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A Distinct Pattern of Beclin-1 Staining Helps Distinguish Sessile Serrated Adenomas

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INTRODUCTION

Autophagy, a lysosomal degradation system, has both cell survival and cell death-promoting capabilities, and its versatility is exploited in many pathologic entities. In neoplastic processes, autophagy has been demonstrated to contribute to both tumor suppression and tumorigenesis in a relatively tumor-specific fashion. Beclin-1 is a protein involved in the formation of the autophagosome, the core unit of autophagy, and serves as one of the general markers for this process. Previous studies have shown Beclin-1 overexpression in both pre-neoplastic and invasive colon carcinoma but weak to absent expression in normal colonic mucosa.

Serrated polyps (SPs) of the colon represent morphologically and molecularly unique precursor lesions in the serrated adenoma-carcinoma pathway. The pathophysiology of the serrated pathway and its natural progression is of great interest. The specific role of autophagy in SPs is not fully described.

We evaluated SPs and autophagy using Beclin-1 protein, a general autophagy marker, to aid in the assessment of autophagy along the serrated pathway. Difference in Beclin-1 staining may represent variation in autophagy among polyp subtypes, exposing biological and possible clinically useful properties.

METHODS

After approval from the Institutional Review Board of Thomas Jefferson University Hospital, cases were considered from randomly selected colonic biopsies with diagnoses of serrated polyps (hyperplastic polyps, sessile serrated adenomas, sessile serrated adenomas with low/high grade dysplasia, and traditional serrated adenomas) collected in 2014 in the Department of Surgical Pathology of Thomas Jefferson University Hospital.

Immunohistochemistry using anti- Beclin-1 antibody (Abcam, Cambridge, MA) was performed on 58 paraffin-embedded SPs (9 hyperplastic polyps, 38 sessile serrated adenomas (SSAs), 4 SSAs with dysplasia, 4 traditional serrated adenomas +/- dysplasia) and normal colonic mucosa from the patients with SPs.

Staining was graded by:

- proportion of cells staining: 0 (no staining), 1, 2, 3 diffuse (>50%)
- Staining intensity: 0 (negative), 1, 2, 3 (strong)

Surface staining score (proportion x intensity) was calculated. Two-sample independent t-test assessed the difference between the SSA mean surface staining score versus the mean surface staining score of the other samples.

RESULTS

82% of SSAs demonstrated a distinct pattern of Beclin-1 staining: diffuse, strong staining of the crypt with weaker surface staining. The difference between the mean surface staining scores of the SSA group versus other samples (HPs, SSAs with dysplasia, TSAs +/- dysplasia) is statistically significant ($P = 0.00001$).

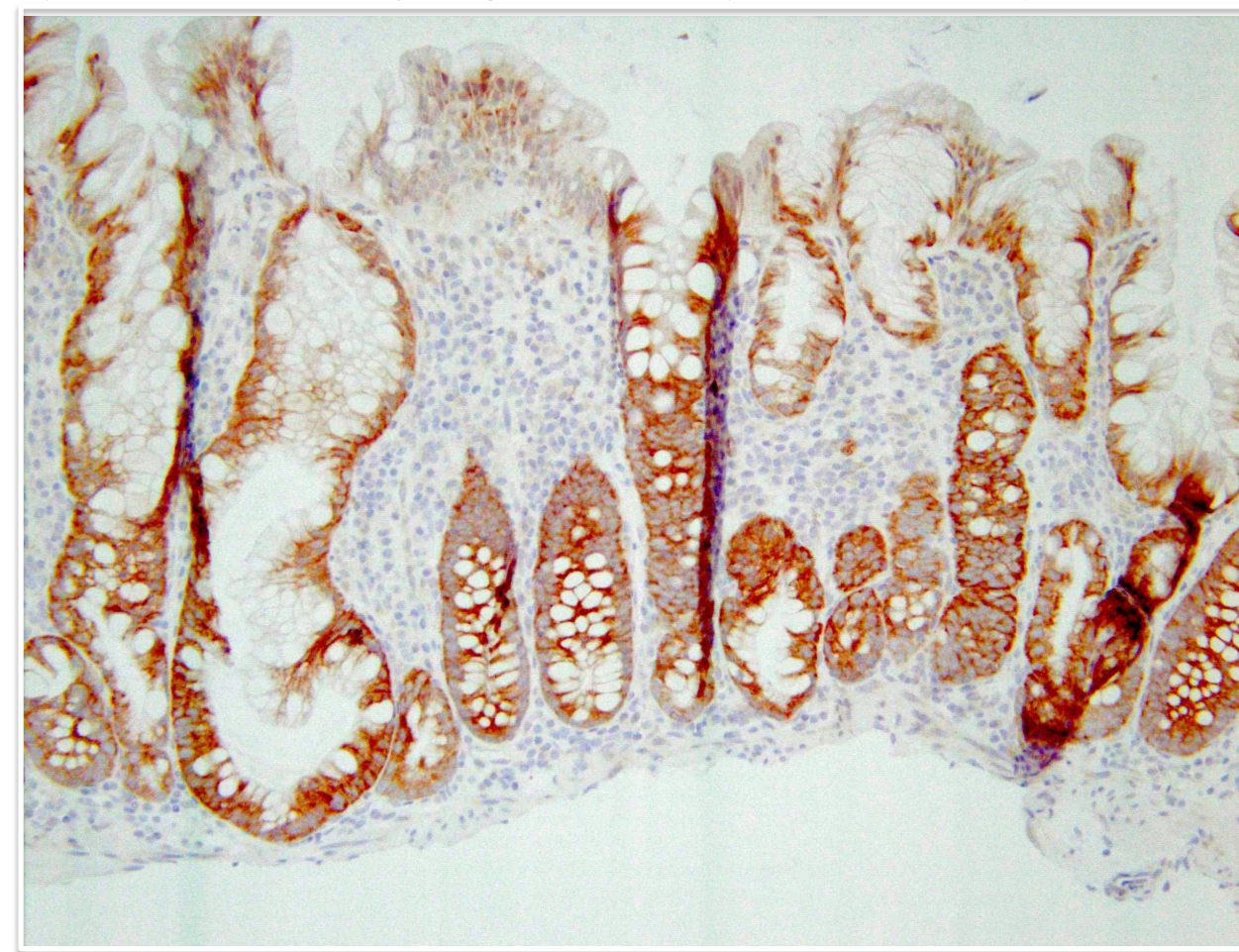
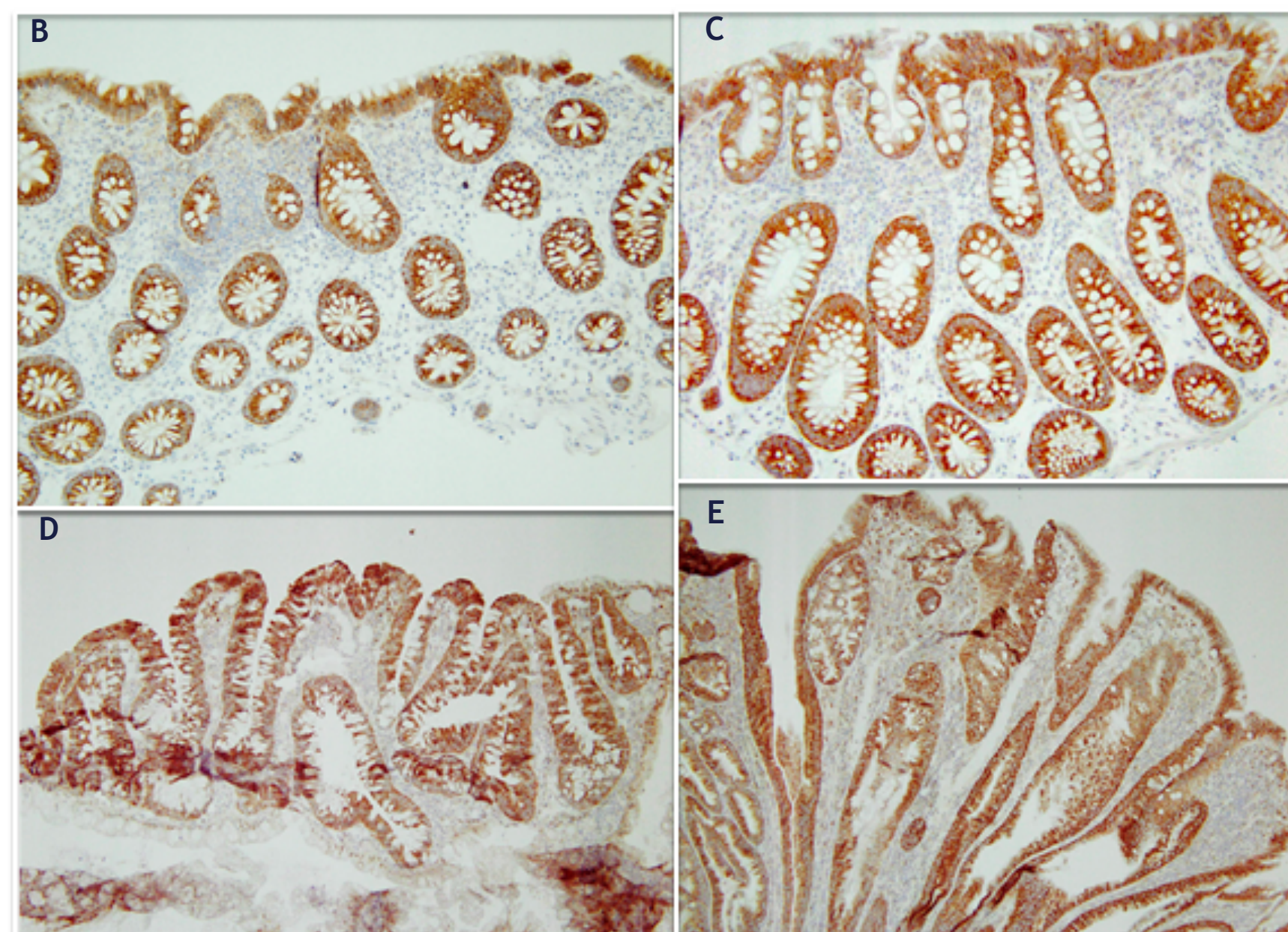


Figure A. Sessile serrated adenoma showing a distinct pattern of Beclin-1 staining: diffuse, strong staining of the crypt with weaker surface staining.



Figures B-E. Normal colonic mucosa (B), hyperplastic polyp (C), SSA with dysplasia (D), and TSA (E) show diffuse, strong staining throughout the crypt and surface.

RESULTS

Diffuse, strong staining throughout the crypt and surface was seen in SSAs with dysplasia, TSAs +/- dysplasia, 67% of HPs, and sections of histologically normal colonic mucosa of patients with SPs. 33% of hyperplastic polyps displayed SSA-type surface staining pattern.

80% of histologically normal colon in the background of the serrated polyps showed diffuse, moderate to strong staining.

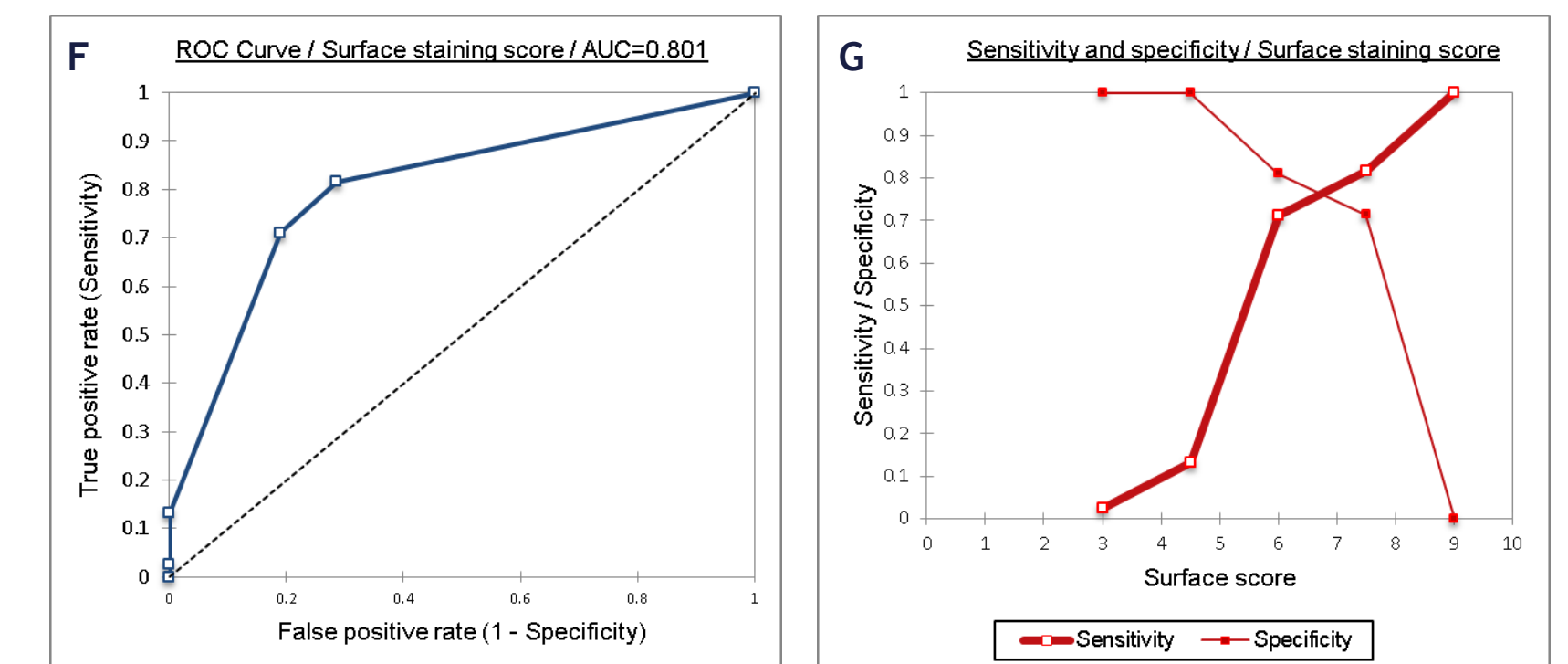


Figure F-G. Receiver operating curve (F) and sensitivity/specificity graph (G) for Beclin-1 surface staining scores.

At a cut-off of 7.5 surface staining score, this distinct staining pattern of Beclin-1 has an 81.6% sensitivity and 71.4% specificity for distinguishing sessile serrated adenomas.

CONCLUSIONS

- The strong Beclin-1 staining in SPs and concurrent normal colonic mucosa suggests that autophagy is significantly altered in the serrated pathway.
- Changes in autophagy may precede the characteristic, morphologic alterations of serration that are seen in these polyps.
- Hyperplastic polyps with the SSA-type staining pattern may represent intermediate SPs.
- The distinct Beclin-1 staining pattern suggests a potentially useful tool to distinguish SSAs in diagnostic challenges.