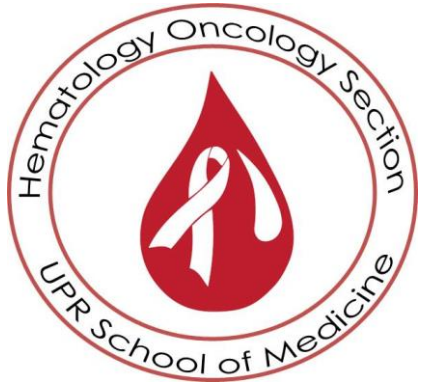
UNIVERSITY OF PUERTO RICO SCHOOL OF MEDICINE
HEMATOLOGY AND MEDICAL ONCOLOGY SECTION



HEREDITARY CANCER SYNDROME

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HISTORY OF PRESENT ILLNESS

- 51 year-old man with past medical history of a testicular seminoma diagnose 14 years ago
- Presented with low hemoglobin levels associated with general weakness, one year prior to admission.
- Manage with iron replacement therapy with no improvement.
- Colonoscopy was done with unremarkable results.
- One year later, patient developed, sudden-onset, non-painfull rectal bleeding.
- Colonoscopy and Upper GI Endoscopy found unremarkable.
- Capsule endoscopy revealed a jejunal ulcer, so the patient was taken to OR for surgical removal of lesion.
- Denies weight loss, nausea, vomiting, fever, chills, night sweats, bowel habits changes.

HISTORY OF PRESENT ILLNESS

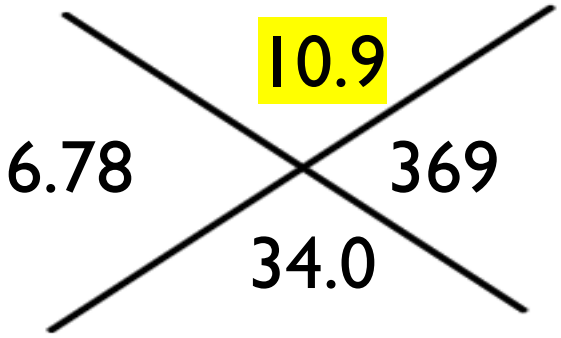
- **PMHx:**
  - 1994: Accidental gun-shot to head, requiring surgical extraction of the bullet
  - 2000: Traumatic fall, requiring thoracic spinal cord surgery
  - 2009: Left testicular seminoma, manage with left sided orchiectomy, and radiation
  - 2022: Anemia of 7, requiring transfusion of 2 PRBCs units
  - Nephrolithiasis
- **FMHx:**
  - Father had colon cancer, Mother suffered breast cancer, Brother with brain tumor, Paternal grandmother had colon cancer, Maternal grandfather had throat cancer, and two cousins with colon cancer
- **Medications:**
  - Omeprazole, Ferrous sulfate, Cannabis (Vape and oils)
- **Social:**
  - No toxic habits.

PHYSICAL EXAM

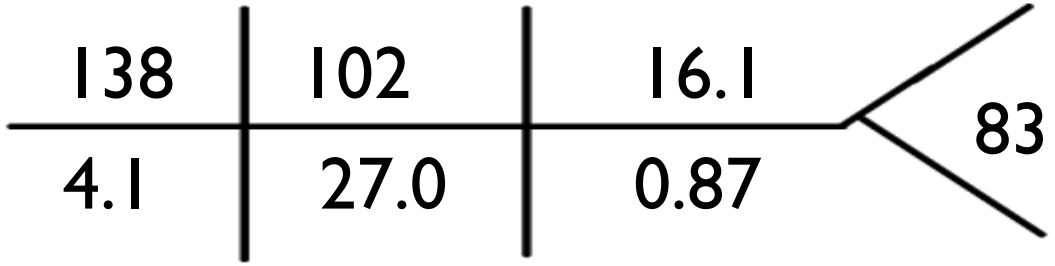
- **Vital Signs**: T: 36.4; HR: 62; RR: 17; BP: 107/65

- **GEN**: Awake and alert. Oriented to person, place and time. No distress.
- **HEENT**: Pale conjunctiva. Normocephalic. PERRLA, EOMI
- **RESP**: Clear to auscultation bilaterally
- **CV**: Regular rate and rhythm, no murmurs
- **ABD**: + bowel sounds, non tender to palpation
- **EXT**: No edema or cyanosis. Strength and sensation preserve

LABORATORIES



MCV: 76.6
MCH: 24.5
RDW: 15.3



- LDH: 127
- CEA: 2.0
- AST: 19
- ALT: 20
- ALKP: 55

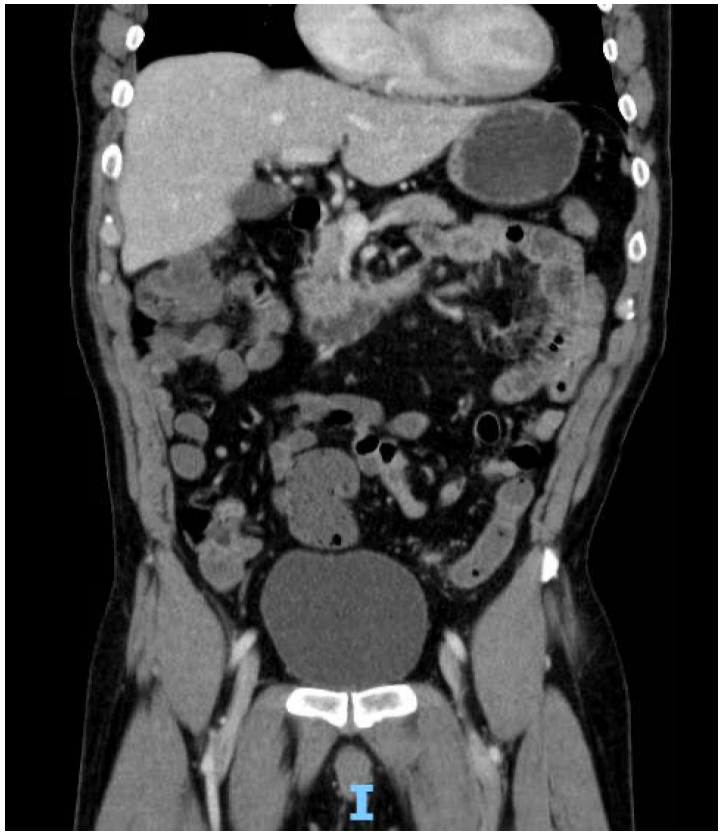
IMAGING

Chest CT Scan with IV Contrast

- Normal examination.

Abdomen/Pelvis CT Scan with IV Contrast

- Normal examination.

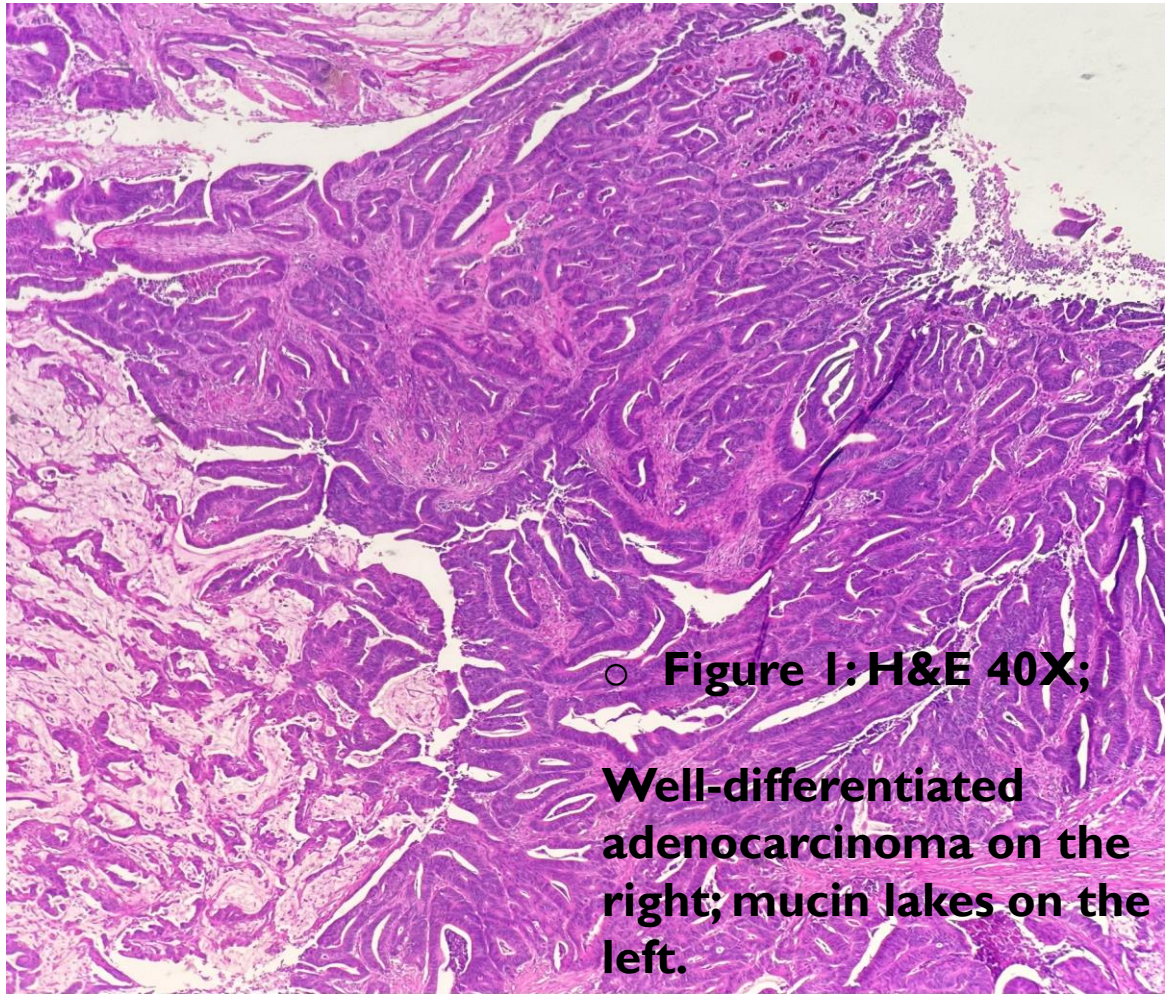


TISSUE BIOPSY: JEJUNUM, 15CM, SEGMENTAL RESECTION

- Final Pathologic Diagnosis:
  - Adenocarcinoma, well differentiated Grade 1, focally mucin producing
  - Tumor site: Jejunum
  - Tumor size: 6 x 3 x 1cm
  - Macroscopic tumor perforation: Not identified
  - Tumor extension: Tumor invades through the muscularis propria into the subserosa, or extends into non-peritonealized perimuscular tissue (mesentery) without serosal penetration
  - Margins not involved by invasive carcinoma, carcinoma in situ, or adenoma
  - Lymphovascular invasion not identified
  - Perineural invasion not identified
  - Eight lymph nodes received, all negative for malignancy

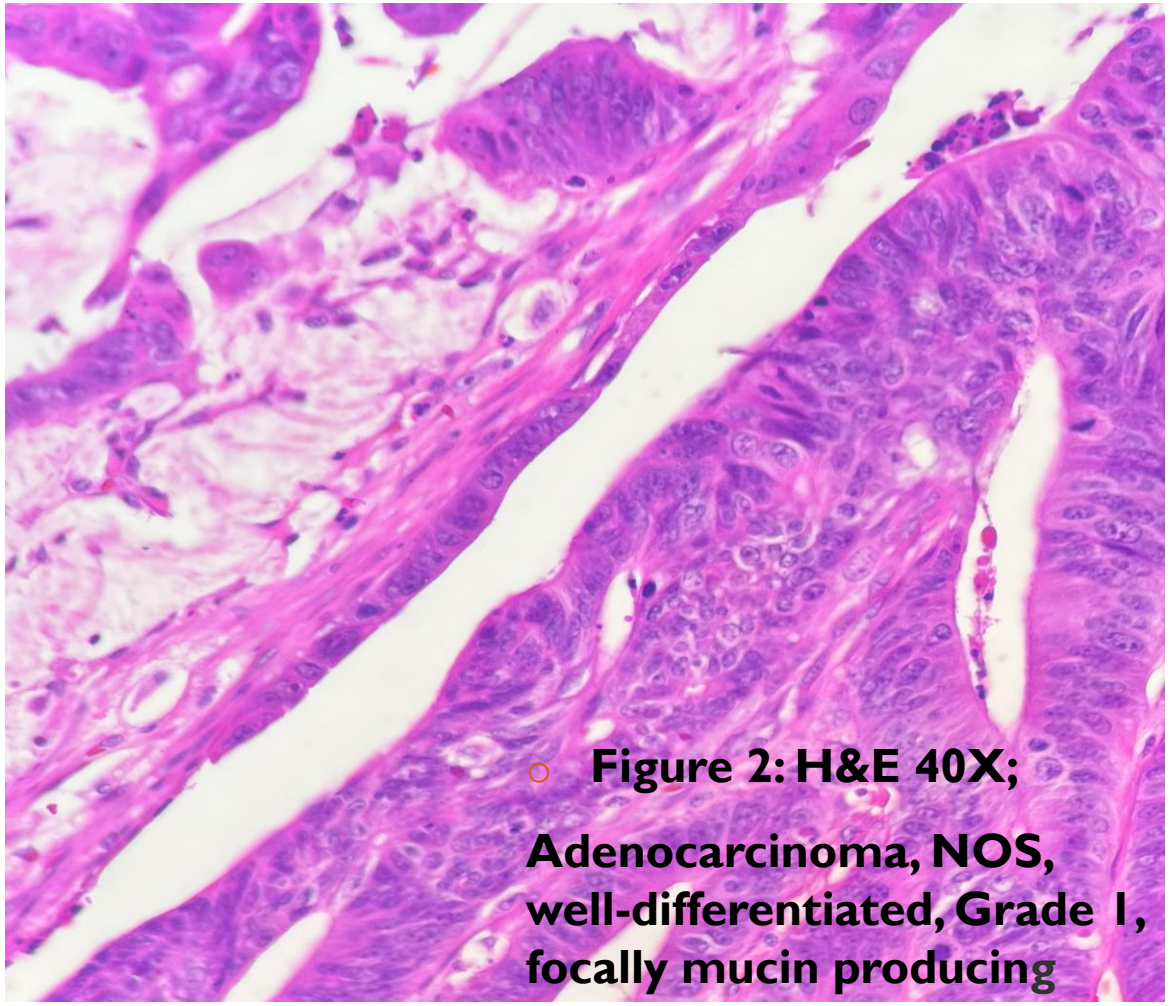
- **Pathologic staging:**
  - **T3 N0 M0**
    - **Stage IIa**

PATHOLOGIC ASSESSMENT



- **Figure 1: H&E 40X;**

Well-differentiated adenocarcinoma on the right; mucin lakes on the left.

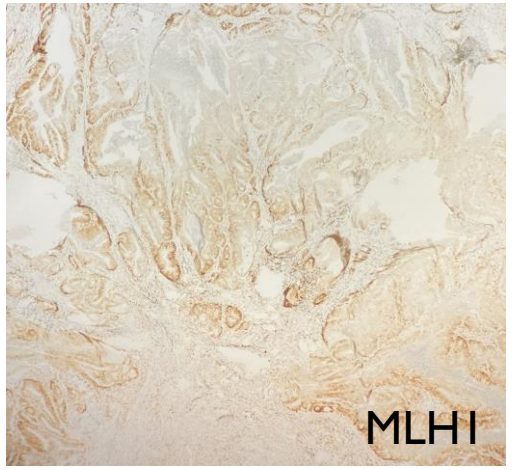


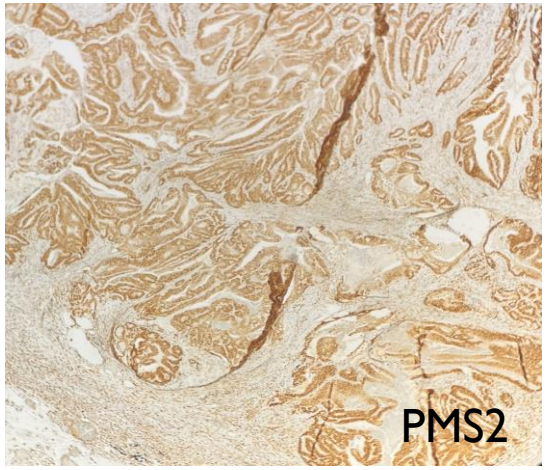
- **Figure 2: H&E 40X;**

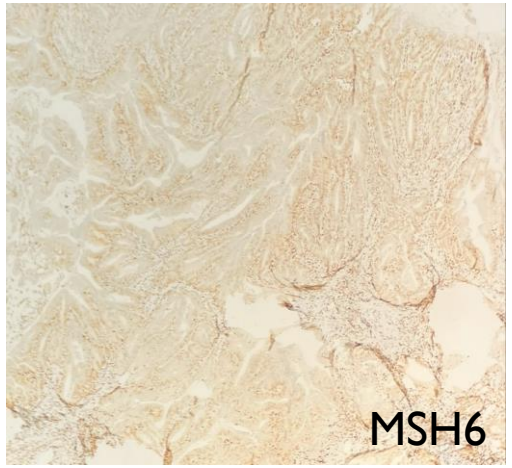
Adenocarcinoma, NOS, well-differentiated, Grade 1, focally mucin producing

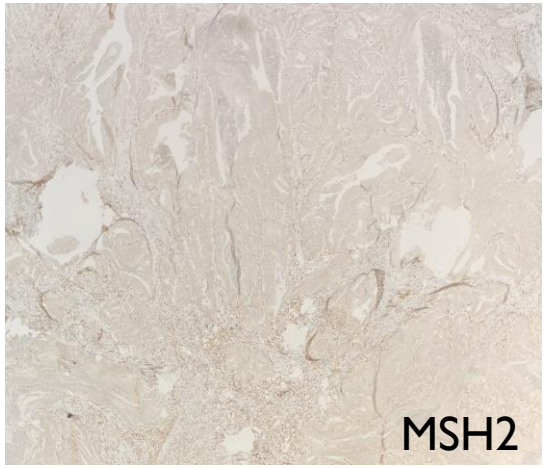
ANCILLARY STUDIES

- Immunohistochemistry testing for Mismatch Repair Proteins:
  - MLH1: Expressed
  - PMS2: Expressed
  - **MSH2: Not Expressed**
  - MSH6: Expressed

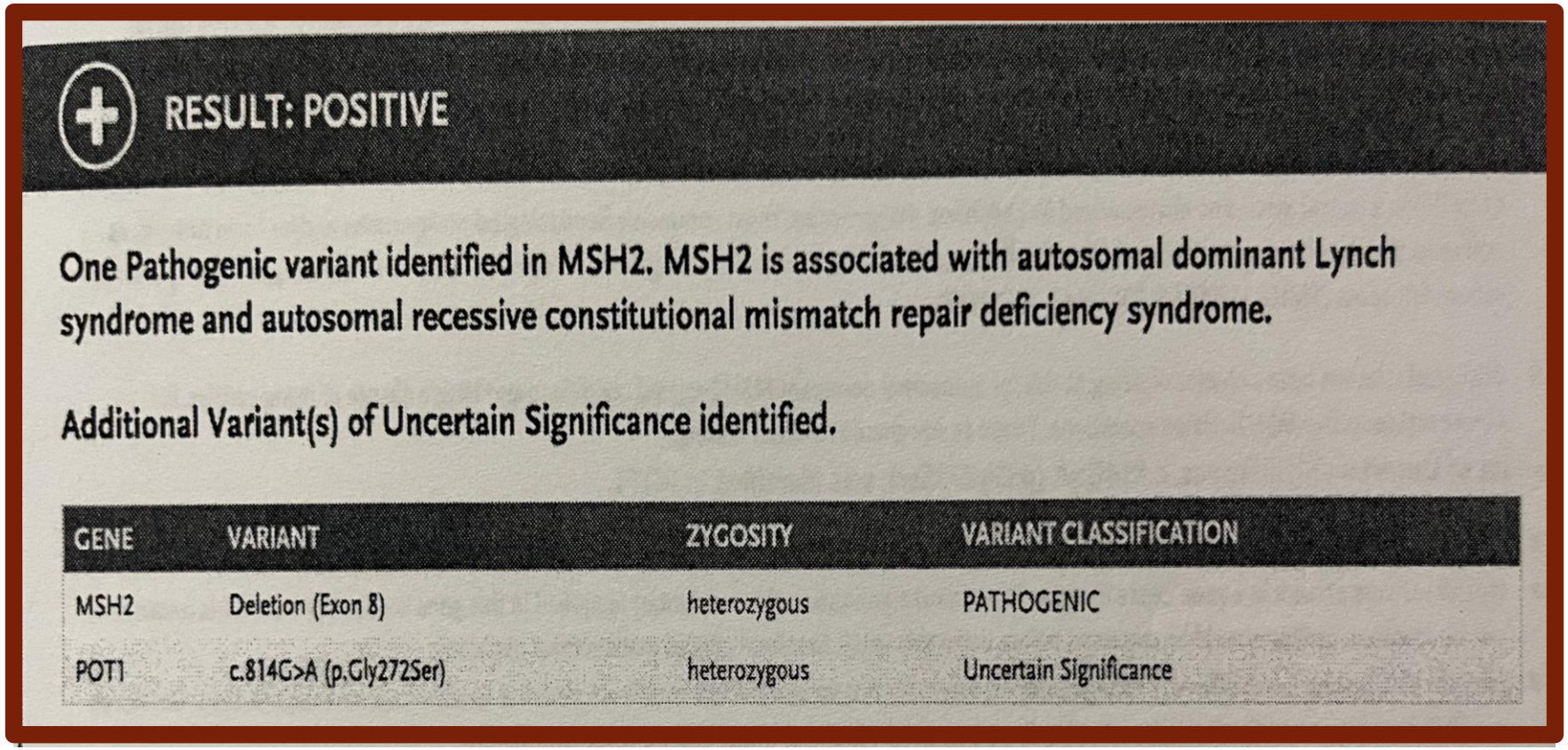








GENETIC TESTING



RESULT: POSITIVE

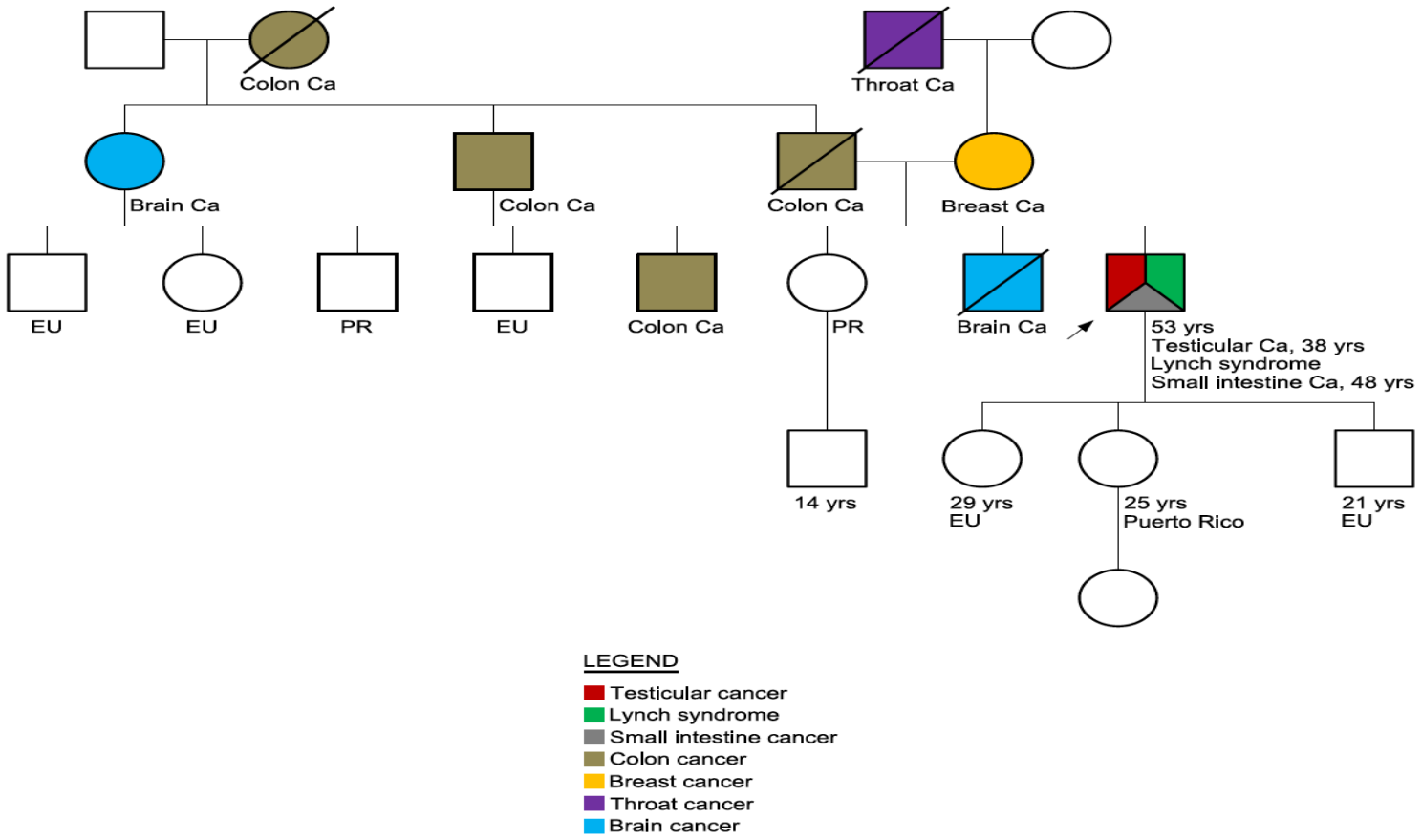
One Pathogenic variant identified in MSH2. MSH2 is associated with autosomal dominant Lynch syndrome and autosomal recessive constitutional mismatch repair deficiency syndrome.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
MSH2	Deletion (Exon 8)	heterozygous	PATHOGENIC
POT1	c.814G>A (p.Gly272Ser)	heterozygous	Uncertain Significance

FOLLOW UP

- The patient was diagnose with Lynch Syndrome.
- Considering pathologic staging, no adjuvant chemotherapy was administer.



DISCUSSION

- Small-bowel adenocarcinoma (SBA) is a rare cancer, and current understanding of its genomic alterations is limited.
  - Comprises only 3% of the gastrointestinal malignancies and is most commonly located on the duodenum.

- Due to the relative rarity of SBA, and the disease's association with several genetic syndromes, the NCCN Panel recommends that all patients with SBA should be counseled for familial malignancies and considered for risk assessment of various genetic syndromes, including Lynch syndrome.

- It may represent the initial manifestations of Lynch syndrome.

DISCUSSION

- Lynch syndrome is a hereditary syndrome resulting from germline mutations in DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, and *PMS2*).
- Individuals with Lynch syndrome are estimated to have a lifetime risk of 4% of developing SBA.
- SBA has a higher percentage of MSI-high tumors compared to CRC.
  - Supports the idea for screening of small bowel adenocarcinoma to identify patients at risk for Lynch syndrome.
  - MSH2 is the most commonly altered in small bowel adenocarcinoma.
  - Up to 8% risk of small bowel cancer if found mutated.

DISCUSSION

- The American Society of Clinical Oncology (ASCO) recommends that Lynch Syndrome patients receive:
  - colonoscopies every 1–2 years to detect colorectal cancers
  - gastroduodenoscopies every 1–3 years to detect stomach cancers

CONCLUSION

- In conclusion, small bowel adenocarcinoma can be the first and the only manifestation of Lynch syndrome.

- Strategies for adequate small bowel tumors screening are needed.
  - There are currently no testing techniques that have proven to be reliable and cost effective enough to detect early-stage small intestine cancer in asymptomatic individuals.

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THANK YOU