

World Journal of *Clinical Cases*

World J Clin Cases 2022 July 16; 10(20): 6759-7186



Contents

Thrice Monthly Volume 10 Number 20 July 16, 2022

OPINION REVIEW

- 6759 Semaglutide might be a key for breaking the vicious cycle of metabolically associated fatty liver disease spectrum?

Cigrovski Berkovic M, Rezig T, Bilic-Curcic I, Mrzljak A

MINIREVIEWS

- 6769 Drainage of pancreatic fluid collections in acute pancreatitis: A comprehensive overview
- Bansal A, Gupta P, Singh AK, Shah J, Samanta J, Mandavdhare HS, Sharma V, Sinha SK, Dutta U, Sandhu MS, Kochhar R*

- 6784 Frontiers of COVID-19-related myocarditis as assessed by cardiovascular magnetic resonance

Luo Y, Liu BT, Yuan WF, Zhao CX

ORIGINAL ARTICLE

Case Control Study

- 6794 Urinary and sexual function changes in benign prostatic hyperplasia patients before and after transurethral columnar balloon dilatation of the prostate

Zhang DP, Pan ZB, Zhang HT

- 6803 Effects of the information-knowledge-attitude-practice nursing model combined with predictability intervention on patients with cerebrovascular disease

Huo HL, Gui YY, Xu CM, Zhang Y, Li Q

Retrospective Cohort Study

- 6811 Effects of Kampo medicine hangebyakujutsutemmato on persistent postural-perceptual dizziness: A retrospective pilot study

Miwa T, Kanemaru SI

Retrospective Study

- 6825 Longitudinal changes in personalized platelet count metrics are good indicators of initial 3-year outcome in colorectal cancer

Herold Z, Herold M, Lohinszky J, Szasz AM, Dank M, Somogyi A

- 6845 Efficacy of Kegel exercises in preventing incontinence after partial division of internal anal sphincter during anal fistula surgery

Garg P, Yagnik VD, Kaur B, Menon GR, Dawka S

Observational Study

- 6855 Influence of the water jet system vs cavitron ultrasonic surgical aspirator for liver resection on the remnant liver

Hanaki T, Tsuda A, Sunaguchi T, Goto K, Morimoto M, Murakami Y, Kihara K, Matsunaga T, Yamamoto M, Tokuyasu N, Sakamoto T, Hasegawa T, Fujiwara Y

- 6865** Critical values of monitoring indexes for perioperative major adverse cardiac events in elderly patients with biliary diseases

Zhang ZM, Xie XY, Zhao Y, Zhang C, Liu Z, Liu LM, Zhu MW, Wan BJ, Deng H, Tian K, Guo ZT, Zhao XZ

- 6876** Comparative study of surface electromyography of masticatory muscles in patients with different types of bruxism

Lan KW, Jiang LL, Yan Y

Randomized Controlled Trial

- 6890** Dural puncture epidural technique provides better anesthesia quality in repeat cesarean delivery than epidural technique: Randomized controlled study

Wang SY, He Y, Zhu HJ, Han B

SYSTEMATIC REVIEWS

- 6900** Network pharmacology-based strategy for predicting therapy targets of Sanqi and Huangjing in diabetes mellitus

Cui XY, Wu X, Lu D, Wang D

META-ANALYSIS

- 6915** Endoscopic submucosal dissection for early signet ring cell gastric cancer: A systematic review and meta-analysis

Weng CY, Sun SP, Cai C, Xu JL, Lv B

- 6927** Prognostic value of computed tomography derived skeletal muscle mass index in lung cancer: A meta-analysis

Pan XL, Li HJ, Li Z, Li ZL

CASE REPORT

- 6936** Autosomal dominant osteopetrosis type II resulting from a *de novo* mutation in the *CLCN7* gene: A case report

Song XL, Peng LY, Wang DW, Wang H

- 6944** Clinical expression and mitochondrial deoxyribonucleic acid study in twins with 14484 Leber's hereditary optic neuropathy: A case report

Chuenkongkaew WL, Chinkulkitnivat B, Lertrit P, Chirapapaisan N, Kaewsutthi S, Suktitipat B, Mitrpant C

- 6954** Management of the enteroatmospheric fistula: A case report

Cho J, Sung K, Lee D

- 6960** Lower lip recurrent keratoacanthoma: A case report

Liu XG, Liu XG, Wang CJ, Wang HX, Wang XX

- 6966** Optic disc coloboma associated with macular retinoschisis: A case report

Zhang W, Peng XY

- 6974** A 7-year-old boy with recurrent cyanosis and tachypnea: A case report
Li S, Chen LN, Zhong L
- 6981** Schwannomatosis patient who was followed up for fifteen years: A case report
Li K, Liu SJ, Wang HB, Yin CY, Huang YS, Guo WT
- 6991** Intentional replantation combined root resection therapy for the treatment of type III radicular groove with two roots: A case report
Tan D, Li ST, Feng H, Wang ZC, Wen C, Nie MH
- 6999** Clinical features and genetic variations of severe neonatal hyperbilirubinemia: Five case reports
Lin F, Xu JX, Wu YH, Ma YB, Yang LY
- 7006** Percutaneous transhepatic access for catheter ablation of a patient with heterotaxy syndrome complicated with atrial fibrillation: A case report
Wang HX, Li N, An J, Han XB
- 7013** Secondary positioning of rotationally asymmetric refractive multifocal intraocular lens in a patient with glaucoma: A case report
Fan C, Zhou Y, Jiang J
- 7020** Laparoscopic repair of diaphragmatic hernia associating with radiofrequency ablation for hepatocellular carcinoma: A case report
Tsunoda J, Nishi T, Ito T, Inaguma G, Matsuzaki T, Seki H, Yasui N, Sakata M, Shimada A, Matsumoto H
- 7029** Hypopituitary syndrome with pituitary crisis in a patient with traumatic shock: A case report
Zhang XC, Sun Y
- 7037** Solitary plasmacytoma of the left rib misdiagnosed as angina pectoris: A case report
Yao J, He X, Wang CY, Hao L, Tan LL, Shen CJ, Hou MX
- 7045** Secondary coronary artery ostial lesions: Three case reports
Liu XP, Wang HJ, Gao JL, Ma GL, Xu XY, Ji LN, He RX, Qi BYE, Wang LC, Li CQ, Zhang YJ, Feng YB
- 7054** Bladder perforation injury after percutaneous peritoneal dialysis catheterization: A case report
Shi CX, Li ZX, Sun HT, Sun WQ, Ji Y, Jia SJ
- 7060** Myotonic dystrophy type 1 presenting with dyspnea: A case report
Jia YX, Dong CL, Xue JW, Duan XQ, Xu MY, Su XM, Li P
- 7068** Novel mutation in the *SALL1* gene in a four-generation Chinese family with uraemia: A case report
Fang JX, Zhang JS, Wang MM, Liu L
- 7076** Malignant transformation of primary mature teratoma of colon: A case report
Liu J

- 7082** Treatment of pyogenic liver abscess by surgical incision and drainage combined with platelet-rich plasma: A case report
Wang JH, Gao ZH, Qian HL, Li JS, Ji HM, Da MX
- 7090** Left bundle branch pacing in a ventricular pacing dependent patient with heart failure: A case report
Song BX, Wang XX, An Y, Zhang YY
- 7097** Solitary fibrous tumor of the liver: A case report and review of the literature
Xie GY, Zhu HB, Jin Y, Li BZ, Yu YQ, Li JT
- 7105** MutL homolog 1 germline mutation c.(453+1_454-1)_(545+1_546-1)del identified in lynch syndrome: A case report and review of literature
Zhang XW, Jia ZH, Zhao LP, Wu YS, Cui MH, Jia Y, Xu TM
- 7116** Malignant histiocytosis associated with mediastinal germ cell tumor: A case report
Yang PY, Ma XL, Zhao W, Fu LB, Zhang R, Zeng Q, Qin H, Yu T, Su Y
- 7124** Immunoglobulin G4 associated autoimmune cholangitis and pancreatitis following the administration of nivolumab: A case report
Agrawal R, Guzman G, Karimi S, Giulianotti PC, Lora AJM, Jain S, Khan M, Boulay BR, Chen Y
- 7130** Portal vein thrombosis in a noncirrhotic patient after hemihepatectomy: A case report and review of literature
Zhang SB, Hu ZX, Xing ZQ, Li A, Zhou XB, Liu JH
- 7138** Microvascular decompression for a patient with oculomotor palsy caused by posterior cerebral artery compression: A case report and literature review
Zhang J, Wei ZJ, Wang H, Yu YB, Sun HT
- 7147** Topical halometasone cream combined with fire needle pre-treatment for treatment of primary cutaneous amyloidosis: Two case reports
Su YQ, Liu ZY, Wei G, Zhang CM
- 7153** Simultaneous robot-assisted approach in a super-elderly patient with urothelial carcinoma and synchronous contralateral renal cell carcinoma: A case report
Yun JK, Kim SH, Kim WB, Kim HK, Lee SW
- 7163** Nursing a patient with latent autoimmune diabetes in adults with insulin-related lipodystrophy, allergy, and exogenous insulin autoimmune syndrome: A case report
He F, Xu LL, Li YX, Dong YX
- 7171** Incidental diagnosis of medullary thyroid carcinoma due to persistently elevated procalcitonin in a patient with COVID-19 pneumonia: A case report
Saha A, Mukhopadhyay M, Paul S, Bera A, Bandyopadhyay T
- 7178** Macular hole following phakic intraocular lens implantation: A case report
Li XJ, Duan JL, Ma JX, Shang QL

LETTER TO THE EDITOR

- 7184** Is every microorganism detected in the intensive care unit a nosocomial infection? Isn't prevention more important than detection?

Yildirim F, Karaman I, Yildirim M

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Jie-Feng Huang, PhD, Associate Chief Physician, Associate Professor, Department of Orthopaedics and Traumatology, The First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou 310006, Zhejiang Province, China. 40983285@qq.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Hua-Ge Yin, Production Department Director: Xu Guo, Editorial Office Director: Jin-Lei Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

July 16, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



MutL homolog 1 germline mutation c.(453+1_454-1)_(545+1_546-1)del identified in lynch syndrome: A case report and review of literature

Xi-Wen Zhang, Zan-Hui Jia, Li-Ping Zhao, Yi-Shi Wu, Man-Hua Cui, Yan Jia, Tian-Min Xu

Specialty type: Obstetrics and gynecology

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Dabravolski SA, Belarus; Yoshida H, Japan

A-Editor: Yao QG, China

Received: December 18, 2021

Peer-review started: December 18, 2021

First decision: January 25, 2022

Revised: February 4, 2022

Accepted: May 27, 2022

Article in press: May 27, 2022

Published online: July 16, 2022



Xi-Wen Zhang, Zan-Hui Jia, Li-Ping Zhao, Yi-Shi Wu, Man-Hua Cui, Yan Jia, Tian-Min Xu, Department of Gynecology, The Second Hospital of Jilin University, Changchun 130000, Jilin Province, China

Corresponding author: Man-Hua Cui, MD, PhD, Chief Doctor, Department of Gynecology, The Second Hospital of Jilin University, No. 218 Ziqiang Road, Changchun 130000, Jilin Province, China. cuimh@jlu.edu.cn

Abstract

BACKGROUND

Lynch syndrome (LS) is an autosomal dominant hereditary disorder because of germline mutations in DNA mismatch repair genes, such as MutL homolog 1 (*MLH1*), PMS1 homolog 2, MutS homolog 2, and MutS homolog 6. Gene mutations could make individuals and their families more susceptible to experiencing various malignant tumors. In Chinese, *MLH1* germline mutation c.(453+1_454-1)_(545+1_546-1)del-related LS has been infrequently reported. Therefore, we report a rare LS patient with colorectal and endometrioid adenocarcinoma and describe her pedigree characteristics.

CASE SUMMARY

A 57-year-old female patient complained of irregular postmenopausal vaginal bleeding for 6 mo. She was diagnosed with LS, colonic malignancy, endometrioid adenocarcinoma, secondary fallopian tube malignancy, and intermyometrial leiomyomas. Then, she was treated by abdominal hysterectomy, bilateral oviduct oophorectomy, and sentinel lymph node resection. Genetic testing was performed using next-generation sequencing technology to detect the causative genetic mutations. Moreover, all her family members were offered a free genetic test, but no one accepted it.

CONCLUSION

No tumor relapse or metastasis was found in the patient during the 30-mo follow-up period. The genetic panel sequencing showed a novel pathogenic germline mutation in *MLH1*, c.(453+1_454-1)_(545+1_546-1)del, for LS. Moreover, cancer genetic counseling and testing are still in the initial development state in China, and maybe face numerous challenges in the further.

Key Words: Lynch syndrome; Colorectal cancer; Endometrial cancer; *MLH1* gene; Gene testing; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Lynch syndrome (LS) is an autosomal dominant hereditary disorder because of germline mutations in DNA mismatch repair genes, such as MutL homolog 1 (*MLH1*) gene, PMS1 homolog 2 gene, MutS homolog 2 gene, and MutS homolog 6 gene, which make the patient more susceptible to other malignancies. In Chinese, *MLH1* germline mutation c.(453+1_454-1)_(545+1_546-1)del-induced LS has been infrequently reported. In this paper, we report a rare LS patient with colorectal and endometrioid adenocarcinoma. The genetic panel sequencing showed a novel pathogenic germline mutation in *MLH1*, c.(453+1_454-1)_(545+1_546-1)del, for LS.

Citation: Zhang XW, Jia ZH, Zhao LP, Wu YS, Cui MH, Jia Y, Xu TM. MutL homolog 1 germline mutation c.(453+1_454-1)_(545+1_546-1)del identified in lynch syndrome: A case report and review of literature. *World J Clin Cases* 2022; 10(20): 7105-7115

URL: <https://www.wjgnet.com/2307-8960/full/v10/i20/7105.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i20.7105>

INTRODUCTION

Lynch syndrome (LS) is an autosomal dominant inherited disorder because of germline mutations in DNA mismatch repair (MMR) genes, such as MutL homolog 1 (*MLH1*), PMS1 homolog 2 (*PMS2*), MutS homolog 2 (*MSH2*), and MutS homolog 6 (*MSH6*), which make the patient more susceptible to other malignancies[1,2]. *MLH1*, *MSH2*, *MSH6*, and *PMS2* mutations in LS account for approximately 50%[3-5], 40%[5], 7%-20%[3-8], and < 6%[3,4,9] of all cases, respectively. Additionally, specific MMR gene deficiencies might result in different ages of onset, types of malignancy, and clinical signs[10]. The *MLH1* gene defects could decrease the expression of *MLH1* protein, affecting the MMR function, leading to errors in DNA replication and ultimately inducing neoplasms[11,12].

LS can be classified as types I and II according to the location of tumors[3,13,14]. Type I is an intestinal neoplasm, such as colorectal cancer[14]. Besides, type II is defined as colorectal malignancy complicated with parenteral cancers, including gastric cancer[15], renal cell cancer[16], epithelial ovarian cancer[17], endometrial cancer[2], bladder cancer[18,19], breast cancer[20], and even repeated stroke[10]. Endometrial cancer is the most frequent parenteral tumor among LS patients[21,22], which ranks 3rd in the mortality of all gynecological cancers[23]. In recent years, LS-associated endometrial cancer (LSAEC) has received increasing attention in the medical field[24]. Furthermore, the offspring of LS patients will have a 50% incidence of inheritance[24]. More than 2600 mutations have been reported worldwide[10,24,25], but *MLH1* exon 6 c.(453+1_454-1)_(545+1_546-1)del-induced LS has been rarely described in Chinese. Therefore, we present a rare case with an *MLH1* germline mutation, analyze her pedigree characteristics, and review the *MLH1* gene mutation loci.

CASE PRESENTATION

Chief complaints

A 57-year-old Chinese female patient complained of irregular postmenopausal vaginal bleeding. The demographic characteristics of the patient are listed in Table 1.

History of present illness

The patient had the clinical symptom of irregular vaginal bleeding for 6 mo.

History of past illness

The patient had a medical history of colon cancer and received a radical colon cancer operation 20 years ago.

Personal and family history

The patient and many of her family members had a cancer history.

Table 1 Demographic characteristics

Parameter	Outcome
Sex	Female
Age (yr)	57
Sample type	Peripheral venous blood
Genes	<i>EPCAM</i> , <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>PMS2</i> , <i>STK11</i> , <i>TP53</i> , <i>PTEN</i> , <i>MUTYH</i> , <i>BRCA1</i> , <i>MLH3</i>
Length of the target region (bp)	49287
Target area coverage	100%
Average depth of target area (×)	608.777386
Average depth of target area > 30 × the proportion of sites	99.78%
Detection range	Exon and its adjacent ± 20 bp intron region

EPCAM: Epithelial cell adhesion molecule; *MLH1*: MutL homolog 1; *MSH2*: MutS homolog 2; *MSH6*: MutS homolog 6; *PMS2*: PMS1 homolog 2; *STK11*: Serine-Threonine Kinase 11; *TP53*: tumor protein 53; *PTEN*: Phosphatase and tensin homolog; *MUTYH*: Mut Y homolog; *BRCA1*: Breast cancer gene 1; *MLH3*: MutL homolog 3.

Physical examination

A small amount of white secretions with no odor was found in the vagina. A smooth cervical surface was detected. The vulva was atrophic, the vagina was patent, and mucosal fold atrophy was palpated. Moreover, the uterus was in an anterior position, with a smooth surface and good range of motion. No obvious abnormality was found in the bilateral adnexal areas.

Laboratory examinations

No abnormality was found in the routine blood tests.

Imaging examinations

Ultrasound

Preoperative abdominal Doppler ultrasound showed that the uterus, with a size of 3.8 cm × 3.5 cm × 3.1 cm, was located in an anterior position, the uterine cavity line was clear, the endometrial thickness was 1.1 cm (significantly greater than the normal value of endometrial thickness in postmenopausal women), and the ultrasonic echo of the endometrium was uneven. In addition, bilateral ovaries and adnexa presented no abnormality. Color Doppler flow imaging showed no abnormal blood flow signal.

Magnetic resonance imaging

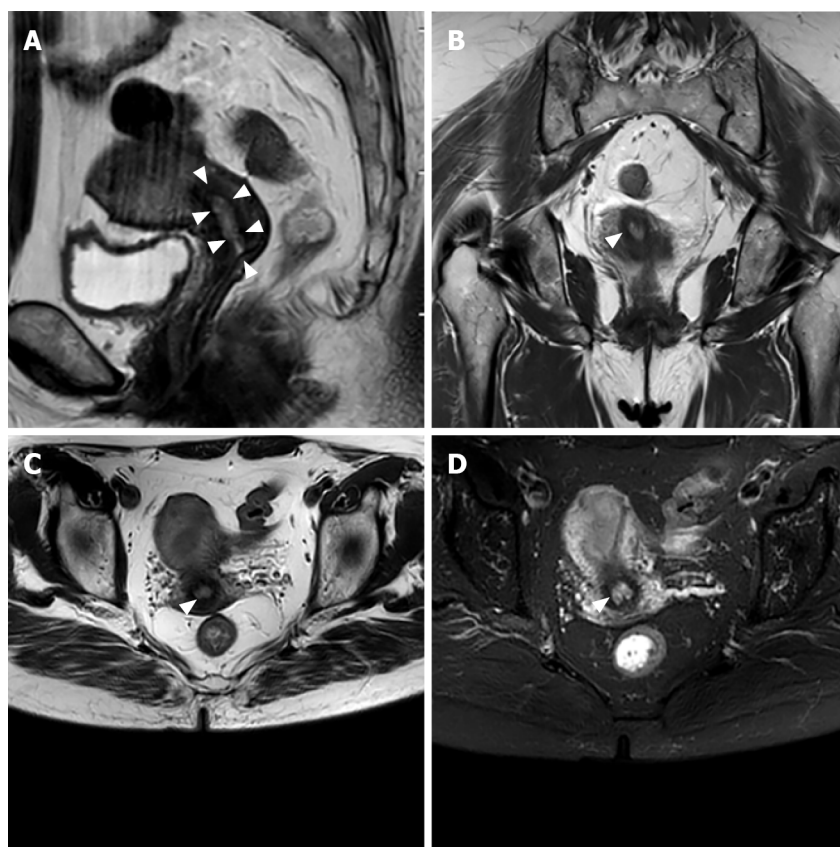
Abdominal magnetic resonance imaging showed that the uterus was in an anteversion and flexion position. A mass with an equal T1 and slightly long T2 signal was found in the uterine cavity, with an unclear boundary (Figure 1A). The tumor size was about 31 mm × 23 mm, and the display of the uterine junction was not clear (Figure 1B and C). The enhanced images showed that the lesions exhibited inhomogeneous enhancement. Diffusion-weighted imaging showed that the lesions exhibited a high signal. The shape and signal of the bilateral adnexa were normal (Figure 1D). There was no obvious abnormal signal in the bladder and rectum. No abnormality was found in bilateral iliac vessels and inguinal lymph nodes. No effusion was found in the pelvic cavity, and no obvious abnormal signal was found in pelvic wall soft tissue.

FINAL DIAGNOSIS

The clinical diagnosis was endometrioid adenocarcinoma (IIIA1) and LS.

TREATMENT

After general anesthesia, abdominal hysterectomy and bilateral oviduct oophorectomy were performed. The whole uterus and bilateral appendages were examined during the operation by fast-frozen histopathology. It revealed a poorly differentiated adenocarcinoma of the uterus, which infiltrated the



DOI: 10.12998/wjcc.v10.i20.7105 Copyright ©The Author(s) 2022.

Figure 1 Preoperative abdominal magnetic resonance imaging. A: Sagittal magnetic resonance imaging (MRI) showed an equal T1 and slightly longer T2 signal in the uterine cavity; B: Coronal MRI image; C: Axial MRI image. D: Enhanced MRI image showing that the lesions were inhomogeneous enhanced. The white arrowheads represent lesions. The tumor size was approximately 31 mm × 23 mm (B and C).

superficial muscularis. Subsequently, sentinel lymph node resection was also performed. After surgery, the patient was treated with regular chemotherapy for six courses, including paclitaxel (Nanjing Green Leaf Pharmaceutical Co., Ltd., Nanjing, China) and carboplatin injection (Qilu Pharmaceutical Co., Ltd., Jinan, China).

OUTCOME AND FOLLOW-UP

The biopsy histochemical (hematoxylin-eosin) staining showed that endometrial cancer was moderately to poorly differentiated. A few of its lesions were accompanied by squamous differentiation. The tumor infiltrated into the superficial muscle wall. Noticeably, one side of the fallopian tube showed cancerous lesions, while the other side of the fallopian tube and bilateral ovaries showed no cancerous lesions. However, cervical vessels, blood vessels, lymphatic vessels, and nerves were not invaded. Bilateral pelvic lymph nodes were normal.

Immunohistochemical (IHC) staining results showed *MLH1* (-), *PMS2* (-), *MSH6* (+/-), *MSH2* (+/-), *BRAF* V600E mutation-specific antibody (VE1) (Ventana IHC enhanced amplification kit) (-), *CD31* (-), *D2-40* (-), *CK5/6* (partial lesions +/-), *p63* (+/-), and *CDX2* (-) (Figure 2). Besides, the positive rate of PR was 90+ACU- (+/-). The positive rate of ER was 90+ACU- (+/-). The positive rate of Ki67 was 60+ACU-. P53 was scattered weak positive, and P16 was partially positive. Based on these findings, the patient was diagnosed with endometrioid adenocarcinoma (IIIA1).

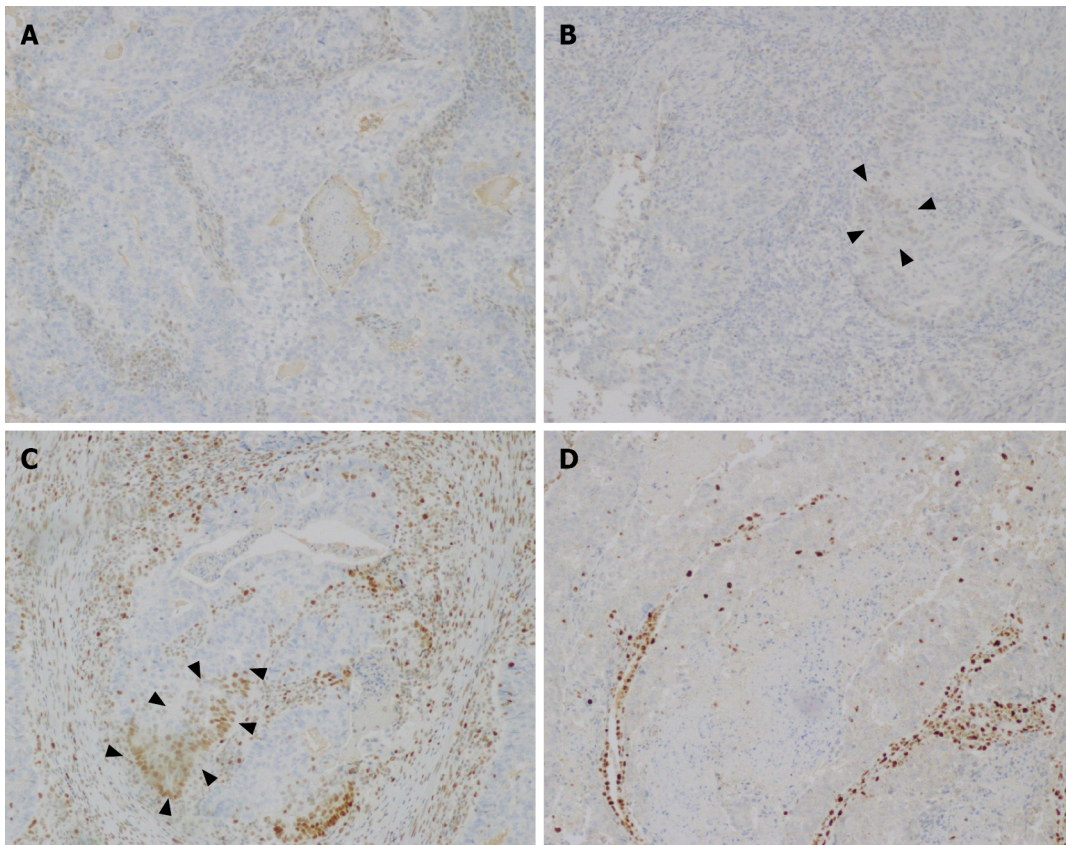
No tumor recurrence or metastasis was found during a 2.5-year follow-up period. Computed tomography was performed after six chemotherapy courses and showed no abnormality in the head, liver, gallbladder, spleen, pancreas, bilateral kidney, bilateral ureter, rectum, or lung.

The results of gene sequencing are shown in Tables 2 and 3. A heterozygous deletion mutation of exon 6 was detected in the *MLH1* gene, which was named c.(453+1+AF8-454-1)+AF8-(545+1+AF8-546-1)del according to the Human Genome Variation Society (Figure 3). Postoperatively, the patient was diagnosed with LS, endometrioid adenocarcinoma (IIIA1), colonic malignancy, secondary fallopian tube malignancy, and intermyometrial leiomyomas.

Table 2 Gene detection of hereditary endometrial cancer

Parameter	Outcome
Diagnosis	Hereditary EC
Gene (NM number)	<i>MLH1</i> (NM_000249.3)
Nucleotide changes	Exon 6 del
Amino acid changes	-
Gene subregion	Exon 6
Heterozygous	Heterozygous mutation
Functional changes	Deletion
Genetic model	AD
Gene mutation type	Known pathogenic mutation

EC: Endometrial cancer; AD: Autosomal dominant inheritance; *MLH1*: MutL homolog 1.



DOI: 10.12998/wjcc.v10.i20.7105 Copyright ©The Author(s) 2022.

Figure 2 Immunohistochemical images. A: Loss of MLH1 proteins was found in the tumor cells; B: Expression of MSH2 protein was detected in the tumor cells; C: Expression of MSH6 protein was detected in the tumor cells; D: Loss of PMS2 protein was found in the tumor cells.

The patient's eldest sister was diagnosed with colon cancer at age 60, the second sister with endometrial cancer at age 60, the third sister with colon cancer at age 40, the older brother with colon polyps three times between the ages of 40 and 50, the mother with endometrial cancer at age 48, and the mother with colon cancer at age 50. The prevalence spectrum of the four generations of patients is shown in [Figure 4](#).

Genetic counseling was conducted among the family relatives. Moreover, we provided free Sanger mutation site verification tests for the family members of the patient. However, all relatives refused to be tested.

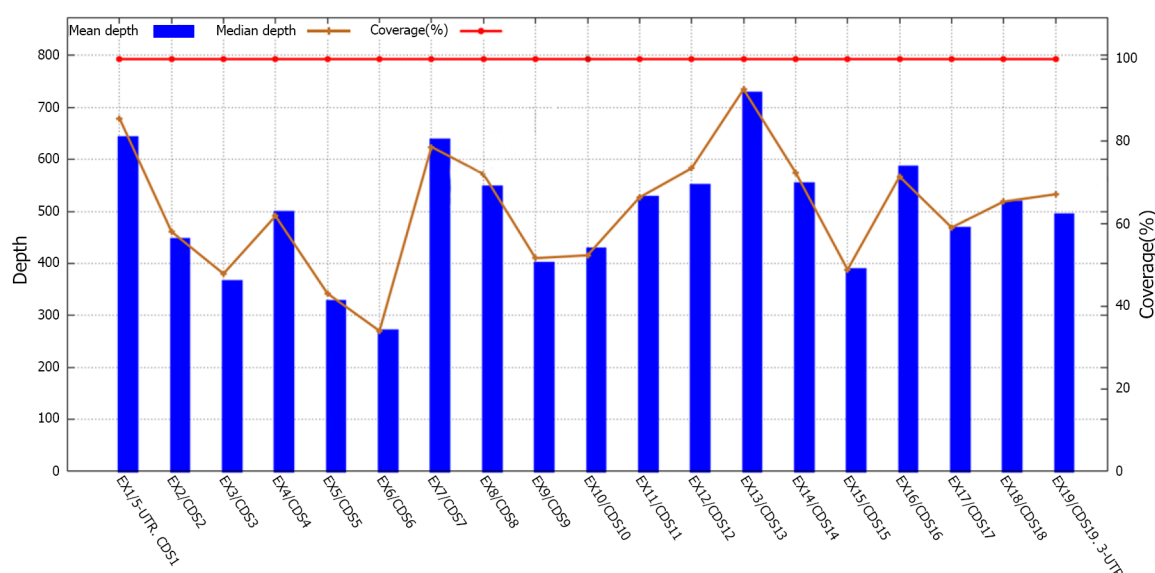
Table 3 Variation information of exon region and its adjacent ± 20 bp intron region in hereditary endometrial cancer

No.	Gene	Transcript	NV	AAC	GS	Heterozygous	Rs NO.	FC	MT
1	<i>MLH1</i>	NM_000249.3	EX6 DEL	-	EX6	Het	-	Deletion	Kv
2	<i>MLH1</i>	NM_000249.3	c.1151T>A	p.Val384Asp	CDS12	Het	rs63750447	Missense	Bp
3	<i>MUTYH</i>	NM_001128425.1	c.74G>A	p.Gly25Asp	CDS2	Het	rs75321043	Missense	Uv
4	<i>MUTYH</i>	NM_001128425.1	c.53C>T	p.Pro18Leu	CDS2	Het	rs79777494	Missense	Uv
5	<i>MUTYH</i>	NM_001128425.1	c.36+11C>T	-	IN1	Het	rs2275602	Splice	Bp
6	<i>MUTYH</i>	NM_001128425.1	c.1014G>C	p.Gln338His	CDS12	Het	rs3219489	Missense	Bp
7	<i>BRCA1</i>	NM_007294.3	c.2612C>T	p.Pro871Leu	CDS9	Het	rs799917	Missense	Bp
8	<i>BRCA1</i>	NM_007294.3	c.4837A>G	p.Ser1613Gly	CDS14	Het	rs1799966	Missense	Bp
9	<i>BRCA1</i>	NM_007294.3	c.3548A>G	p.Lys1183Arg	CDS9	Het	rs16942	Missense	Bp
10	<i>BRCA1</i>	NM_007294.3	c.3113A>G	p.Glu1038Gly	CDS9	Het	rs16941	Missense	Bp
11	<i>EPCAM</i>	NM_002354.2	c.344T>C	p.Met115Thr	CDS3	Het	rs1126497	Missense	Bp
12	<i>MLH3</i>	NM_014381.2	c.2531C>T	p.Pro844Leu	CDS1	Het	rs175080	Missense	Bp
13	<i>MLH3</i>	NM_014381.2	c.2476A>G	p.Asn826Asp	CDS1	Hom	rs175081	Missense	Bp
14	<i>MSH2</i>	NM_000251.2	c.211+9C>G	-	IN1	Het	rs2303426	Splice	Bp
15	<i>MSH6</i>	NM_000179.2	c.3438+14A>C	-	IN5	Hom	rs2020911	Splice	Bp
16	<i>PMS2</i>	NM_000535.6	c.1408C>T	p.Pro470Ser	CDS11	Het	rs1805321	Missense	Bp
17	<i>PMS2</i>	NM_000535.6	c.2570G>C	p.Gly857Ala	CDS15	Hom	rs1802683	Missense	Bp
18	<i>PMS2</i>	NM_000535.6	c.706-4delT	-	IN6	Het	rs6079473	Splice	Bp
19	<i>PMS2</i>	NM_000535.6	c.59G>A	p.Arg20Gln	CDS2	Het	rs10254120	Missense	Bp
20	<i>PMS2</i>	NM_000535.6	c.1621A>G	p.Lys541Glu	CDS11	Hom	rs2228006	Missense	Bp
21	<i>PMS2</i>	NM_000535.6	c.705+17A>G	-	IN6	Het	rs62456182	Splice	Bp
22	<i>PMS2</i>	NM_000535.6	c.2007-4G>A	-	IN11	Het	rs1805326	Splice	Bp
23	<i>PMS2</i>	NM_000535.6	c.2007-7C>T	-	IN11	Het	rs55954143	Splice	Bp
24	<i>PTEN</i>	NM_000314.6	c.802-3dupT	-	IN7	Het	rs762344516	Splice	Bp
25	<i>TP53</i>	NM_000546.5	c.215C>G	p.Pro72Arg	CDS3	Het	rs1042522	Missense	Bp

EC: Endometrial cancer; NV: Nucleotide variation; AAC: Amino acid changes; GS: Gene subregion; Rs NO.: rs number; FC: Functional changes; MT: Mutation types; Kv: Known variation; Uv: Unknown variation; Bp: Benign polymorphism; Het: Heterozygous; Hom: Homozygous.

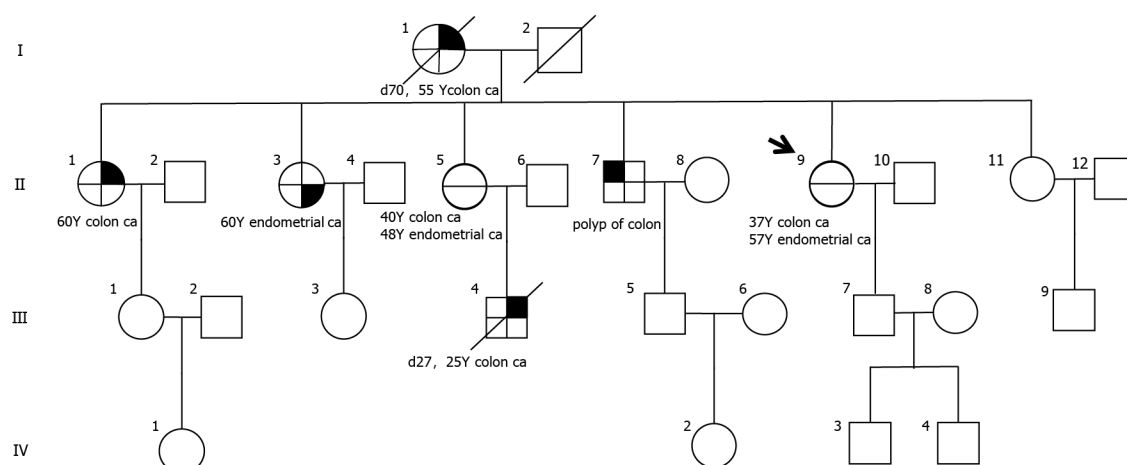
DISCUSSION

Colorectal cancer is the 5th commonly diagnosed cancer in China[23,26]. In 2015, the number of colorectal cancer-related deaths and new cases in China was approximately 191000 and 376300, respectively. Moreover, hereditary colorectal malignancy accounts for 5%-10% of colorectal malignancies, including LS, Li-Fraumeni syndrome, MUTYH-associated polyposis, juvenile polyposis syndrome, familial adenomatous polyposis, and Peutz-Jeghers syndrome[27]. In this study, the patient had a medical history of colon cancer 20 years ago and has experienced endometrial adenocarcinoma. We found that the patient carries a novel pathogenic genetic deletion mutation in *MLH1*. Many researchers have reported diseases caused by *MLH1* gene mutations[28-31]. Hong *et al*[31] detected that the deletion of exon 7 to exon 19 of the *MLH1* gene was a pathogenic mutation causing colorectal cancer. Jia *et al*[28] reported that the p.K618del variant in *MLH1* was the causative pathogenic genetic variant for LS. Solassol *et al*[29] found that an *AluY5a* insertion in *MLH1* exon 6 led to exon skipping, which resulted in a pathogenic frameshift in patients who developed colorectal adenocarcinomas. Li *et al*[30] reported that the insertion of a truncated *AluSx* like element into *MLH1* intron 7 resulted in aberrant splicing and transcription, thus inducing LS. Lagerstedt-Robinson *et al*[32] reported an LS patient with the deletion of *MLH1* c.(453+1_454-1)_(545+1_546-1) in Switzerland. However, in China, the *MLH1* genetic mutation c.(453+1_454-1)_(545+1_546-1) del has not been reported. Consequently, we present a relatively rare LS patient with *MLH1* c.(453+1_454-1)_(545+1_546-1)del and describe the clinical features, pathological features, and familial morbidity of the proband.



DOI: 10.12998/wjcc.v10.i20.7105 Copyright ©The Author(s) 2022.

Figure 3 Figures related to gene test results. A deletion mutation of exon 6 was found in the *MLH1* gene.



DOI: 10.12998/wjcc.v10.i20.7105 Copyright ©The Author(s) 2022.

Figure 4 Family pedigree. The reconstructed pedigree demonstrates that the proband (II-9), her mother (I-1), her sisters (II-1, II-3, and II-5) and her brother (II-7), and her sister's son (IV-4) experienced cancer. I-1 was diagnosed with colon cancer at 55 years and died at 70 years. II-1 and II-3, both at 60 years, suffered from colon cancer and endometrial cancer, respectively. II-5 experienced colon cancer at 40 years and endometrial cancer at 48 years. II-7 developed polyps of the colon at unknown age. III-4 had colon cancer at 25 years and died at 27 years. The arrow indicates the proband. Solid symbols reveal persons affected by malignancy. The symbol with a slash indicates a deceased individual with age at death. Circles indicate female family members, and squares suggest male family members.

The demographic characteristics of LSAEC are as follows: First, the pathological types are diverse and poorly differentiated. Second, the onset age is between 46 and 54 years old. Third, the majority of the pathological changes are situated in the lower segment of the corpus uteri[33]. The potential risk of LS patients experiencing another cancer at 10 and 15 years was 25% and 50%, respectively[34]. The present case had colon cancer at age 37. Twenty years later, she was diagnosed with endometrioid adenocarcinoma. The demographic characteristics of the present patient were similar to those reported in the previous studies[21,34].

Concerning the diagnosis of LS, Amsterdam II[35] and Bethesda[36] criteria have been widely used to screen for LS. In the present study, the patient met the criteria of the Amsterdam standard II and the revision of the Bethesda guidelines. Nonetheless, the two standards' sensitivity is low because they are based on clinical background and family history[37-39]. Thus, Amsterdam II and Bethesda criteria are inadequate as independent screening tools.

IHC was a useful method for LS screening[37,40,41], particularly in colorectal malignancy patients. The sensitivity and specificity of IHC in patients with MMR mutations are 83% and 89%, respectively [42]. When IHC results suggest deleting *MLH1* and *PMS2* proteins, universal screening including *BRAF* testing and *MLH1* promoter methylation analysis is required[10,22,24,25,28,38-40,43,44]. In the present

study, the IHC results showed the loss of *MLH1* and *PMS2* proteins, but expression of *MSH2* and *MSH6* proteins in the tumor cells. Subsequently, *MLH1* mutation was considered. The patient had a medical history of colon cancer and a family history of LS-related cancers. Then, she was diagnosed with LS. Also, we advised the patient and her family members to receive genetic counseling.

Before genetic testing, we provided genetic counseling for the patient and obtained a clear LS family history. We found that the proband's mother (I-1) suffered from primary colon cancer at 55 years and died at 70 years, two of her sisters [(II-1) and (II-3)] were affected by colon cancer at 60 years and endometrial cancer at 60 years, respectively, one of her sisters (II-5) experienced colon cancer at 40 years and endometrial cancer at 48 years, her brother (II-7) developed polyps of the colon, and her nephew developed colon cancer at 25 years and died at 27 years. Besides, standard processes of cancer-related genetic counseling should include pre-test counseling, results analysis, and follow-up[28]. In our study, the family history suggested the clinical diagnosis of LS. Then, the patient and family members were given detailed pre-test counseling. However, we cannot make a definitive diagnosis of LS without genetic testing[28]. Consequently, genetic testing was recommended for the proband and her relatives.

Furthermore, we provided free genetic tests for all her family members to help at-risk offspring know their risk of developing cancers, thus enabling them to access personalized precision medicine. Unexpectedly, only the proband received the genetic test, but her family members refused. The reasons for the relatives of the proband to refuse genetic testing are as follows: First, they were worried that their genetic problems may cause difficulties in mate selection or affect the stability of marriage. Second, they will be unable to purchase life insurance if they have a genetic defect. Third, they are worried about personal privacy exposure. Wang *et al*[45] investigated the willingness and awareness of genetic screening for patients undergoing colon cancer surgery at Peking Union Medical College Hospital who had any protein (*MLH1/MLH2/MLH6/PMS2*) expression deletion suggested by IHC, and the result indicated that 27.4% (61/219) of the patients explicitly refused to undergo genetic screening. The findings of our study and Wang *et al*[45] indicate that gynecologists should strengthen health education. Therefore, cancer genetic counseling and testing are still in the initial development stage in China, and maybe face numerous challenges in the further[28]. This dilemma is expected to be improved with better preventative education to the general population and a better understanding of cancer genetics among cancer patients and medical practitioners[28].

The patient achieved positive clinical outcomes during the 30-mo follow-up visit period. However, several limitations exist in this study. First, 6 mo after discharge, the proband's 25-year-old offspring (III-4) was diagnosed with colon cancer and died at age 27. We believe that this unfortunate outcome could have been prevented if her family members had taken genetic testing and then received individualized preventive treatment before the malignant tumor onset. Thus, it is essential to enhance genetic testing awareness among the Chinese population, especially in rural areas.

CONCLUSION

MLH1 exon 6 c.(453+1_454-1)_(545+1_546-1)del mutation is a novel pathogenic mutation of LS in Chinese. This case report emphasizes the value of diagnosis and treatment in patients with inherited malignancy syndromes. To date, cancer genetic counseling and testing are still in the initial development state in China, and maybe face numerous challenges in the further.

FOOTNOTES

Author contributions: Zhang XW, Jia ZH, and Zhao LP were the patient's gynecologic surgeons, reviewed the literature, and contributed to manuscript drafting; Wu YS, Xu TM, and Jia Y were responsible for the revision of the manuscript for important intellectual content; Cui MH analyzed and interpreted the imaging findings; all authors issued final approval for the version to be submitted.

Supported by the Natural Science Fund of Science and Technology Department, Jilin, No. 20180101010JC; Jilin Provincial Department of Education, No. JJKH20201049KJ.

Informed consent statement: The approval for using the medical records for retrospective studies of this case study was provided by the Ethics Committee of the Second Hospital of Jilin University (2021. No.197). The patient signed an informed consent form.

Conflict-of-interest statement: The authors declare no conflict of interest for this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-

NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Xi-Wen Zhang 0000-0002-7092-6461; Zan-Hui Jia 0000-0001-7105-7563; Li-Ping Zhao 0000-0001-5684-7022; Yi-Shi Wu 0000-0002-8129-0323; Man-Hua Cui 0000-0001-7694-6917; Yan Jia 0000-0002-3704-4977; Tian-Min Xu 0000-0002-1219-061X.

S-Editor: Chang KL

L-Editor: Wang TQ

P-Editor: Chang KL

REFERENCES

- 1 **Kahn RM**, Gordhandas S, Maddy BP, Baltich Nelson B, Askin G, Christos PJ, Caputo TA, Chapman-Davis E, Holcomb K, Frey MK. Universal endometrial cancer tumor typing: How much has immunohistochemistry, microsatellite instability, and MLH1 methylation improved the diagnosis of Lynch syndrome across the population? *Cancer* 2019; **125**: 3172-3183 [PMID: 31150123 DOI: 10.1002/cnrc.32203]
- 2 **Ryan NAJ**, Glaire MA, Blake D, Cabrera-Dandy M, Evans DG, Crosbie EJ. The proportion of endometrial cancers associated with Lynch syndrome: a systematic review of the literature and meta-analysis. *Genet Med* 2019; **21**: 2167-2180 [PMID: 31086306 DOI: 10.1038/s41436-019-0536-8]
- 3 **Bhattacharya P**, McHugh TW. Lynch Syndrome. StatPearls. Treasure Island (FL), 2019 [DOI: 10.5040/9780571352654.00000004]
- 4 **Borràs E**, Pineda M, Cadiñanos J, Del Valle J, Brieger A, Hinrichsen I, Cabanillas R, Navarro M, Brunet J, Sanjuan X, Musulen E, van der Klift H, Lázaro C, Plotz G, Blanco I, Capellá G. Refining the role of PMS2 in Lynch syndrome: germline mutational analysis improved by comprehensive assessment of variants. *J Med Genet* 2013; **50**: 552-563 [PMID: 23709753 DOI: 10.1136/jmedgenet-2012-101511]
- 5 **Peltomäki P**. Role of DNA mismatch repair defects in the pathogenesis of human cancer. *J Clin Oncol* 2003; **21**: 1174-1179 [PMID: 12637487 DOI: 10.1200/JCO.2003.04.060]
- 6 **Miyaki M**, Konishi M, Tanaka K, Kikuchi-Yanoshita R, Muraoka M, Yasuno M, Igari T, Koike M, Chiba M, Mori T. Germline mutation of MSH6 as the cause of hereditary nonpolyposis colorectal cancer. *Nat Genet* 1997; **17**: 271-272 [PMID: 9354786 DOI: 10.1038/ng1197-271]
- 7 **Berends MJ**, Wu Y, Sijmons RH, Mensink RG, van der Sluis T, Hordijk-Hos JM, de Vries EG, Hollema H, Karrenbeld A, Buys CH, van der Zee AG, Hofstra RM, Kleibeuker JH. Molecular and clinical characteristics of MSH6 variants: an analysis of 25 index carriers of a germline variant. *Am J Hum Genet* 2002; **70**: 26-37 [PMID: 11709755 DOI: 10.1086/337944]
- 8 **Nilbert M**, Wikman FP, Hansen TV, Krarup HB, Orntoft TF, Nielsen FC, Sunde L, Gerdes AM, Cruger D, Timshel S, Bisgaard ML, Bernstein I, Okkels H. Major contribution from recurrent alterations and MSH6 mutations in the Danish Lynch syndrome population. *Fam Cancer* 2009; **8**: 75-83 [PMID: 18566915 DOI: 10.1007/s10689-008-9199-3]
- 9 **Senter L**, Clendenning M, Sotamaa K, Hampel H, Green J, Potter JD, Lindblom A, Lagerstedt K, Thibodeau SN, Lindor NM, Young J, Winship I, Dowty JG, White DM, Hopper JL, Baglietto L, Jenkins MA, de la Chapelle A. The clinical phenotype of Lynch syndrome due to germ-line PMS2 mutations. *Gastroenterology* 2008; **135**: 419-428 [PMID: 18602922 DOI: 10.1053/j.gastro.2008.04.026]
- 10 **Zhang M**, Yang H, Chen Z, Fan Y, Hu X, Liu W. Lynch syndrome-associated repeated stroke with MLH1 frame-shift mutation. *Neurol Sci* 2021; **42**: 1641 [PMID: 33528673 DOI: 10.1007/s10072-021-05098-1]
- 11 **Ahadova A**, Gallon R, Gebert J, Ballhausen A, Endris V, Kirchner M, Stenzinger A, Burn J, von Knebel Doeberitz M, Bläker H, Kloor M. Three molecular pathways model colorectal carcinogenesis in Lynch syndrome. *Int J Cancer* 2018; **143**: 139-150 [PMID: 29424427 DOI: 10.1002/ijc.31300]
- 12 **Menahem B**, Alves A, Regimbeau JM, Sabbagh C. Lynch Syndrome: Current management In 2019. *J Visc Surg* 2019; **156**: 507-514 [PMID: 31445799 DOI: 10.1016/j.jvisurg.2019.07.009]
- 13 **Vasen HFA**. Progress Report: New insights into the prevention of CRC by colonoscopic surveillance in Lynch syndrome. *Fam Cancer* 2022; **21**: 49-56 [PMID: 33464460 DOI: 10.1007/s10689-020-00225-x]
- 14 **Ahadova A**, Seppälä TT, Engel C, Gallon R, Burn J, Holinski-Feder E, Steinke-Lange V, Möslin G, Nielsen M, Ten Broeke SW, Laghi L, Dominguez-Valentin M, Capella G, Macrae F, Scott R, Hüneburg R, Nattermann J, Hoffmeister M, Brenner H, Bläker H, von Knebel Doeberitz M, Sampson JR, Vasen H, Mecklin JP, Möller P, Kloor M. The "unnatural" history of colorectal cancer in Lynch syndrome: Lessons from colonoscopy surveillance. *Int J Cancer* 2021; **148**: 800-811 [PMID: 32683684 DOI: 10.1002/ijc.33224]
- 15 **Ladigan-Badura S**, Vangala DB, Engel C, Bucksch K, Hueneburg R, Perne C, Nattermann J, Steinke-Lange V, Rahner N, Schackert HK, Weitz J, Kloor M, Kuhlkamp J, Nguyen HP, Moeslein G, Strassburg C, Morak M, Holinski-Feder E, Buettner R, Aretz S, Loeffler M, Schmiegler W, Pox C, Schulmann K; German Consortium for Familial Intestinal Cancer. Value of upper gastrointestinal endoscopy for gastric cancer surveillance in patients with Lynch syndrome. *Int J Cancer* 2021; **148**: 106-114 [PMID: 32930401 DOI: 10.1002/ijc.33294]
- 16 **Therkildsen C**, Joost P, Lindberg LJ, Ladelund S, Smith-Hansen L, Nilbert M. Renal cell cancer linked to Lynch syndrome: Increased incidence and loss of mismatch repair protein expression. *Int J Urol* 2016; **23**: 528-529 [PMID: 26883684 DOI: 10.1002/ijc.33224]

- 27168032 DOI: [10.1111/iju.13094](https://doi.org/10.1111/iju.13094)]
- 17 **Ketabi Z**, Bartuma K, Bernstein I, Malander S, Grönberg H, Björck E, Holck S, Nilbert M. Ovarian cancer linked to Lynch syndrome typically presents as early-onset, non-serous epithelial tumors. *Gynecol Oncol* 2011; **121**: 462-465 [PMID: [21388660](https://pubmed.ncbi.nlm.nih.gov/21388660/) DOI: [10.1016/j.ygyno.2011.02.010](https://doi.org/10.1016/j.ygyno.2011.02.010)]
 - 18 **Groth JV**, Prabhu S, Periakaruppan R, Ohlander S, Emmadi R, Kothari R. Coexistent Dedifferentiated Endometrioid Carcinoma of the Uterus and Adenocarcinoma of the Bladder in Lynch Syndrome: Case Report and Review of the Literature. *Appl Immunohistochem Mol Morphol* 2020; **28**: e26-e30 [PMID: [32167968](https://pubmed.ncbi.nlm.nih.gov/32167968/) DOI: [10.1097/PAL.0000000000000553](https://doi.org/10.1097/PAL.0000000000000553)]
 - 19 **Phelan A**, Lopez-Beltran A, Montironi R, Zhang S, Raspollini MR, Cheng M, Kaimakiotis HZ, Koch MO, Cheng L. Inherited forms of bladder cancer: a review of Lynch syndrome and other inherited conditions. *Future Oncol* 2018; **14**: 277-290 [PMID: [29345160](https://pubmed.ncbi.nlm.nih.gov/29345160/) DOI: [10.2217/fon-2017-0346](https://doi.org/10.2217/fon-2017-0346)]
 - 20 **Ten Broeke SW**, Suerink M, Nielsen M. Response to Roberts et al. 2018: is breast cancer truly caused by MSH6 and PMS2 variants or is it simply due to a high prevalence of these variants in the population? *Genet Med* 2019; **21**: 256-257 [PMID: [29795439](https://pubmed.ncbi.nlm.nih.gov/29795439/) DOI: [10.1038/s41436-018-0029-1](https://doi.org/10.1038/s41436-018-0029-1)]
 - 21 **Tjalsma AS**, Wagner A, Dinjens WNM, Ewing-Graham PC, Alcalá LSM, de Groot MER, Hamoen KE, van Hof AC, Hofhuis W, Hofman LN, Hoogduin KJ, Kaijser J, Makkus ACF, Mol SJJ, Plaisier GM, Schelfhout K, Smedts HPM, Smit RA, Timmers PJ, Vencken PMLH, Visschers B, van der Wurff AAM, van Doorn HC. Evaluation of a nationwide Dutch guideline to detect Lynch syndrome in patients with endometrial cancer. *Gynecol Oncol* 2021; **160**: 771-776 [PMID: [33419609](https://pubmed.ncbi.nlm.nih.gov/33419609/) DOI: [10.1016/j.ygyno.2020.12.028](https://doi.org/10.1016/j.ygyno.2020.12.028)]
 - 22 **Stinton C**, Fraser H, Al-Khudairy L, Court R, Jordan M, Grammatopoulos D, Taylor-Phillips S. Testing for lynch syndrome in people with endometrial cancer using immunohistochemistry and microsatellite instability-based testing strategies - A systematic review of test accuracy. *Gynecol Oncol* 2021; **160**: 148-160 [PMID: [33190932](https://pubmed.ncbi.nlm.nih.gov/33190932/) DOI: [10.1016/j.ygyno.2020.10.003](https://doi.org/10.1016/j.ygyno.2020.10.003)]
 - 23 **Chen W**. Cancer statistics: updated cancer burden in China. *Chin J Cancer Res* 2015; **27**: 1 [PMID: [25717219](https://pubmed.ncbi.nlm.nih.gov/25717219/) DOI: [10.3978/j.issn.1000-9604.2015.02.07](https://doi.org/10.3978/j.issn.1000-9604.2015.02.07)]
 - 24 **Cui MH**, Zhang XW, Yu T, Huang DW, Jia Y. PMS2 germline mutation c.1577delA (p.Asp526Alafs*69)-induced Lynch syndrome-associated endometrial cancer: A case report. *Medicine (Baltimore)* 2019; **98**: e18279 [PMID: [31860975](https://pubmed.ncbi.nlm.nih.gov/31860975/) DOI: [10.1097/MD.00000000000018279](https://doi.org/10.1097/MD.00000000000018279)]
 - 25 **Kumar A**, Paramasivam N, Bandapalli OR, Schlesner M, Chen T, Sijmons R, Dymerska D, Golebiewska K, Kuswik M, Lubinski J, Hemminki K, Försti A. A rare large duplication of MLH1 identified in Lynch syndrome. *Heredit Cancer Clin Pract* 2021; **19**: 10 [PMID: [33468175](https://pubmed.ncbi.nlm.nih.gov/33468175/) DOI: [10.1186/s13053-021-00167-0](https://doi.org/10.1186/s13053-021-00167-0)]
 - 26 **Song XJ**, Liu ZL, Zeng R, Ye W, Liu CW. A meta-analysis of laparoscopic surgery vs conventional open surgery in the treatment of colorectal cancer. *Medicine (Baltimore)* 2019; **98**: e15347 [PMID: [31027112](https://pubmed.ncbi.nlm.nih.gov/31027112/) DOI: [10.1097/MD.00000000000015347](https://doi.org/10.1097/MD.00000000000015347)]
 - 27 **Rohlin A**, Rambech E, Kvist A, Törngren T, Eiengård F, Lundstam U, Zagoras T, Gebre-Medhin S, Borg Å, Björck J, Nilbert M, Nordling M. Expanding the genotype-phenotype spectrum in hereditary colorectal cancer by gene panel testing. *Fam Cancer* 2017; **16**: 195-203 [PMID: [27696107](https://pubmed.ncbi.nlm.nih.gov/27696107/) DOI: [10.1007/s10689-016-9934-0](https://doi.org/10.1007/s10689-016-9934-0)]
 - 28 **Jia S**, Zhang M, Sun Y, Yan H, Zhao F, Li Z, Ji J. A Chinese family affected by lynch syndrome caused by MLH1 mutation. *BMC Med Genet* 2018; **19**: 106 [PMID: [29929473](https://pubmed.ncbi.nlm.nih.gov/29929473/) DOI: [10.1186/s12881-018-0605-x](https://doi.org/10.1186/s12881-018-0605-x)]
 - 29 **Solassol J**, Larrieux M, Leclerc J, Ducros V, Corsini C, Chiésa J, Pujol P, Rey JM. Alu element insertion in the MLH1 exon 6 coding sequence as a mutation predisposing to Lynch syndrome. *Hum Mutat* 2019; **40**: 716-720 [PMID: [30815977](https://pubmed.ncbi.nlm.nih.gov/30815977/) DOI: [10.1002/humu.23725](https://doi.org/10.1002/humu.23725)]
 - 30 **Li Y**, Salo-Mullen E, Varghese A, Trotter M, Stadler ZK, Zhang L. Insertion of an Alu-like element in MLH1 intron 7 as a novel cause of Lynch syndrome. *Mol Genet Genomic Med* 2020; **8**: e1523 [PMID: [33058565](https://pubmed.ncbi.nlm.nih.gov/33058565/) DOI: [10.1002/mgg3.1523](https://doi.org/10.1002/mgg3.1523)]
 - 31 **Hong J**, Kim H, Hong YS, Lee W, Lim S-B, Byeon J-S, Chun S, Min W-K. A Case of Lynch Syndrome with the Deletion of Multiple Exons of the MLH1 Gene, Detected by Next-Generation Sequencing. *J Lab Med Qual Assur* 2019; **41**: 220-224 [DOI: [10.15263/jlmqa.2019.41.4.220](https://doi.org/10.15263/jlmqa.2019.41.4.220)]
 - 32 **Lagerstedt-Robinson K**, Rohlin A, Aravidis C, Melin B, Nordling M, Stenmark-Askmalin M, Lindblom A, Nilbert M. Mismatch repair gene mutation spectrum in the Swedish Lynch syndrome population. *Oncol Rep* 2016; **36**: 2823-2835 [PMID: [27601186](https://pubmed.ncbi.nlm.nih.gov/27601186/) DOI: [10.3892/or.2016.5060](https://doi.org/10.3892/or.2016.5060)]
 - 33 **Singh S**, Resnick KE. Lynch Syndrome and Endometrial Cancer. *South Med J* 2017; **110**: 265-269 [PMID: [28376523](https://pubmed.ncbi.nlm.nih.gov/28376523/) DOI: [10.14423/SMJ.0000000000000633](https://doi.org/10.14423/SMJ.0000000000000633)]
 - 34 **Wang Y**, Wang Y, Li J, Cragun J, Hatch K, Chambers SK, Zheng W. Lynch syndrome related endometrial cancer: clinical significance beyond the endometrium. *J Hematol Oncol* 2013; **6**: 22 [PMID: [23531335](https://pubmed.ncbi.nlm.nih.gov/23531335/) DOI: [10.1186/1756-8722-6-22](https://doi.org/10.1186/1756-8722-6-22)]
 - 35 **Vasen HF**, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* 1999; **116**: 1453-1456 [PMID: [10348829](https://pubmed.ncbi.nlm.nih.gov/10348829/) DOI: [10.1016/s0016-5085\(99\)70510-x](https://doi.org/10.1016/s0016-5085(99)70510-x)]
 - 36 **Umar A**, Boland CR, Terdiman JP, Syngal S, de la Chapelle A, Rüschoff J, Fishel R, Lindor NM, Burgart LJ, Hamelin R, Hamilton SR, Hiatt RA, Jass J, Lindblom A, Lynch HT, Peltomäki P, Ramsey SD, Rodriguez-Bigas MA, Vasen HF, Hawk ET, Barrett JC, Freedman AN, Srivastava S. Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. *J Natl Cancer Inst* 2004; **96**: 261-268 [PMID: [14970275](https://pubmed.ncbi.nlm.nih.gov/14970275/) DOI: [10.1093/jnci/djh034](https://doi.org/10.1093/jnci/djh034)]
 - 37 **Buchanan DD**, Tan YY, Walsh MD, Clendenning M, Metcalf AM, Ferguson K, Arnold ST, Thompson BA, Lose FA, Parsons MT, Walters RJ, Pearson SA, Cummings M, Oehler MK, Blomfield PB, Quinn MA, Kirk JA, Stewart CJ, Obermair A, Young JP, Webb PM, Spurdle AB. Tumor mismatch repair immunohistochemistry and DNA MLH1 methylation testing of patients with endometrial cancer diagnosed at age younger than 60 years optimizes triage for population-level germline mismatch repair gene mutation testing. *J Clin Oncol* 2014; **32**: 90-100 [PMID: [24323032](https://pubmed.ncbi.nlm.nih.gov/24323032/) DOI: [10.1200/JCO.2013.51.2129](https://doi.org/10.1200/JCO.2013.51.2129)]
 - 38 **Provenzale D**, Gupta S, Ahnen DJ, Bray T, Cannon JA, Cooper G, David DS, Early DS, Erwin D, Ford JM, Giardiello FM,

- Grady W, Halverson AL, Hamilton SR, Hampel H, Ismail MK, Klapman JB, Larson DW, Lazenby AJ, Lynch PM, Mayer RJ, Ness RM, Regenbogen SE, Samadder NJ, Shike M, Steinbach G, Weinberg D, Dwyer M, Darlow S. Genetic/Familial High-Risk Assessment: Colorectal Version 1.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2016; **14**: 1010-1030 [PMID: [27496117](#) DOI: [10.6004/jnccn.2016.0108](#)]
- 39 **Giardiello FM**, Allen JI, Axilbund JE, Boland CR, Burke CA, Burt RW, Church JM, Dominitz JA, Johnson DA, Kaltenbach T, Levin TR, Lieberman DA, Robertson DJ, Syngal S, Rex DK. Guidelines on genetic evaluation and management of Lynch syndrome: a consensus statement by the US Multi-society Task Force on colorectal cancer. *Am J Gastroenterol* 2014; **109**: 1159-1179 [PMID: [25070057](#) DOI: [10.1038/ajg.2014.186](#)]
- 40 **Goodfellow PJ**, Billingsley CC, Lankes HA, Ali S, Cohn DE, Broadus RJ, Ramirez N, Pritchard CC, Hampel H, Chassen AS, Simmons LV, Schmidt AP, Gao F, Brinton LA, Backes F, Landrum LM, Geller MA, DiSilvestro PA, Pearl ML, Lele SB, Powell MA, Zaino RJ, Mutch D. Combined Microsatellite Instability, MLH1 Methylation Analysis, and Immunohistochemistry for Lynch Syndrome Screening in Endometrial Cancers From GOG210: An NRG Oncology and Gynecologic Oncology Group Study. *J Clin Oncol* 2015; **33**: 4301-4308 [PMID: [26552419](#) DOI: [10.1200/JCO.2015.63.9518](#)]
- 41 **Kwon JS**, Scott JL, Gilks CB, Daniels MS, Sun CC, Lu KH. Testing women with endometrial cancer to detect Lynch syndrome. *J Clin Oncol* 2011; **29**: 2247-2252 [PMID: [21537049](#) DOI: [10.1200/JCO.2010.32.9979](#)]
- 42 **Piñol V**, Castells A, Andreu M, Castellvi-Bel S, Alenda C, Llor X, Xicola RM, Rodríguez-Moranta F, Payá A, Jover R, Bessa X; Gastrointestinal Oncology Group of the Spanish Gastroenterological Association. Accuracy of revised Bethesda guidelines, microsatellite instability, and immunohistochemistry for the identification of patients with hereditary nonpolyposis colorectal cancer. *JAMA* 2005; **293**: 1986-1994 [PMID: [15855432](#) DOI: [10.1001/jama.293.16.1986](#)]
- 43 **Yoshihama T**, Hirasawa A, Sugano K, Yoshida T, Ushima M, Ueki A, Akahane T, Nanki Y, Sakai K, Makabe T, Yamagami W, Susumu N, Kameyama K, Kosaki K, Aoki D. Germline multigene panel testing revealed a *BRC1A2* pathogenic variant in a patient with suspected Lynch syndrome. *Int Cancer Conf J* 2021; **10**: 6-10 [PMID: [33489693](#) DOI: [10.1007/s13691-020-00449-9](#)]
- 44 **Kasela M**, Nyström M, Kansikas M. PMS2 expression decrease causes severe problems in mismatch repair. *Hum Mutat* 2019; **40**: 904-907 [PMID: [30946512](#) DOI: [10.1002/humu.23756](#)]
- 45 **Wang WM**. Optimization strategy and screening status of colorectal cancer related Lynch syndrome with MLH1 deletion in Chinese population. *Annals of Oncology* 2018; **29**: viii176-viii177 [DOI: [10.1093/annonc/mdy281.073](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

