Envoi SPECIALIST PATHOLOGISTS inside insights

Update No.5 - 2017 Dr Christophe Rosty

Adenomatous polyposis syndromes

- 5% of all colorectal carcinomas are caused by a known genetic syndrome
- Lynch syndrome is the most common inherited condition predisposing to CRC but is usually not associated with colonic polyposis
- Polyposis syndromes include adenomatous polyposis, serrated polyposis and hamartomatous polyposis
- Familial adenomatous polyposis (FAP) was the first described adenomatous polyposis syndrome associated with inevitable development of CRC. Other adenomatous polyposis syndromes have been identified more recently: *MUTYH*-associated polyposis, polymerase proofreading-associated polyposis and *NTHL1*-associated tumour syndrome (Table 1). Adenomas in this context include conventional tubular, tubulovillous and villous adenomas but not sessile serrated adenomas.

Syndrome	Gene	Inheritance	Gastrointestinal polyposis	Other tumour risk
FAP, classic form	*APC*	Autosomal dominant	Multiple (≥100) colonic adenomas; gastric fundic gland polyps and pyloric gland adenomas; small intestinal adenomas	Cancer of small intestine, stomach; desmoid tumours; hepatoblastoma; some brain and thyroid tumours; osteoma
FAP, attenuated form	*APC*	Autosomal dominant	10-99 adenomas predominant in proximal colon; gastric fundic gland polyps and pyloric gland adenomas; small intestinal adenomas	Rare
***MUTYH*-associated polyposis**	*MUTYH*	Autosomal recessive	Multiple colonic adenomas (some >100) with serrated polyps; gastric fundic gland polyps; duodenal adenomas	Cancer of bladder, ovary, duodenum
Polymerase proofreading-associated polyposis	*POLE, POLD1*	Autosomal dominant	Multiple colonic adenomas, duodenal adenomas	Cancer of endometrium; brain tumours
***NTHL1*-associated tumour syndrome**	*NTHL1*	Autosomal recessive	Multiple colonic adenomas (up to 200)	Cancer of breast, duodenum, bladder, brain, endometrium, head and neck, hematologic system

Table 1. Summary of the currently known inherited adenomatous polyposis syndromes predisposing to colorectal carcinoma

When to refer a patient with multiple colonic polyps for genetic counselling?

Patients with one of these findings may be tested for *APC* and *MUTYH* mutation:

- ≥ 20 colonic adenomas
- 10-20 adenomas with family history of multiple adenomas, early age of onset, or extra-colonic tumours associated with one of the polyposis syndromes

The prevalence of mutation identified varies by adenoma count:

Number of adenomas	Prevalence of mutation	
	APC	MUTYH
>1000	80%	2%
100-999	56%	7%
20-99	10%	7%
10-19	5%	4%

There is phenotypic overlap between serrated polyposis and *MUTYH*-associated polyposis, and between Lynch syndrome and *MUTYH*-associated polyposis.

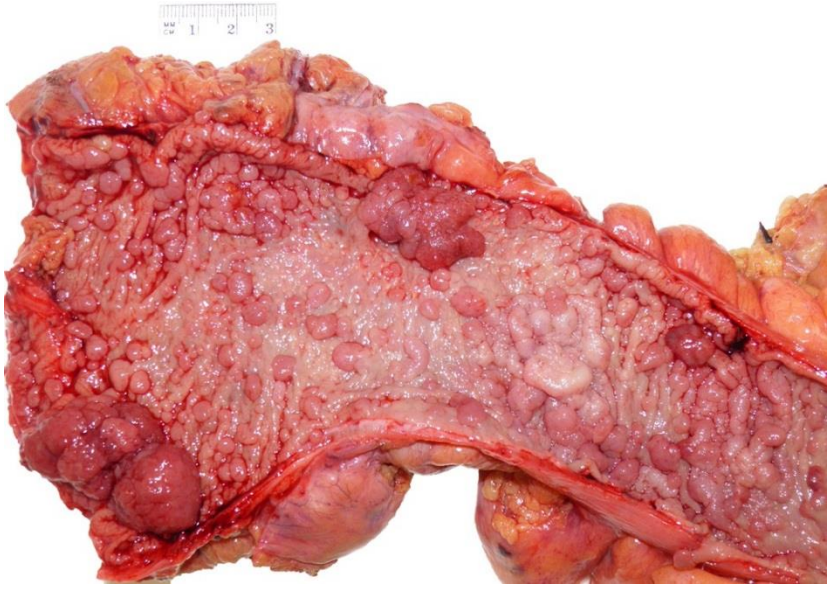

Fig. 1. Multiple colonic polyps in FAP

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