A Patient with Granular Cell Tumor of the Colon

by John E. Poulos, Alexandros G. Georgakilas, Peter T. Kalogerinis, Thomas Daignaut, Giovanni Lujan

We report a case of granular cell tumor of the large intestine in a 50-year-old black female who presented with constipation, weight loss, hematochezia and abdominal pain. Radiographic and endoscopic evaluation of this lesion is presented as well as the histologic findings of this lesion with S-100 immunostaining. Granular cell tumors of the colon are of low malignant potential and are being recognized with increasing frequency. Treatment options are similar to those for other benign submucosal lesions of the colon and may include conservative therapy, endoscopic resection for lesions smaller than 2 cm and surgical resection for larger lesions if there is a threat of obstruction or question of underlying malignancy. A review of the literature in relation to this submucosal colonic lesion is presented.

CASE REPORT

A 50-year-old black female with a history of cutaneous lupus erythematosus and hypertension presented with a six-month history of chronic constipation. She reported having a hard stool once a week with straining and intermittent episodes of bright red blood per rectum. She also reported a fifteen-pound weight loss over the period of several months. Her medications included irbesartan, hydrochlorothiazide, and lactulose. Her past medical and surgical history was significant for cutaneous lupus erythematosus and hypertension.

The patient denied any significant alcohol use and had a 30-pack-year history of cigarette use. Her family history was negative for colon polyps or colon cancer. On physical exam there was no evidence of adenopathy. Chest and abdominal examinations were normal. Rectal examination revealed guiac-negative stool. Pertinent laboratory examinations revealed the following: elevated serum amylase of 123 with a normal lipase and hepatic profile. She had a normal basic metabolic panel and complete blood count. Due to her history of weight loss a computed tomography (CT) of the abdomen and pelvis was performed in order to exclude any occult malignancy. CT revealed a small well circumscribed 0.7 cm simple cyst in the tail of the pancreas which was confirmed on endoscopic ultrasonography of the pancreas. No other intra-abdominal abnormalities were noted. Colonoscopy revealed two 10 mm submucosal lesions in the ascending colon and one in the transverse colon (Figure 1). Uprooting of these lesions with cold biopsy forceps revealed firm nonflucuent submucosa with a firm yellow base. Sigmoid diverticuli and small grade I internal hemorrhoids were also noted.

Histologic evaluation of biopsies from these submucosal lesions located in the colon revealed submucosal proliferation of eosinophilic granular cells with bland nuclear features, no mitotic activity and low N/C ratio. Immunohistochemistry revealed reactivity with S-100. Gross description of the polyp was stated to have contained multiple portions of light tan mucosal tissue ranging from 0.3 cm to 0.2 cm in greatest.

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A CASE TO REMEMBER

Due to the absence of symptoms in this patient, size of this lesion, and benign histologic features of this submucosal lesion it was felt that conservative therapy was warranted in this patient. She is currently undergoing colonscopic surveillance.

DISCUSSION

Granular cell tumors (GCT) occur throughout the body most commonly in the tongue and skin, but also in the breast, respiratory tract, biliary tree, nervous system, and gastrointestinal tract (1). Granular cell tumors are submucosal neoplasms that are thought to derive from Schwann cells. They are the least common submuco-
sosal lesions of the colon and less than 100 cases of colorectal GCT have been reported (2). Colonic GCT range in size from 10 mm to 30 mm in size and are submucosal with intact surface mucosa (1). They have also been described in the literature as having a white-yellow appearance and being very firm (1). The presence of a firm base may distinguish them endoscopically from other benign submucosal lesions of the colon. Immunochemistry reports show strong expression of S-100 protein and nestin, a class VI intermediate filament protein (1–3).

The differential diagnosis of submucosal lesions of the colon involves malignant and benign lesions. Malignant lesions include carcinoids, lymphomas, leukemia, malignant melanoma and metastatic carcinomas (4). The differential of benign submucosal lesions of the colon include GCT, stromal cell tumors or leiomyomas, endometriosis, lymphatic cyst, lipomas, lymphoid hyperplasia, pneumatosis, colitis cystica profunda (CCP) and hemangiomas.

Submucosal lesions may occur throughout the colon and tend to have a normal overlying mucosa. GCTs, lipomas, gastrointestinal stromal tumors (GISTs) and lymphatic cyst may appear yellowish to tan to white and are predominately smaller than 3 cm in size (4). Endometriosis may appear to have a bluish-purple hue; however, in the majority of cases presents as nodular colonic mucosa or as an extraluminal obstructing mass (5). Hemangiomas are apparent as cherry red or vascular lesions and should not be biop-sied due to the risk of bleeding (4). Lymphatic cysts and pneumatosis appear as transparent lesions and similar to lipomas may be easily compressible with biopsy forceps. Pneumatosis however, release air and decompress upon biopsy (6). Pneumatosis and lymphoid hyperplasia tend to be multifocal; however, pneumatosis may be associated with ischemia, immunosuppression, infection, chronic obstructive pulmonary disease or divertic-ular disease (6). Lymphoid hyperplasia is usually an incidental finding and without clinical significance; however, lymphoma has been associated with these lesions (4). CCP may also be multifocal, associated with ischemia or inflammatory events, and similar to lymphoid hyperplasia tends to be polypoid in nature and often indistinguishable from colonic polyps (4).

Radiographically submucosal lesions of the colon appear as radiolucent defects similar to colonic polyps. For lymphatic cysts or pneumatosis computed tomography utilizing contrast may reveal high density nonehancing lesions. Lipomas, GCT, GIST or lymphatic hyperplasia may be visualized as low density lesions. Endoscopic ultrasound (EUS) with or without the utilization of an endoluminal probe may allow for the determination of the depth of involvement, presence of malignant features and suggest the etiology of submu-co sal lesions based on the presence of echoic or anechoic features. The utilization of fine needle biopsy in combination with EUS may allow for an increase in the diagnostic specificity and sensitivity due to the ability to obtain cytological specimens for pathologic interpretation. Lymphatic cyst, pneumatosis may appear cystic and anechoic, GISTs, GCT, endometriosis and lymphatic hyperplasia may appear hypoechoic and lipomas may appear hyperechoic (5,7–9). EUS may also
exclude lesion involvement of the muscularis mucosa allowing for favorable endoscopic removal (9).

The gold standard for the diagnosis of submucosal lesions of the colon is histologic or cytologic diagnosis utilizing cold forceps, polypectomy, endoscopic mucosal resection (EMR), fine needle aspiration or surgical resection. GCT and GIST are stromal in appearance with histocyte appearing cells. GCT express positivity to S-100 protein and nestin whereas GIST express positivity to CD117 (1–3,8). Lymphoid hyperplasia reveals lymphocytic infiltration of the lamina propria with distention of the overlying epithelium and lipomas are characterized by adipose tissue (4). Pneumatosis reveals air filled cysts within the submucosa while CCP contains epithelium lined mucous cysts within the muscularis mucosa.

Colorectal GCT are often asymptomatic and are usually incidental findings during colonoscopy. Most gastrointestinal GCT are solitary but multiplicity is not uncommon, with 10% of GCT being multiple (10). In this case report, colonic GCT presented as synchronous lesions in both the ascending colon and hepatic flexure. Disagreement does exist however, concerning GCT potential for malignancy. While reports of malignant GCT have been described for the esophagus they comprise less than 4% of all cases (1,10,11). To date no cases of malignant colonic GCT have been described and Johnston, et al failed to find evidence of reoccurrence or malignant degeneration in their review of over 100 cases involving GCT of the gastrointestinal tract (13). Literature review has suggested both surgical and endoscopic treatment of colonic GCT (1,2,14). These treatments range from hemicolecotomy, local excision and snare polypectomy. However, Parfitt, et al did report of a perforation from snare polypectomy in a patient undergoing endoscopic treatment of a colonic GCT (1). Due to submucosal nature of these lesions endoscopist may wish to consider EUS and proceed with caution prior to attempted snare polypectomy of colonic GCT. The utilization of EUS in combination with EMR may offer a theoretical advantage over traditional polypectomy due to its ability to determine involvement of the muscularis mucosa and allow removal of the mucosa and submucosal without involvement of other remaining layers. As with other benign submucosal lesions of the gastrointestinal tract, conservative therapy may be warranted if the lesion is asymptomatic, smaller than 2 cm and fails to display histological features associated with malignancy (15). Histologic features of malignancy include necrosis, spindling, vesicular nuclei, large nucleoli, increased mitotic activity and a high N/C ration with pleomorphism (16). As with other GCT of the gastrointestinal tract, conservative options may include surveillance endoscopy to detect any potential malignant degeneration. However, further studies are needed to determine the optimal treatment of GCT.

With the increasing utilization of screening colonoscopy in the prevention of colorectal cancer colon GCTs may be discovered incidentally. These submucosal lesions may be associated with nonspecific symptoms and have a low-risk of malignancy. Treatment of these lesions may involve conservative surveillance, polypectomy, EMR or surgical resection. The decision of whether to treat and choice of modalities to use may be dependant on the size of the lesion, histologic features, and the risk of perforation.

References