Hereditary Colorectal Cancer and Polyposis Syndromes

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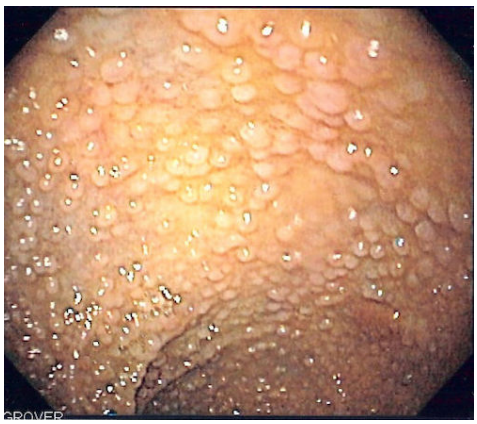
Syndromes

Familial Adenomatous Polyposis (FAP)

- Includes:
  - *Classical FAP*
  - *Attenuated FAP (AFAP)*
  - *Gastric Adenocarcinoma and Proximal Polyposis of the Stomach (GAPPS)*
  - *Gardner's Syndrome*
  - *Turcot's Syndrome*
- *See Familial Adenomatous Polyposis (FAP)


FAP on Colonoscopy [1]

Lynch Syndrome

- Also Known as "Hereditary Nonpolyposis Colon Cancer (HNPCC)"
- *See Lynch Syndrome/Hereditary Nonpolyposis Colon Cancer (HNPCC)

Juvenile Polyposis Syndrome (JPS)

- Also Known as "Familial Juvenile Polyposis"
- *See Juvenile Polyposis Syndrome (JPS)

MUT Y Homolog (MUTYH)-Associated Polyposis (MAP)

- *See MUT Y Homolog (MUTYH)-Associated Polyposis (MAP)

Serrated Polyposis Syndrome (SPS)

- Historically Known as “Hyperplastic Polyposis Syndrome”
- *See Serrated Polyposis Syndrome (SPS)

Peutz-Jeghers Syndrome (PJS)

- *See Peutz-Jeghers Syndrome

PTEN Hamartoma Tumor Syndrome (PHTS)

- Includes:
  - *Cowden Syndrome*
  - *Bannayan-Riley-Ruvalcaba Syndrome (BRRS)*
  - *Proteus-Like Syndrome/SOLAMEN Syndrome*
- *See PTEN Hamartoma Tumor Syndrome (PHTS)

Other Rare Polyposis Syndromes [2,3]

- *GREM1*-Associated Polyposis *(Hereditary Mixed Polyposis Syndrome/HMPS)*
  - Mutations: GREM1 (Autosomal Dominant)
  - Associated with Multiple Polyps of Mixed Histology (Adenomas, Hyperplastic, Hematomas, and Juvenile)
  - Increased Risk of Colorectal Cancer
  - Associated with Desmoid Tumors, Prostate Cancer, and Duodenal Cancer
- Other Adenomatous Polyposis Syndromes (Autosomal Dominant):
  - *POLE-Associated Polyposis*
  - *POLD1-Associated Polyposis*
  - *AXIN2-Associated Polyposis (Oligodontia-Colorectal Cancer Syndrome)*
- Other Adenomatous Polyposis Syndromes (Autosomal Recessive):
  - *NTHL1-Associated Polyposis*
  - *MLH3-Associated Polyposis*
  - *MSH3-Associated Polyposis*

Comparisons

Genetic Mutations

- *Familial Adenomatous Polyposis (FAP)*: APC
- *Lynch Syndrome*: MLH1, MSH2, MSH6, PMS2, or EpCAM
- *Juvenile Polyposis Syndrome (JPS)*: SMAD4 (MADH4) or BMPR1A
- *MUTYH-Associated Polyposis (MAP)*: MUT Y Homolog (MUTYH) Gene
- *Serrated Polyposis Syndrome (SPS)*: Genetic Basis is Mostly Unknown, RNF43 Most Closely Related

- *Peutz-Jeghers Syndrome (PJS)*: STK11
- *PTEN Hamartoma Tumor Syndrome (PHTS)*: PTEN
- Others: GREM1, POLE, POLD1, AXIN2, NTHL1, MLH3, or MSH3

Malignancy of the GI Tract

	Risk of Colorectal Cancer	Stomach	Duodenum/SI
FAP	100%	X	X
Lynch Syndrome	20-80%	~	
MAP	80-90%	~	X
Peutz-Jeghers	39%	X	X
PTEN	9%		
JPS	68%	X	X
SPS	25-70%		

X: Common Association
~: Less Common Association

Extraintestinal Manifestations

	Breast	Endometrium	Ovarian	Thyroid	Pancreatic	Hepatobiliary	Brain	Desmoid	Osteoma	Other
FAP				~	~	~	X	X	X	CHRPE Epidermal Cysts
Lynch Syndrome	~	X	X		~	~	~			Urinary Tract Cancers
MAP	X	X	X	~	~			~		Bladder Cancer Epidermal Cysts
Peutz-Jeghers	X	X	X		X					Melanin Spots Testicle Cancer Lung Cancer
PTEN	X	X		X						Kidney Cancer Mucocutaneous Lesions
JPS										Telangiectasias Skeletal Stigmata
SPS										

X: Common Association
~: Less Common Association

References

1. Makarewicz W, Bobowicz M, Sawicka W, Rzyman W. The treatment of chronic pleural empyema with laparoscopic omentoplasty. Initial Report. Wideochir Inne Tech Maloinwazyjne. 2014 Dec;9(4):548-53. (License: CC BY-NC-ND 3.0)
2. Jelsig AM, Karstensen JG, Jespersen N, Ketabi Z, Lautrup C, Rønlund K, Sunde L, Wadt K, Thorlacius-Ussing O, Qvist N. Danish guidelines for management of non-APC-associated hereditary polyposis syndromes. Hered Cancer Clin Pract. 2021 Oct 7;19(1):41.
3. Lieberman S, Walsh T, Schechter M, Adar T, Goldin E, Beeri R, Sharon N, Baris H, Ben Avi L, Half E, Lerer I, Shirts BH, Pritchard CC, Tomlinson I, King MC, Levy-Lahad E, Peretz T, Goldberg Y. Features of Patients With Hereditary Mixed Polyposis Syndrome Caused by Duplication of GREM1 and Implications for Screening and Surveillance. Gastroenterology. 2017 Jun;152(8):1876-1880.e1.