BEYOND THE POLYPS AND COLON CANCER MANAGEMENT

Case presentation and panel discussion
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CASE 1

33 years old lady referred to you for consultation about colonoscopy requirement. Her father died of a colorectal cancer at the age of 44. No other significant family history was mentioned.

She had history of crampy abdominal pain, alleviate with diarrhea and mucous passing. No history of rectorrhagia.

Upon examination, no abnormality was detected and rectal examination was normal as well.

Some laboratory tests requested which were unremarkable (CBC, ESR, Stool OB X3, CEA)
WHAT DO YOU ADVISE HER TO DO?

A. Total colonoscopy at this time
B. Total colonoscopy one year later
C. Total colonoscopy at the age of 40
D. Total colonoscopy at the age of 50
CORRECT ANSWER IS B

Panel discussion ....
Colonoscopy was performed, a 10 x 10 mm polyp was detected at sigmoid, other parts were NL till terminal ileum. What do you recommended that to do?

A. Biopsy and polypectomy if pathology showed adenomatous polyp in next session

B. Biopsy and polypectomy if pathology showed adenoma with moderate to severe dysplasia

C. Polypectomy at the same session
Supporting data:

Almost all colon cancers arise within an adenoma.

The risk of colon cancer increases with larger and increasing numbers of adenomatous polyps.

The risk of cancer in unresected polyps is:

- 4% after 5 years
- 14% after 10 years
CORRECT ANSWER IS ... C

Panel discussion
SNARE POLYPECTOMY WAS DONE AND WAS SENT FOR PATHOLOGY

_Tubular adenoma with low grade dysplasia, no high grade dysplasia was detected_
DOES THIS POLYP HAVE CRITERIA FOR ADVANCED ADENOMA?

A. Yes
B. No
CORRECT ANSWER IS B

Panel discussion ...
ADENOMATOUS POLYPS

- About **two-thirds** of all colonic polyps are adenomas.
- Adenomatous polyps are neoplastic polyps.
- Adenomas are by definition dysplastic and thus have malignant potential.
- Nearly **all colorectal cancers** arise from adenomas,
- But only a small minority of adenomas progress to cancer (**5% or less)**.
- The time for development of adenomas to cancer is **about 7 to 10 years**.
- The risk of progression is faster for advanced adenomas.
ADVANCED ADENOMA

1. High-grade dysplasia
2. >10 mm in size
3. Villous component
Epidemiology of Adenomas

<table>
<thead>
<tr>
<th>Type</th>
<th>Prevalence</th>
<th>% Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubular Adenoma</td>
<td>75%</td>
<td>5%</td>
</tr>
<tr>
<td>Tubulovillous</td>
<td>15%</td>
<td>22%</td>
</tr>
<tr>
<td>Villous Adenoma</td>
<td>10%</td>
<td>40%</td>
</tr>
<tr>
<td>Weighted Chance</td>
<td>100%</td>
<td>10.5%</td>
</tr>
</tbody>
</table>
## Size and % of Ca

<table>
<thead>
<tr>
<th>Type</th>
<th>&lt;1 cm</th>
<th>1-2 cm</th>
<th>&gt;2 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubular Adenoma</td>
<td>1%</td>
<td>10%</td>
<td>34%</td>
</tr>
<tr>
<td>Tubulo-Villous</td>
<td>4%</td>
<td>9%</td>
<td>45%</td>
</tr>
<tr>
<td>Villous Adenoma</td>
<td>10%</td>
<td>10%</td>
<td>54%</td>
</tr>
</tbody>
</table>
CONTINUE ,,,

1. Sex ( men > women )
2. Age ( > 50 )
3. Family history
The patient ask about diet and medications that can prevent polyp recurrence. What is your dietary recommendation?

A. Low fat diet
B. Low red meat diet
C. Reduce weight
D. Stop smoking
E. High fiber diet
ALL OF THE ABOVE

Panel discussion ...
RISK FACTORS

LIFESTYLE

- high fat diet
- high red meat
- low fiber diet
- Cigarette smoking
- Obesity
DO YOU RECOMMEND THAT SHE HAVE TO USE ANY MEDICATION FOR PREVENTION?

A. Yes, ASA
B. Yes, calcium
C. Yes, statins
D. No, not at all
**Statins**

Based on solid evidence, statins do not reduce the incidence or mortality from CRC.

**Aspirin**

Based on solid evidence, daily aspirin for at least 5 years reduces CRC incidence and mortality.

**Nonsteroidal anti-inflammatory drugs (NSAIDs)**

There is inadequate evidence that the use of NSAIDs reduces the risk of CRC.

Based on solid evidence, NSAIDs reduce the risk of adenomas, but the extent to which this translates into a reduction of CRC is uncertain.

**Calcium supplementation**

The evidence is inadequate to determine whether calcium supplementation reduces the risk of CRC.
Hormone therapy (estrogen plus progestin)

Based on solid evidence, combined hormone therapy (conjugated equine estrogen and progestin) decreases the incidence of invasive CRC.

Based on solid evidence, harms of postmenopausal combined estrogen-plus-progestin hormone use include increased risk of breast cancer, coronary heart disease, and thromboembolic events.

Based on fair evidence, conjugated equine estrogens do not affect the incidence of, or survival from, invasive CRD.
FOLIC ACID AND FOLATE ?
Data from animal and human studies have demonstrated that folate inhibits pathogenesis of cancer in a number of tissues including the colon.

However, whether folate and folic acid have a role in prevention of colorectal cancer is unclear. By contrast, the possibility that folic acid supplementation increases the risk of colon cancer has also been raised.
Drugs

Currently there are no generally accepted chemopreventive recommendations for patients at average risk for CRC but several agents have been shown to have modest to moderate chemopreventive effects in average and high risk populations.
CORRECT ANSWER ...?

Panel discussion...
IN A FOLLOW UP REVISIT, THE PATIENT MENTIONED THAT ONE OF HER COUSIN HAD ALSO A MALIGNANT POLYP.

Is your strategy change?

A. Yes, we increase the follow up visits and colonoscopies
B. No, not at all
People who have

1. One first-degree relative before the age of 60 years (parent, brother, sister, or child) with colorectal cancer or an advanced type of adenomatous polyps

2. two first-degree relatives diagnosed at any age

should begin screening for colon cancer earlier, typically at age 40, or 10 years younger than the earliest diagnosis in their family, whichever comes first
People with:

a **second-degree relative** (grandparent, aunt, or uncle) or **third-degree relative** (great-grandparent or cousin) with colorectal cancer should be screened for colon cancer similar to a person with an **average risk**.
WHAT DO YOU SUGGESTED THAT TO DO NOW?

A. The next colonoscopy six months later
B. The next colonoscopy one year later
C. The next colonoscopy 5 years later
D. The next colonoscopy 10 years later
ACG AND ACS GUIDELINES:

If a single first-degree relative was diagnosed at age 60 years or older with CRC or an advanced adenoma (≥1 cm, or high-grade dysplasia, or villous elements), screening with colonoscopy is recommended every 10 years beginning at age 50, consistent with one option for average risk screening.
If a single first-degree relative was diagnosed before 60 years with CRC or an advanced adenoma, or two or more first-degree relatives had colorectal cancer or advanced adenomas at any age, screening with colonoscopy is recommended at age 40 or 10 years before the youngest relative's diagnosis, to be repeated every five years.
CASE 2

A 48-year-old, patient of yours referred with a stool test, which showed one plus occult blood positive in one occasion. He is worried about the risk of colon cancer. In family history, he has no evidence for colon cancer in family at all.
WHAT DO YOU ADVISE HIM TO DO NOW?

A. Repeat OB test and perform colonoscopy if it will be positive
B. Perform rectosigmoidoscopy immediately
C. Perform total colonoscopy immediately
D. Perform a double contrast barium enema (DCBE) and if it is normal, nothing would be necessary to do
False-negative results may be caused by
- vitamin C supplements
- antacids
- delaying transport of the stool samples for analysis

False-positive results may result from
- failure to follow dietary or medication restrictions
- presence of bleeding gums
- hemorrhoids
- menstrual blood
- watery stools
Before the Fecal Occult Blood Test

For **seven days** before the test, do not take any antacids, iron supplements, steroids or **NSAID** such as aspirin, ibuprofen. (Your doctor may also instruct you to avoid certain other medications).

The following instructions should be carried out for **three days** before the test to maximize the accuracy of results.

- Avoid eating red meat (especially meat that is cooked rare), poultry, fish or peroxidase-rich fruits and vegetables (especially turnips, melons, carrots, broccoli, cauliflower, cucumbers, grapefruit, mushrooms, radishes and horseradish).

- Do not take vitamin C supplements or eat large quantities of foods, such as citrus fruits, that contain this vitamin.

- Eat a high-fiber diet, containing whole grains, beans and vegetables that do not contain peroxidase, to increase the bulk of the stools.

- Do not drink alcohol and avoid any other substances that may irritate the digestive tract.

- If your gums tend to bleed, avoid brushing your teeth.

- Women should not begin testing during their-menstrual period or during the first three days after the end of their period.
gFOBT: guaiac-based fecal occult blood test

Two to three stool samples collected at home are needed to complete testing; a single sample of stool gathered during a digital exam in the clinical setting is not an acceptable stool test and should not be done.
CORRECT ANSWER IS C

Panel discussion
Colonoscopy was performed. 3 polyps were detected in the sigmoid, descending and hepatic flexure, their size was 15 mm, 10 mm and 7 mm consequently.

Polypectomy was performed and 3 samples were sent to pathologist.

Report:

1\textsuperscript{st} sample villous adenoma, tip with HGD, stalk about 2 mm free of dysplasia

2\textsuperscript{nd}, tubular adenoma with moderate dysplasia

3\textsuperscript{rd}, compatible with hyperplastic polyp
WHAT IS YOUR RECOMMENDATION?

A. Local resection of polyp area in sigmoid
B. Left hemicolecctomy
C. Colectomy
D. No recent further intervention
Multiple adenomas (or carcinoma)
two or more neoplasms

Multiple adenomatous polyposis syndromes
tens to hundreds of polyps

The risks of colon cancer and of high-grade dysplasia both rise with the number of adenomas present
Haggitt classification

Submucosal invasion in pedunculated
1-head
2-neck
3-stalk
4-base
or
4-Submucosal invasion in sessile
Superficial, middle and deep thirds of the submucosa, i.e. so-called Kikuchi levels sm1, sm2 and sm3.
Both the Kikuchi (for non-polypoid tumours) and the Haggitt (for pedunculated tumours) systems may be difficult to use in practice, especially if there is fragmentation or suboptimal orientation of the tissue.
Pedunculated polyp

submucosa of the former projects up into the stalk

Sessile polyp

submucosa is in direct continuity with the bowel wall proper

If cancer in a pedunculated polyp is confined to the submucosa of the stalk and all other histologic features are favorable, surgery is not indicated because the chance of an adverse outcome from endoscopic polypectomy is less than the operative mortality.

Once the submucosa of the bowel wall is involved with cancer (a situation that occurs more readily in sessile polyps), the chance of an adverse outcome often outweighs the operative mortality, thereby justifying surgical resection.
Studies have examined the depth of submucosal invasion as a predictor of lymph node metastasis.

Two studies found the rate of lymph node metastasis was zero when depth of submucosal invasion was less than 1 mm in one study and 2 mm in the other.
Summary of malignant colorectal polyps that should have an oncologic bowel resection

A. Lesions in Colon
   a. Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesions with lymphovascular invasion
   b. Lesions removed with margin < 2 mm
   c. Sessile lesions removed piecemeal
   d. Sessile lesions with depth of invasion into distal third of submucosa (Sm3)
   e. Sessile lesions with lymphovascular invasion

B. Lesions in Middle Third and Upper Third Rectum
   Same as lesions in colon

C. Lesions in Distal Third Rectum
   a. Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesions with lymphovascular invasion
   b. All sessile lesions

Table 2

Suggested Criteria for Polypectomy and Observation for Cancer In a Polyp

- Complete excision of lesion
- \( \geq 2 \) mm clear margins
- Well or moderately differentiated
- No lymphovascular invasion
- Haggitt levels 1, 2, or 3 in pedunculated polyps
- Haggitt level 4 (pedunculated or sessile polyp) with Sm1 invasion

Adapted from Rothenberger.[8]
All of the following criteria must be met in order for a complete polypectomy to be considered as an adequate treatment:

— The polyp must be pedunculated
— The tumor does not extend beyond the head or neck of the polyp (Haggitt’s levels 1 and 2, respectively)
— The distance between the tumor edge and the margin of the specimen exceeds 2 mm
— The histology is favorable (not poorly differentiated and no lymphatic or vascular invasion)
Risk factors for high-grade dysplasia and cancer

- Villous histology, increasing polyp size, and high-grade dysplasia are risk factors for focal cancer within an individual adenoma.

- Number and size are the most consistent risk factors for metachronous adenomas including advanced adenomas and cancer.
NUMBER OF POLYP ?
NUMBER OF POLYPS

- The risk for metachronous advanced adenomas increased with the number of adenomas at baseline and was 9, 13, 15, 20, and 24 percent for 1, 2, 3, 4, or ≥5 adenomas at baseline, respectively.
- Patients with multiple large or villous rectosigmoid adenomas had a 6.6-fold higher risk of subsequent malignancy than the control population.
- Large polyp size (>1 cm) and proximally located adenomas were independent predictors of recurrent high-risk adenomas.
- The number of adenomas, particularly three or more, was the sole risk factor for development of metachronous adenomas with advanced pathologic features.
WHAT DO YOU ADVISE HIM TO DO IN FUTURE?

A. Recolonoscopy after a 6 months period
B. Recolonoscopy after a one -year period
C. Recolonoscopy after a 3 to 5- year period
D. Recolonoscopy after a 10 - year period
<table>
<thead>
<tr>
<th>FINDINGS ON COLONOSCOPY</th>
<th>NEXT COLONOSCOPY</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small rectal hyperplastic polyps</td>
<td>10 years</td>
<td>Considered equivalent to normal colonoscopy</td>
</tr>
<tr>
<td>One or two small (&lt;1 cm) tubular adenomas with only LGD (low-risk adenoma)</td>
<td>5-10 years</td>
<td>Specific follow-up interval is determined by prior colonoscopic findings, family history, patient preference, and clinical judgment</td>
</tr>
<tr>
<td>3-10 adenomas, any adenoma ≥1 cm, or any adenoma with villous features or HGD</td>
<td>3 years</td>
<td>If the 3-year examination is normal, or shows only a low-risk adenoma, repeat again in 5 years</td>
</tr>
<tr>
<td>&gt;10 adenomas at one examination</td>
<td>&lt;3 years</td>
<td>Use clinical judgment; consider familial syndrome</td>
</tr>
<tr>
<td>Suggestive of HNPCC*</td>
<td>2-3 years</td>
<td>Consider more frequent intervals</td>
</tr>
<tr>
<td>Piecemeal removal of a sessile adenoma</td>
<td>2-6 months</td>
<td>Follow-up interval based on clinical judgment</td>
</tr>
<tr>
<td>Baseline colonoscopy: most advanced finding(s)</td>
<td>Recommended surveillance interval (years)</td>
<td>Quality of evidence supporting the recommendation</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>No polyps</td>
<td>10</td>
<td>Moderate</td>
</tr>
<tr>
<td>Small (&lt;10 mm) hyperplastic polyps in rectum or sigmoid</td>
<td>10</td>
<td>Moderate</td>
</tr>
<tr>
<td>1 to 2 small (&lt;10 mm) tubular adenomas</td>
<td>5 to 10</td>
<td>Moderate</td>
</tr>
<tr>
<td>3 to 10 tubular adenomas</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;10 adenomas</td>
<td>&lt;3</td>
<td>Moderate</td>
</tr>
<tr>
<td>One or more tubular adenomas ≥10 mm</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>One or more villous adenomas</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>Adenoma with HGD</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>Sessile lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sessile serrated polyp(s) &lt;10 mm with no dysplasia</td>
<td>5</td>
<td>Low</td>
</tr>
<tr>
<td>Sessile serrated polyp(s) ≥10 mm OR Sessile serrated polyp with dysplasia OR Traditional serrated adenoma</td>
<td>3</td>
<td>Low</td>
</tr>
<tr>
<td>Serrated polyposis syndrome*</td>
<td>1</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
If the primary (index) polyp contains high-grade dysplasia or carcinoma on histology, the chance of an early histologically significant metachronous lesion is high. Hence, in such a case the recommendation is for the first follow-up at one year.