch Syndrome .
- Lynch syndrome previously known as Hereditary Non-polyposis colorectal cancer syndrome (HNPCC) (9).
- Lynch syndrome the preponderance of an innate cancer syndrome, the most common cause of heritable colorectal cancer, and the only known heritable cause of endometrial cancer. Lynch syndrome is associated with cancers of the ovary, stomach, urothelial tract, small bowel, less frequently, cancers of the brain (glioblastoma), biliary tract, pancreas, and prostate (3).



U.S. National Library of Medicine, 2013.

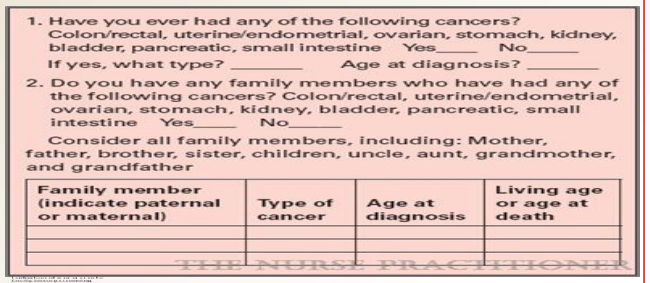
Pathophysiological Process

- Underlying Pathophysiology
- Lynch Syndrome is confirmed by a mutation in one of several mismatch repair (MMR) genes.(10)
- DNA is the genetic material that embodies instructions for every chemical process in the body. As cells grow and divide, DNA is copied, and it is common for minor mistakes to occur. (8)
- MMR normally responsible for correcting mistakes in the deoxyribonucleic acid (DNA) sequence. (8)
- MMR genes include *MLH1*, *MSH2*, *MSH6*, *PMS2* or by a mutation in the *EPCAM* gene. (10)
- *EPCAM* gene is not involved in DNA repair (2)
- The *EPCAM* gene has been shown to cause Lynch Syndrome by turning off its neighboring MSH2 gene (2)
- The errors preferentially accumulate in regions of the genome called microsatellites.
- Microsatellites are areas where repeating of DNA sequences, in which one to a few nucleotides (e.g., adenine-, cytosine-, guanine-, or thymine-based DNA elements) are repeated"(3) The linear sequence of DNA is symbolized by the first letter of the nucleotide base. When describing nucleotides, the first letter is used for identification, adenine (A), cytosine (C), guanine (G), thymine (T). (3)
- Normal cells have mechanisms to recognize these mistakes and repair them.(8) but during DNA synthesis, mutations can occur in microsatellites causing misalignments of the repetitive sequences. (3)
- However, people who inherit a mutated version of one of the genes associated with Lynch syndrome cannot repair these minor mistakes leading to permanent changes or mutations in the DNA sequences (8)
- An accumulation of such misalignments can lead to the cells becoming cancerous. (8)

Significance of Pathophysiology

United States, approximately has 140,000 new cases of colorectal cancer are diagnosed each year. About three to five percent of these cancers are caused by Lynch syndrome (U.S. National Library of Medicine, 2013). The significance of understanding genetics and genetic mutations and individual risk factors is imperative to preventative treatment and early detection

Implications for Nursing Care


1. Have you ever had any of the following cancers? Colon/rectal, uterine/endometrial, ovarian, stomach, kidney, bladder, pancreatic, small intestine Yes_____ No_____
   If yes, what type? _____ Age at diagnosis? _____
2. Do you have any family members who have had any of the following cancers? Colon/rectal, uterine/endometrial, ovarian, stomach, kidney, bladder, pancreatic, small intestine Yes_____ No_____

Consider all family members, including: Mother, father, brother, sister, children, uncle, aunt, grandmother, and grandfather

Family member (indicate paternal or maternal)	Type of cancer	Age at diagnosis	Living age or age at death

THE NURSE PRACTITIONER

- Completing genetic family history screening (GFHS) questionnaires during initial family history survey (4).
- Utilizing the GFHS questionnaire supports the identification of at-risk individuals for Lynch Syndrome who would benefit from genetic evaluation and testing (4)
- Serum (blood) Germline sequencing of the MMR genes remains the gold standard for confirming the causative gene mutation for Lynch Syndrome (5)
- The questionnaire encompasses multiple testing and diagnostic criteria from Original Amsterdam Criteria, Revised Amsterdam Criteria(Amsterdam Criteria II), Original Bethesda Criteria, Revised Bethesda Guidelines (1)
- People diagnosed with LS will need preventive screening and surgical procedures to reduce the incidence of a cancer diagnosis.
- Addition screening and testing will need to be ordered for these patients including having a family discussion and being sent for their genetic counseling and potential testing.

Sign & Symptoms

- The median age for diagnosis for Lynch Syndrome is between 44 and 61 in contrast to 66 years of age in sporadic cases of Colorectal Cancer (CRC) (Harrison & Handley, 2017).
- Signs of LS include a genetic predisposition to many primary cancers in the same person or on one side of the family; these cancers may be the same or different types of cancers known to be genetically linked. (Pasalodos-Sanchez, Howard, & Scotting, 2013).
- Identification may also include some rare cancers clustered in a family, diagnosis younger than average age, a particular genetic ancestry (Pasalodos-Sanchez et al., 2013) Understanding the family tree or family pedigree for determining carrier of mutated genes.

Top symptoms
80-99% Have the following

- Abdominal pain
- Colon cancer
- Constipation,
- Fatigue
- Gastrointestinal hemorrhage,
- Glioblastoma multiforme
- Malabsorption,
- Weight loss.

30-79%

- Anxiety
- Attention deficit hyperactivity disorder (ADHD)
- death in early adulthood
- death in infancy depression
- Hypertonia
- Increased intracranial pressure
- Irritability
- Migraine
- Muscular hypotonia, Nausea and vomiting
- Neoplasm of the rectum
- Seizures

National Institute of Health Genetic and rare disease center [NIH & GARD], 2018).

Conclusion

Lynch Syndrome is a genetic mutation that can lead to cancer. Identification and preventive screening is key to surviving and thriving with LS.
Below is the recommendation for individuals with LS.
5

Variable associated with LS	*Recommendation*	*Screening/Testing*
Colonoscopy	Annually or biennial	Starting at age 20-25 years or 2 – 5 years before earliest CRC diagnosis in the family
Endometrial cancer	Annually	Pelvic exam, endometrial sampling starting 30-35 years
Ovarian cancer	Annually	Transvaginal ultrasound starting age 30-35 years
Prophylactic hysterectomy and oophorectomy	Recommendation	Hysterectomy and bilateral salpingo-oophorectomy who have finished childbearing or 40 years
Gastric cancer	Consideration for at risk	Esoghagogastroduodenoscopy with gastric biopsy of antrum at 30-35 years
Small Intestinal cancer	No routine screening recommended at this time	
Cancers of the urinary tract	Annually	Urinalysis starting at 30-35 years
Pancreatic cancer	No routine screening recommended at this time	
Breast and prostate cancer	No special recommendations for LS	Routine general population screening
Treatment/Prevention	Colectomy and Aspirin	Colectomy with ileorectal anastomosis primary treatment for colon cancer or colon neoplasia not removable by endoscopy. Aspirin treatment is growing but is not conclusive.

References

1. (2014). *Diagnostic & Tumor Testing Criteria*. Available from Lynch Syndrome Screening Network.
2. *A Patient's Guide to Lynch Syndrome*. (2016). Hereditary Colon Cancer Foundation.
3. Cox, V. L., Saeed Bamashmos, A. A., Foo, W. C., Gupta, S., Yedururi, S., Garg, N., & Kang, H. C. (2018). Lynch Syndrome: Genomics Update and Imaging Review. *Radiographics,38*, 483-499.
4. Harrison, D. S., & Handley, M. (2017, August 17). Evaluation of a new genetic family history screening questionnaire for identifying Lynch Syndrome. *The Nurse Practitioner, 42(8)*, 48-51. https://doi.org/10.1097/01.NPR.0000515425.45908.af
5. Herzig, D. O., Buie, W., Weiser, M. R., You, Y., Rafferty, J. F., Feingold, D., & Steele, S. R. (2017). Clinical Practice Guidelines for the Surgical Treatment of Patients with Lynch Syndrome. *Disease of the Colon & Rectum, 60*, 137-143. https://doi.org/10.1097/DCR.0000000000000785
6. National Institute of Health Genetic and rare disease center. (2018). *Lynch Syndrome*. Retrieved from https://rarediseases.info.nih.gov/diseases/9905/lynch-syndrome
7. Offit, K. (2012, May 24). *Understanding Lynch Syndrome: Facts and Statistics* [Video file]. Retrieved from https://www.youtube.com/watch?v=NbRj2vjDw4c
8. Pasalodos-Sanchez, S., Howard, P., & Scotting, P. (2013). Identifying Familial Cancer Risk. *Cancer Nursing Practice, 12*, 16-22.
9. Shulman, L. P. (2015). Lynch Syndrome: Identification and surveillance will help carriers avoid cancer. *Contemporary OB/GYN*, 33-47.
10. Solomon, I., Harrington, E., Hooker, G., Erby, L., Axilbund, J., Hampel, H., ... Leonard, L. (2017, January 26). Lynch Syndrome Limbo: Patient Understanding of Variants of Uncertain Significance. *Springer*, 866-877. https://doi.org/10.1007/s10897-071-0066-y
11. U.S. National Library of Medicine. (2013). *Genetic Home Reference, Lynch Syndrome*. Retrieved from https://ghr.nlm.nih.gov/condition/lynch-syndrome#inheritance

OTTERBEIN UNIVERSITY