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USCAP & AACR HIGHLIGHTS

Patología Ginecológica

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USCAP & AACR HIGHLIGHTS 2012

LYNCH SYNDROME IN PATIENTS WITH ENDOMETRIAL CANCER

Genotype in patients < 50 years

	Berend	*Hampel*	*Lu*	*Total*
	8.6%(5/54)	**4.9% (4/81)**	**9% (9/100)**	**7.6% (18/235)**
MLH1	1	1	1	3 (33.3%)
MSH2	3	2	7	**12 (66.6%)**
MSH6	1	1	1	3 (33.3%)

Genotype in patients 50 years or older

	Hampel
	1.3% (6/462)
MLH1	0
MSH2	1 (17%)
MSH6	**5 (83%)**

Berends et al; J Clin Oncol 2003.

Hampel et al; Cancer Res 2006.

Lu et al; J Clin Oncol 2007.

Selection of Endometrial Carcinomas for DNA Mismatch Repair Protein Immunohistochemistry Using Patient Age and Tumor Morphology Enhances Detection of Mismatch Repair Abnormalities

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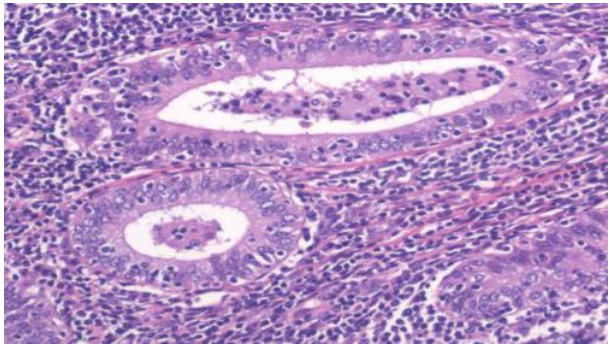
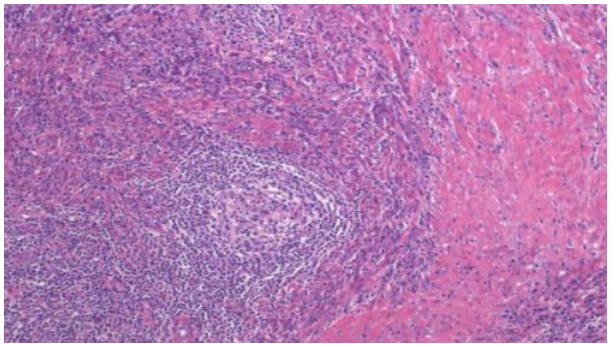
Pathological features

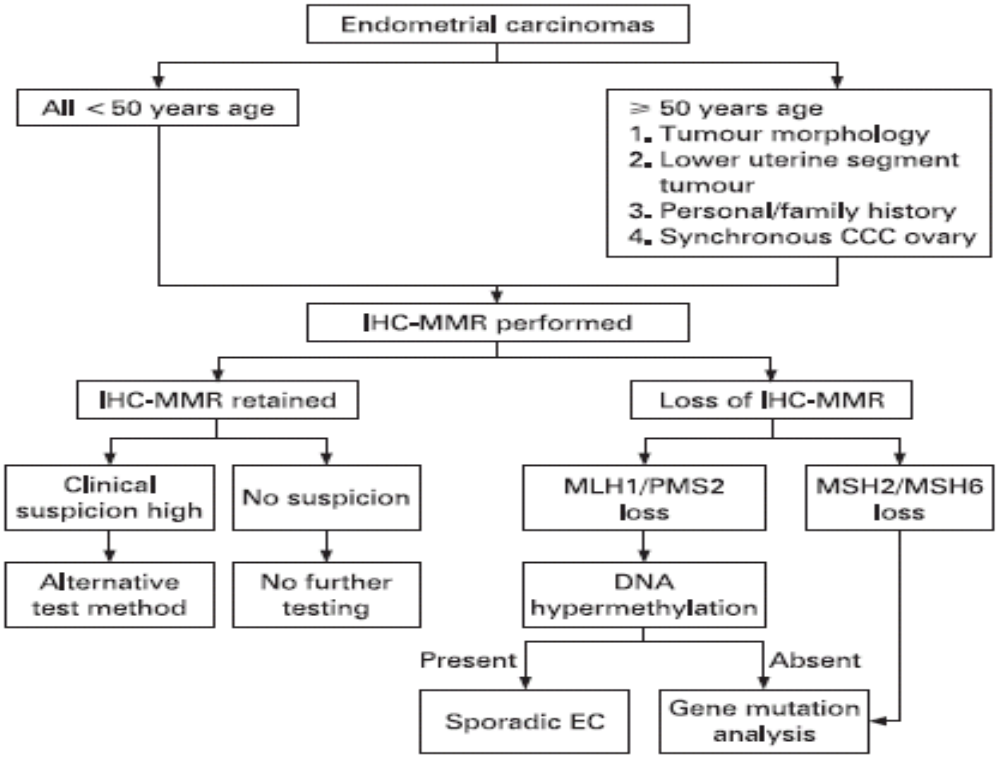
Lower Uterine Segment
Peritumoral lymphocytes
TILs
Dedifferentiated EC
Synchronous clear cell carcinoma of the ovary





Am J Surg Pathol 2008

PROPOSED ALGORITHM FOR DETECTION OF EC PATIENTS AT HIGEST RISK FOR LYNCH SYNDROME



Garg and Soslow, J Clin Pathol 2009

LYNCH SYNDROME IN PATIENTS WITH ENDOMETRIAL CANCER

#1099

- 5/182 (2.7%) EC patients >50 years lacking BG and TM-MMR had IHC-MMR deficiency: 4 MLH1/PMS2 (3 with HMLH1 methylation) and 1 MSH6.
- 35/74 (47%) EC patients >50 years with TM-MMR had IHC-MMR deficiency.
- 4/21 (20%) EC patients >50 years with BG without TM-MMR had IHC-MMR deficiency.
- LS screening is questionable in EC >50 years lacking BG and TM-MMR (MSH6?).

 # 1118

- PMS2 loss without concurrent MLH1 loss occurred in 5/154 sequential EC and 2/45 clinically suspicious (<50 years or family history).
- All cases were endometrioid carcinomas.
- 6 patients were older than 50 years and without family history of LS or had relatives with colon cancer late in life.
- Lynch syndrome associated to PMS2 deficiency may be missed by screening criteria based on age and family history.

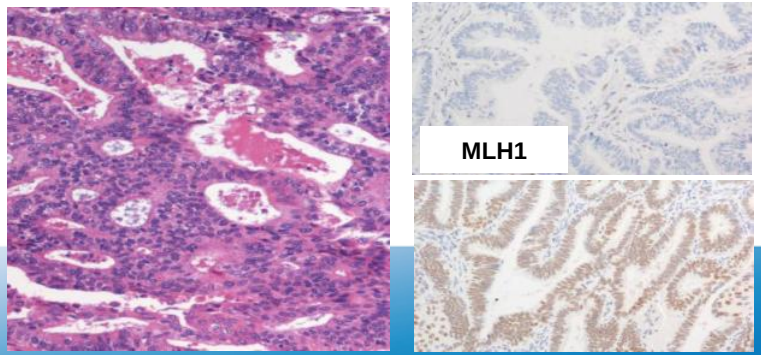
LYNCH SYNDROME IN PATIENTS WITH ENDOMETRIAL CANCER

#1084

- 70/178 ECs (40%) showed loss of MMR proteins and /or MSI
  34 MLH1 methylation (sporadic).

- Loss of MMR proteins without methylation: 10 MLH1, 1 PMS2, 5 MSH2/MSH6, 9 MSH6; 10 MSI without loss of MRR proteins.

- 4-8% of EC in Spanish population are due to Lynch Syndrome.



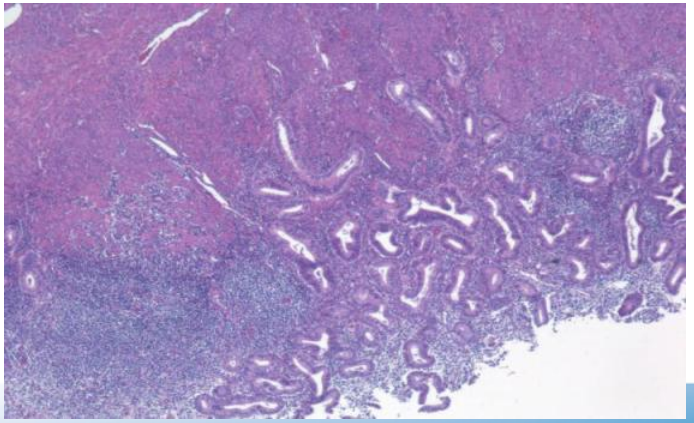
LYNCH SYNDROME IN PATIENTS WITH ENDOMETRIAL CANCER

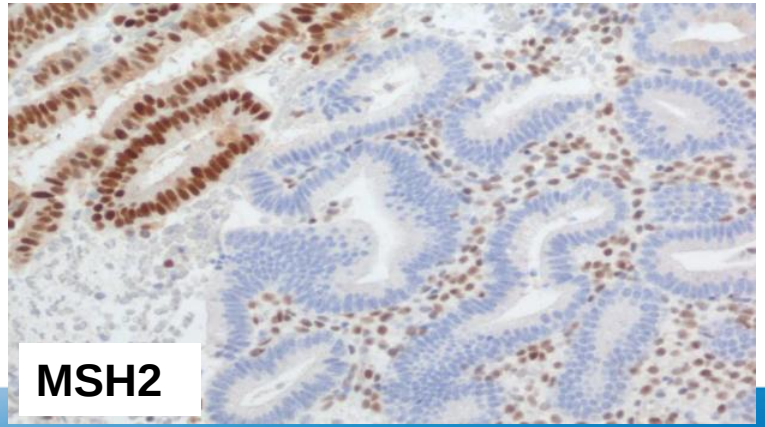
#1173

25 prophylactic hysterectomies in LS patients (31-66 years):

CEH: 2 (8%, 35-52 years); EC: 2 (8%, 54-56 years); OC: 1 (4%; 44 years)

MM: 4 (16%); LA: 5 (20%)

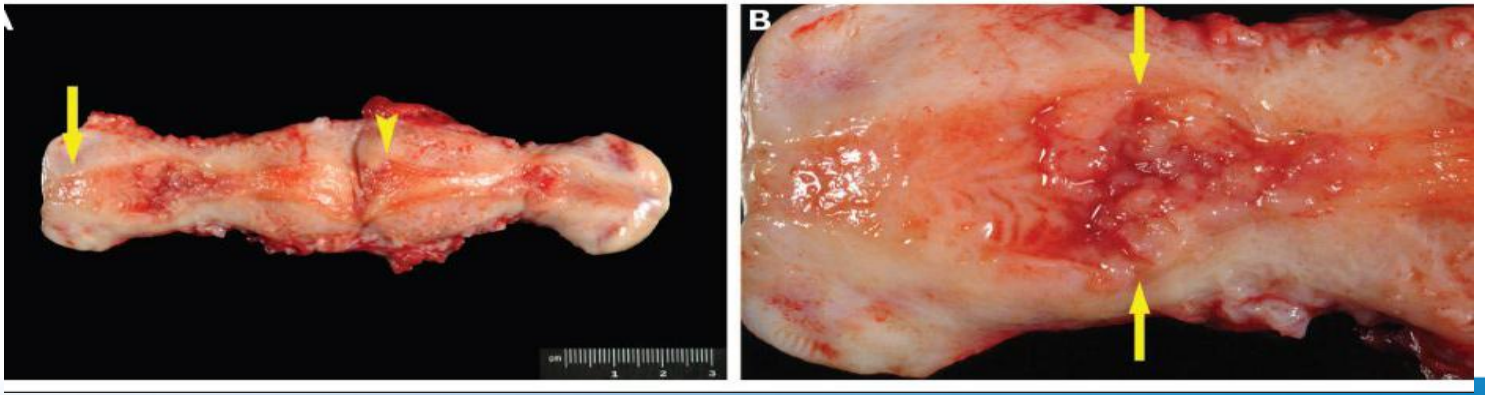




Lower Uterine Segment (LUS) endometrial carcinomas

#1156

Differences between LUS-C with cervical involvement and primary cervical adenocarcinoma (PCAC) (42 cases).
5/42 (11%) LUS: no SIL, p16-negative.
4/5 LUS MMR-IHC deficiency: 2 MSH2/MSH6 (1 serous/endometrioid, 1 undifferentiated), 1 PMS2 (mucinous), 1 MLH1/PMS2 (serous/endometrioid).



Role of ARID1 (BAF250A) in ovarian lesions

#1089

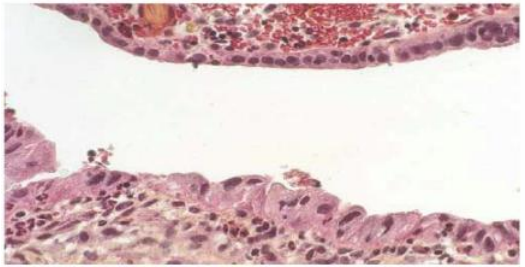
ARID1 was analyzed in endometriotic cysts and concurrent ovarian carcinomas: 25 CCC, 16 WD-EC, 4 mixed.

ARID1 was lost in 30 endometriotic cysts and concurrent carcinomas (67%): 19 CCC, 9 EC, 2 MC.

Endometriosis is a true precursor of CCC and EC and ARID1 mutations frequently occur before malignant transformation.

#1128

ARID1 loss in 32% (12/36) endometriosis, 61% (8/13) atypical endometriosis, and 58% (15/25) CCC.



#1267

ARID1 loss in 58% (15/25) CCC.

ARID1 loss in none of 24 OSC

Role of ARID1 (BAF250A) in Endometrial Cancer

#1086

- Loss of ARID1 occurs in 48% of HG-EEC (46/97), 31% ECCC (5/16) and 10% ESC (10/97).

- LOSS of ARID1 in HG-EEC was associated with lymph node metastasis.

Endometrial clear cell carcinoma
#1115, 1116, 1128, 1130

- Clear cells are present in pure ECC, EC and SC.
- Moderate level (K=0.46) of interobserver agreement in the diagnosis of ECC
- HNF-1β expression is more characteristic of ECC.
- PIK3CA and KRAS occur in 5% of CC
- ARID1 loss was found in 5/22 (23%) of pure ECC.
- ECC with p53 expression present at higher stage and have poor prognosis than those p53-negative (variant of ESC?).