Envoi SPECIALIST PATHOLOGISTS *inside insights*

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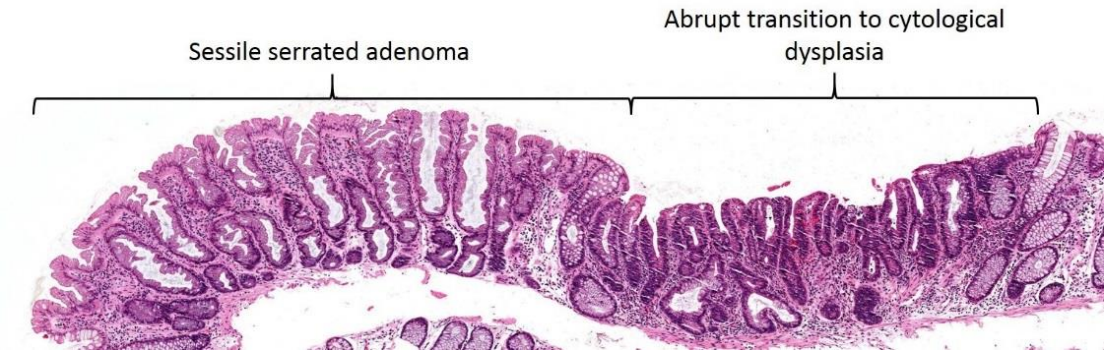
SSA with dysplasia (SSAD)

The sessile serrated adenoma with cytological dysplasia (SSAD) is the progressed form of the SSA and represents the final histological stage before the development of malignancy. Because SSADs progress very rapidly to malignancy they are rarely encountered in clinical practice (only 0.4% of all polyps removed and only 3% of all SSAs). Because they are mostly proximal, small and flat they can be easily missed at colonoscopy and as such are disproportionately represented in series of interval colorectal carcinoma. They give rise to sporadic microsatellite unstable carcinomas that must be distinguished from Lynch syndrome.



Definition: A neoplastic polyp characterised by serrated architectural features and superimposed cytological dysplasia (Note: Grading dysplasia in these polyps is not recommended as any form of dysplasia indicates an advanced polyp with a high risk of malignant progression).

Risk factors: Older age, female gender, smoking, possibly obesity

Clinicopathological features: Mean age 75, female > male, proximal > distal, median size 9mm, 83% flat

Molecular biology: *BRAF* mutation, CpG island methylator phenotype (CIMP), *MLH1* methylation (75%)

Risk of malignant progression: Very high risk of rapid malignant transformation

Risk of metachronous carcinoma: High; odds ratio 4.76; risk of carcinoma by ten years 4.43%

Surveillance guidelines: Current guidelines recommend repeat colonoscopy at 3 years, but closer surveillance may be warranted if there is any doubt about the adequacy of endoscopic resection

Cancer outcome: The sessile serrated adenoma with dysplasia gives rise to the majority of serrated neoplasia pathway carcinomas (approximately 15-20% of all colorectal carcinoma). 75% become *BRAF* mutated, microsatellite unstable (MSI-H) colorectal carcinoma (good prognosis but require distinction from Lynch syndrome) and 25% become *BRAF* mutated, microsatellite stable colorectal carcinoma (poor prognosis).

Distinction from Lynch syndrome: SSADs give rise to about 80% of microsatellite unstable carcinomas, the remaining 20% occur in patients with Lynch syndrome. The following table illustrates the similarities and differences between them.

Feature	Serrated pathway	Lynch syndrome
Age	Mostly older	Mostly younger
Gender	Mostly female	No predilection
Location	Mostly proximal	Mostly proximal
Precursor polyp	Sessile serrated adenoma	Conventional adenoma
Histology	Poorly differentiated (often mucinous)	Poorly differentiated (often mucinous)
Molecular basis of MSI	MLH1 promoter methylation	Germline mutation (MLH1, PMS2, MSH2, MSH6)
BRAF mutation	Usually (70%)	Absent
CIMP	Yes	No

Further reading:

Bettington et al; Clinicopathological and molecular features of sessile serrated adenomas with dysplasia or carcinoma. Gut 2015, epub ahead of print.

Rune et al; Increased risk of colorectal cancer development among patients with serrated polyps. Gastroenterology 2015, epub ahead of print.

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