

Germline testing for Lynch syndrome in patients with endometrial cancer in RHH

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INTRODUCTION:

- Lynch syndrome is an inherited genetic condition associated with an increased risk of several cancers, particularly endometrial and colorectal cancer.
- It is caused by mutations in, or near, the DNA sequence of mismatch repair (MMR) genes.
- NICE recommends testing for Lynch syndrome following colorectal cancer diagnosis, but endometrial cancer is often the first cancer that women with Lynch syndrome will have.
- Lynch syndrome could be identified earlier if women are tested after a diagnosis of endometrial cancer.
- Prevalence of Lynch syndrome in people with endometrial cancer : 3.2%
- Identifying Lynch syndrome at the time of endometrial cancer diagnosis is important because:
 - ✓it could prevent other cancers such as colorectal cancer in these women through surveillance and risk reduction strategies
 - ✓ it could help to identify relatives with Lynch syndrome and reduce their risks of Lynch syndrome associated cancers or increase early detection of cancer
 - ✓relatives diagnosed at an early age with Lynch syndrome could consider family planning and, if they wish, have risk-reducing interventions, for example, a hysterectomy.

OBJECTIVES & DESIGN:

- Audit of all patients diagnosed with endometrial cancer over an 18-month period in a large district general hospital to assess compliance with the NICE guidance DG 42 regarding germline testing for Lynch Syndrome.
- Retrospective audit over an 18-month period

METHODS:

- Retrieval from IT system of all patients with primary diagnosis of ‘Malignant neoplasm of endometrium’ during April 2023-October 2024, analysis of the histopathological reports and review of electronic patient records to assess referral for germline testing.

REFERENCES:

• 'Testing strategies for Lynch syndrome in people with endometrial cancer ', Diagnostics guidance ,Published: 28 October 2020 , [https://www.nice.org.uk/guidance/NG121](#)

• 'Implementing Lynch syndrome testing and surveillance pathways', A handbook to support local systems. NHS '

RESULTS:

- Between April 2023-October 2024, 124 patients were diagnosed with primary endometrial cancer at RHH.
- Average age at diagnosis was 68.7 years. Mean BMI was 36.3 kg/m2.
- 96.7% of the patients (120/124) had their Mismatch Repair Proteins (MMR) status tested via immunohistochemistry of the histopathological specimen.
- Where immunohistochemistry was abnormal with loss of MLH1, or loss of both MLH1 and PMS2 protein expression, MLH1 promoter hypermethylation was tested in the tumour DNA. If MLH1 promoter hypermethylation was not detected, germline testing was offered to confirm Lynch syndrome. In cases of abnormal immunohistochemistry with loss of MSH2, MSH6 or isolated PMS2 protein expression, patients were offered germline genetic testing.
- Of those who had MMR status testing, 85 were found to be MMR proficient (pMMR) and 35 MMR deficient (dMMR):
 - ✓ 10 were offered referral for germline testing and 8/10 patients were finally referred for germling testing to Clinical Genetics at BWH.
 - ✓ 1 patient had negative result, 1 patient with ongoing testing ,2 are awaiting future appointment for testing, 1 patient DNA'd appointment, 2 patients did not book appointment, 1 patient was unfit and family declined testing.
- 4 patients had concomitant cancer (SCC, ovarian, pancreatic, lung cancer) and 5 patients died shortly after diagnosis due to advanced disease.

CONCLUSIONS:

- 97% of patients with endometrial cancer had MMR/IHC testing
- 100% of patients whose IHC was abnormal with loss of MLH1, or loss of both MLH1 and PMS2 protein expression patients went on to have MLH1 promoter hypermethylation testing of tumour DNA.
- 100% of patients in whom MLH1 promoter hypermethylation was not detected or with loss of MSH2, MSH6 or isolated PMS2 protein expression, were offered germline genetic testing to confirm Lynch syndrome.
- Overall, this audit demonstrates local compliance with NICE guideline DG42:
 - 124 patients audited and 97% of them had MMR testing, largest Cohort of patients reviewed
 - MDT following the diagnostic pathway and result discussion in 96%.
- Waiting times for germline testing for Lynch are long : currently at least 6 months for initial appointment with Clinical Genetics at BWH.
- Aim to develop mainstreaming service to improve waiting time and patient’s experience.
- Opportunity to offer additional treatments once diagnosis made.
- Aim to develop a system to track patients and help assist in re-audits.