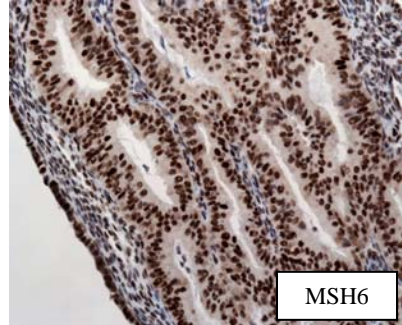
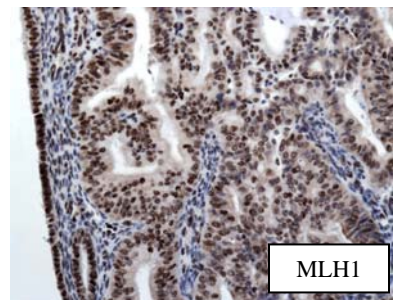
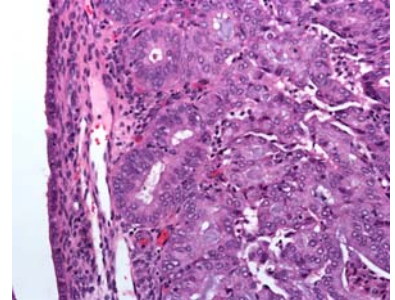


Endometrial Adenocarcinoma: Immunohistochemical Detection of DNA Mismatch Repair Proteins

INTRODUCTION

- Patients with microsatellite instability (MSI), a condition seen in hereditary non-polyposis colon cancer (HNPCC; previously known as Lynch II syndrome) harbor a lifetime risk of 40-60% of developing endometrial carcinoma
- 51% of females with HNPCC may present with endometrial carcinoma
- Female patients fulfilling the criteria for HNPCC need to undergo transvaginal ultrasound endometrial aspirate annually starting at the age of 20-25 years
- Immunohistochemical surrogate that identifies mutations in mismatch repair genes
- Detects protein products of MLH1, MSH2, MSH6 and PMS2 genes



INDICATIONS

- Bethesda Criteria (suggestive of HNPCC)
 - Colon or endometrial cancer at age < 50
 - Two HNPCC cancers in a single individual at any age
 - Colon or endometrial cancer in an individual with one or more 1st degree relatives with an HNPCC cancer, with at least 1 diagnosed < 50
 - Colon or endometrial cancer at any age, in an individual with 2 or more 1st or 2nd degree relatives with HNPCC cancers
- Amsterdam II criteria (diagnostic of HNPCC)
 - 3 relatives w/ HNPCC-associated cancers
 - 1 case 1st degree relative in 2 successive generations
 - At least 1 cancer < 50, excluding FAP

SPECIMEN REQUIREMENTS

Formalin-fixed, paraffin-embedded tissue sections or blocks containing both tumor and nonneoplastic endometrium

SENSITIVITY AND SPECIFICITY

- 90-95% sensitive compared to PCR-based analysis
- Positive test (loss of protein expression) does not discriminate germline versus somatic DNA mismatch repair gene mutations
- Negative test (normal protein expression) does not entirely exclude HNPCC

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Diagnosis at the Speed of Right