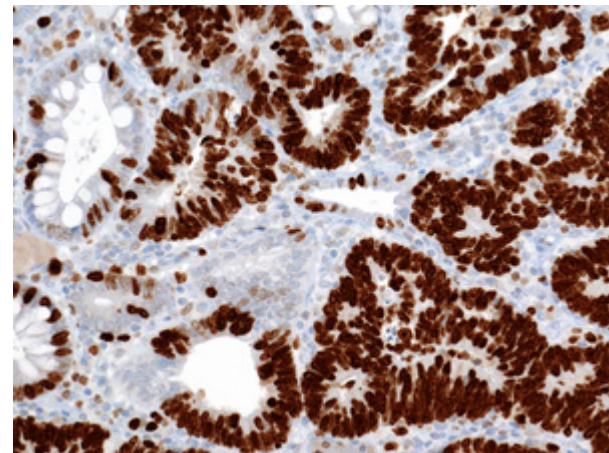
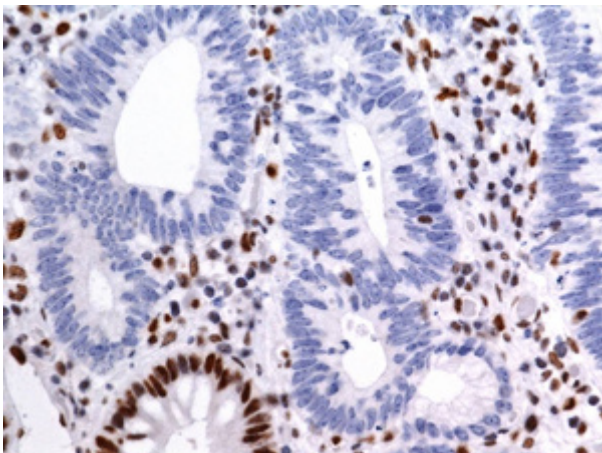
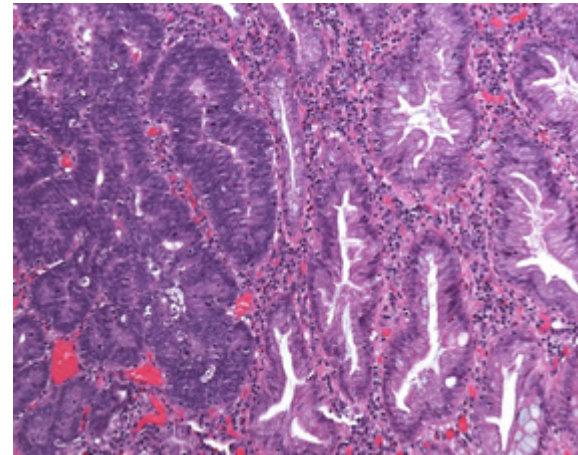
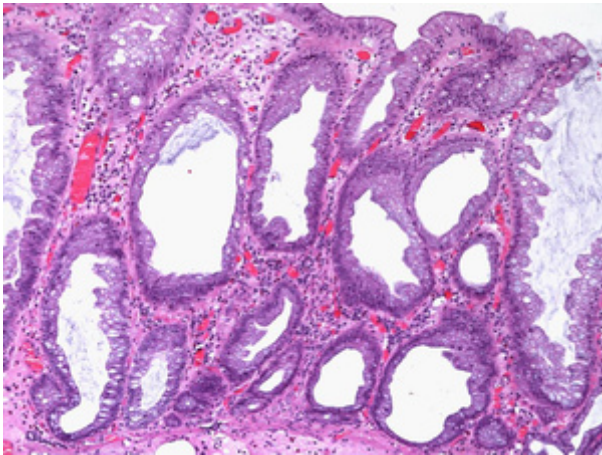
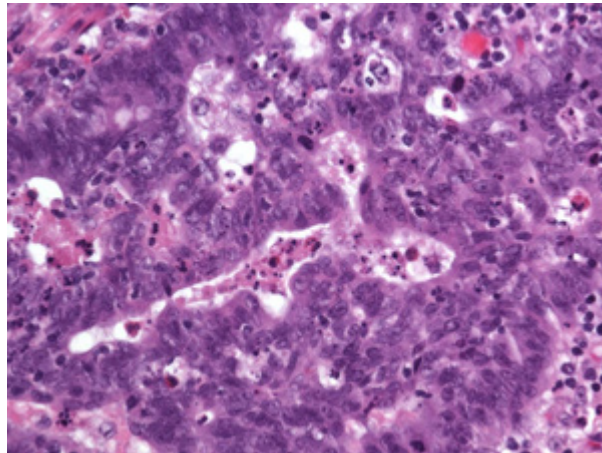
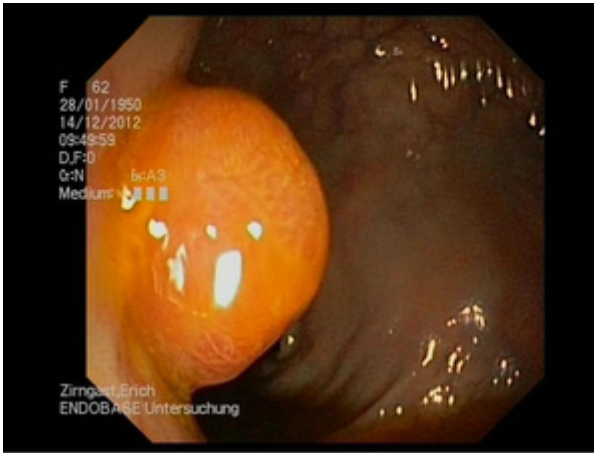
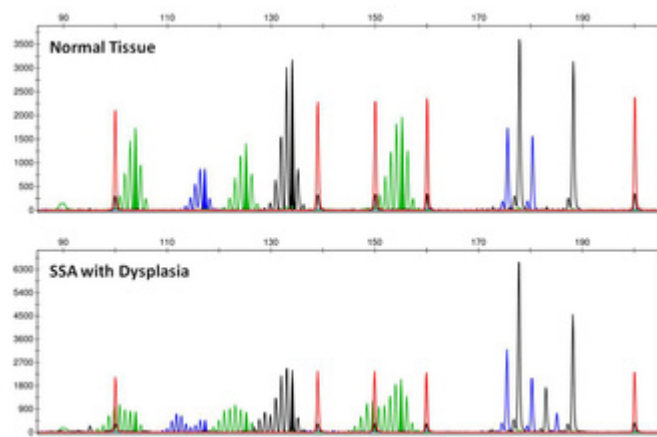
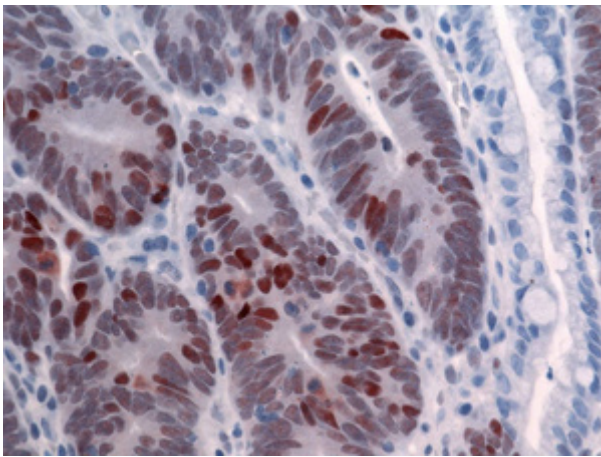


February 2013

Polypectomy specimen obtained from the hepatic flexure of a 62-year-old female.

What is your diagnosis?





Diagnosis

Sessile serrated adenoma/polyp with high grade dysplasia (intraepithelial neoplasia).

Comment

The polypectomy specimen shows a sessile serrated adenoma/polyp (SSA/P). The crypts are often dilated, abundantly filled with mucin, and assume abnormal shapes, including L-shaped and inverted T-shaped crypts (panel B). The presence of tubular structures with unequivocal (cytological) low and high grade dysplasia (panels C-D) identifies the lesion as SSA/P with dysplasia. Invasion through the muscularis mucosae into the submucosa is not observed. Immunohistochemistry reveals lack of MLH1 expression (panel E), high mitotic activity (MIB-1; panel F), and p53 protein stabilization (panel G) in dysplastic glands. Upon molecular analysis, the lesion is microsatellite instable (panel H), positive for BRAF mutation, yet negative for KRAS mutation.

Cytological dysplasia is not present in uncomplicated SSA/P, but develops with progression toward carcinoma, often in conjunction with methylation of the MLH1 gene, as documented by the loss of nuclear MLH1 expression in dysplastic glands, and with increased proliferation (MIB-1). Loss of MLH1 function implies additional molecular changes, such as microsatellite instability (MSI). Nuclear accumulation of p53 protein is present in a subset of SSA/P with cytological dysplasia and may indicate neoplastic progression.

For further reading

- › Snover DC. Update on the serrated pathway to colorectal carcinoma. *Hum Pathol.* 2011;42:1-10.
- › Fujita K, Yamamoto H, Matsumoto T, Hirahashi M, Gushima M, Kishimoto J, Nishiyama K, Taguchi T, Yao T, Oda Y. Sessile serrated adenoma with early neoplastic progression: a clinicopathologic and molecular study. *Am J Surg Pathol.* 2011;35:295-304.
- › Rex DK, Ahnen DJ, Baron JA, Batts KP, Burke CA, Burt RW, Goldblum JR, Guillem JG, Kahi CJ, Kalady MF, O'Brien MJ, Odze RD, Ogino S, Parry S, Snover DC, Torlakovic EE, Wise PE, Young J, Church J. Serrated Lesions of the Colorectum: Review and Recommendations From an Expert Panel. *Am J Gastroenterol.* 2012;107:1315-29.

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