Serrated Neoplasia

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Colorectal Polyps

Adenomas – defined by epithelial dysplasia
Hyperplastic (metaplastic) polyps
Hamartomas (juvenile, Cowden’s, Peutz-Jeghers)

Inflammatory
Non-epithelial
Adenomas
Advanced Adenoma Patients

> 10 mm
>25% villous component
high grade dysplasia
multiple (>3) polyps
Atkin WS et al. Lancet 2010; 375: 1624-33

UK FlexiSig Trial

Cumulative colorectal cancer mortality (%)

Time from randomisation (years)

- Control
- Screened
- Not screened
Increasing neoplastic transformation and acquisition of mutations
Chromosomal Instability in a Colorectal Cancer

Near-triploid pattern & unbalanced translocations (Prof MW Arends, Edinburgh)
Hyperplastic Polyps

- Formerly metaplastic polyps
- Asymptomatic
- 21% of all colonoscopies
- Left > right, Male > female
- Infolded epithelial tufts giving a saw-tooth *serrated* appearance
- No dysplasia
- Failure of anoikis (shedding of mature cells)
- Historically regarded as reactive lesions with no malignant potential
The method by which the free epithelial border extends, and by which the cavities become filled by secondary growths, should be studied under a high power. The process is as follows:—At one or more points in the border the epithelial cells increase in length, so that they stand out like a small bud beyond the heads of their neighbours (Plate XII).

If such a bud be closely examined it will be seen that the two central cells forming the group act as the leaders of the growing branch. At the same time it is seen that these lengthened cells are in an active state of generation, and appear as if multiplying by cleavage of their extremities (Plate XII). As the cells are progressively formed they bend over and gradually assume a direction at right angles to the line between the primary cells. The line of junction between the walls of the two original cells, which at first was barely visible, becomes more strongly marked, assuming a distinctly fibrous character, and increases in thickness at the expense of the cell contents. After a while small dark cells appear in the very centre of this line, as if they were again separating the bond of union by which the two contiguous cell walls had united to form the original fibre.

Such cells become vacuolated, and the central line becomes the channel. In time a considerable amount of retiform tissue is formed in the centre of the growing leaf. It would appear as if the fibres of this tissue were formed from what is left behind of the walls of the epithelial cells, that is to say, that if the line of junction between any two of the contiguous cells forming the surface of the branch were followed inwards it would be continuous with the fibres of the retiform tissue (fig. 1, Plate XII).

W. Harrison Cripps, Surgeon.
*Trans Path Soc Lond*
1881; 32: 87-112
Hyperplastic Polyps

- Increase in frequency with age
- 17 times commoner in colons with carcinoma
- Similar dietary and lifestyle risk factors to CRC
- KRAS or BRAF mutation not uncommon
- Monocryptal and oligocryptal in ‘aberrant crypt foci’
Hyperplastic Polyp Types

Microvesicular
Mostly left colon
*BRAF* mutation >> *KRAS*

Goblet Cell
Exclusively left colon
*KRAS* mutation >> *BRAF*
Serrated Adenoma

Dysplasia by definition, usually low grade
Eosinophilic cytoplasm
Pseudostratified, ‘pencillate’ nuclei
May be tubular, tubulovillous or villous
Invade to give serrated carcinoma

Serrated Adenoma
‘Traditional’ Serrated Adenoma

Â <2% of all adenomas
Â More often left sided
Â Frequently pedunculated
Â Complex architecture, tubulovillous, villous, filiform
Â Short, budding, ‘ectopic’ crypts with ‘clefts’
Â KRAS mutation in ~25%

‘Traditional’ Serrated adenoma (TSA)
Sessile Serrated ‘Adenoma’

- Serrated polyps with unusual architectural features
  - Horizontal orientation of deep crypts
  - Serration down to crypt base
- Often large **sessile**, **indistinct** and poorly defined with a mucus covering
- Prevalence 1-2%
- Usually right colon, Females > males
- Associated with cigarette smoking
- Multiple in some patients (serrated polyposis)

Tolakovic EE & Snover DC. *Gastroenterology* 1996; 110: 748-55
Sessile serrated lesion
Sessile Serrated ‘Adenoma’

- No conventional dysplasia but may have ‘nuclear atypia’, ‘dysmaturation’ or disorganised mixture of goblet cells and non-mucous cells at crypt base
- Basal crypt dilatation
- Abnormal proliferation
- Normal subepithelial collagen plate
- Often express MUC5AC or MUC6 and Annexin A10
- KRAS mutation very uncommon

Nomenclature

Sessile serrated lesion (SSL)

is preferred to

Sessile Serrated Adenoma (SSA)
(there’s no conventional dysplasia)

or

Sessile Serrated Polyp (SSP)
(it’s rarely polypoid)

or even

Sessile Serrated Polyp/Adenoma (SSP/A)