Lynch Syndrome Testing Algorithm

Patient with personal or family history of cancer suspicious for Lynch syndrome

Has genetic testing been previously performed on family member?

Pathogenic mutation identified

Is patient's tumor available for testing?

Consider MSIHC / Microsatellite Instability (MSI)/Mismatch Repair (MMR) Protein Immunohistochemistry Profile

Testing in family member was negative or variant of uncertain significance identified

Consider LYNCH / Lynch Syndrome Panel or testing for the variant of uncertain significance in family member to determine if it segregates with disease

Patient is young (<50) or family history suggestive of Lynch syndrome

Patient is older (>50) and family history is not suggestive of Lynch syndrome

Sporadic in origin; no further testing recommended

Endometrial

Colorectal

No hypermethylation

Hypermethylation

Hypermethylation and BRAF negative

Hypermethylation and BRAF positive

If endometrial tumor:
- consider MLH1Z / MLH1 Gene, Full Gene Analysis

If colorectal tumor:
- consider MLH1Z / MLH1 Gene, Full Gene Analysis

Endometrial

Colorectal

No hypermethylation

Hypermethylation

Hypermethylation and BRAF negative

Hypermethylation and BRAF positive

Sporadic in origin OR if still suspicious of Lynch syndrome consider MLH1Z / MLH1 Gene, Full Gene Analysis and PMS2Z / PMS2 Gene, Full Gene Analysis to detect germline mutation

Consider performing both MLH1Z / MLH1 Gene, Full Gene Analysis and PMS2Z / PMS2 Gene, Full Gene Analysis to detect germline mutation

IHC=Immunohistochemical
MSI=Microsatellite Instability
-MSI-H=MSI-High
-MSI-L=MSI-Low

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