# Management of Constitutional Mismatch Repair Deficiency Syndrome

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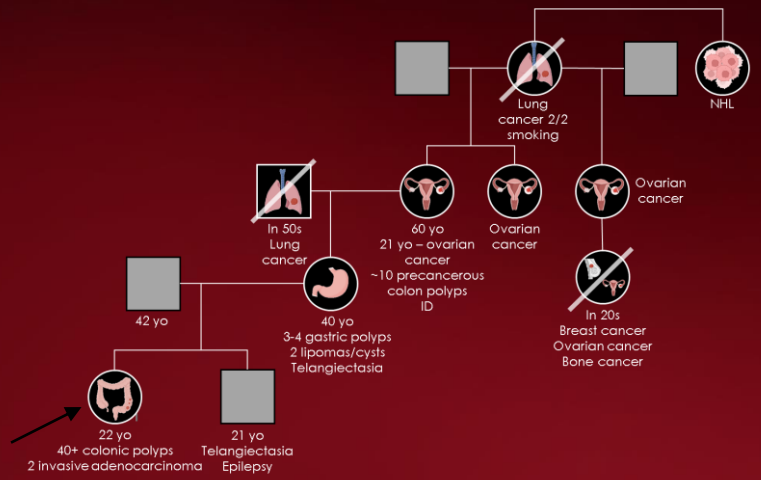
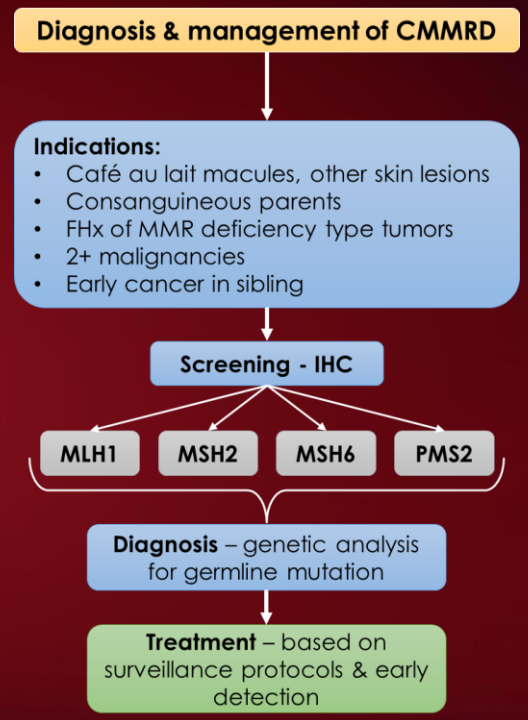
- 22 y/o female with hematochezia, abdominal pain & PMH s/f iron deficiency anemia & previous NF1 diagnosis due to café au lait spots & axillary freckling.




Polyps on colonoscopy: (red: adenomatous polyps; black: invasive adenocarcinoma)


- Genetic analysis: germline biallelic heterozygous *PMS2* mutations
- Total colectomy + ileorectal anastomosis (1 additional invasive adenocarcinoma found) & total hysterectomy + BSO
- Follow-up management:
  - Flexible sigmoidoscopy in January
  - MRI scheduled for May

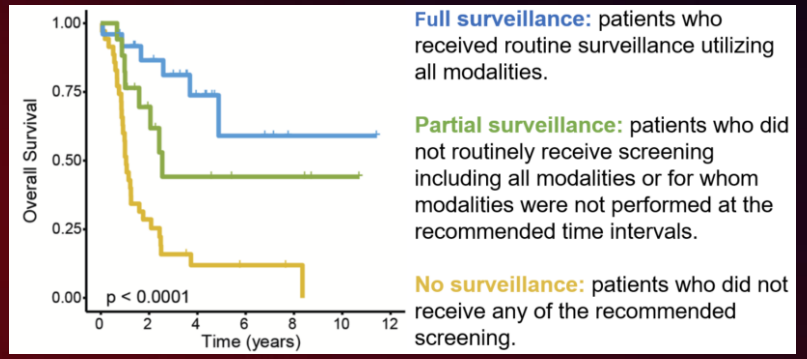
Constitutional mismatch repair deficiency (CMMRD) syndrome is caused by biallelic heterozygous germline mutations in *MLH1, MSH2, MSH6,* or *PMS2*. While single heterozygous mutations in these mismatch repair genes causes Lynch syndrome, CMMRD is associated with a wider variety of lesions, with many patients' signs & symptoms resembling Neurofibromatosis-1 early in life with subsequent development of Lynch syndrome-associated cancers (e.g., colorectal, small bowel, endometrial, & ureteral cancers).[1,2,3]




Though the syndrome is very rare with upwards of 200 cases reported as of 2020, the International Replication Repair Deficiency Consortium (IRRDC) has been developing diagnostic & surveillance recommendations to improve survival, as an estimated ~30% of patients with one cancer will develop another, & ~85% of patients pass away within 4 years.[2,3]

Surveillance & prognosis per IRRDC recommendations & data:[2]

| Exam | Start Age | Frequency | Tumors |
|---|---|---|---|
| Brain MRI | At diagnosis | q6 months | Brain |
| Whole body MRI | 6 yrs | q1 year | All |
| CBC | 1 yr | q6 months | Leukemia |
| Abdominal US | 1 yr | q6 months | Lymphoma |
| Upper GI, VCI, ileocolonoscopy | 4-6 yrs | q1 year | GI |
| Gyn exam, TVUS | 20 yrs | q1 year | GU |




1. Wimmer K, Kratz CP. Constitutional mismatch repair-deficiency syndrome. Haematologica. 2010 May;95(5):699-701. doi: 10.3324/haematol.2009.021626. PMID: 20442441; PMCID: PMC2864372.
2. Durno C, Ercan AB, et al. Survival benefit for individuals with Constitutional Mismatch Repair Deficiency undergoing surveillance. J of Clin Onc. 2021 May;39(25)2779-2790. DOI: 10.1200/JCO.20.02636. PMID: 33945292.
3. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. Constitutional Mismatch Repair Deficiency Syndrome; [updated 2020 Apr 1; [cited 2023 Jan 17]. Available from: https://medlineplus.gov/genetics/condition/constitutional-mismatch-repair-deficiency-syndrome/.

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