Considerations for Diagnosis and Management of Ileostomy-related Malignancy: A Report of Two Cases

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Abstract
Malignancy associated with a long-standing ileostomy is a rare occurrence reported as early as 3 years after ileostomy placement. Patients most commonly present first to their ostomy care nurse with peristomal skin changes unresponsive to conservative measures. To elucidate presentation and management, two cases of male patients with ileostomy-related malignancy (one lymphoma and one squamous cell carcinoma) are discussed. Both patients had undergone proctocolectomy with end ileostomy decades prior. Symptoms in the lymphoma patient included complaints of skin irritation, stoma mucosa changes and friability, and a persistent rash around the ostomy; he was found to have small bowel friability and a peristomal mass arising from the terminal ileum that was resected en bloc with the ileostomy, the surrounding skin, and associated abdominal wall musculature. The patient with squamous cell carcinoma had developed a gray-tan skin lesion around his ileostomy site; he underwent exploratory laparotomy with wide local excision of the abdominal wall including ileostomy site, distal ileum, and squamous cell carcinoma, and resiting of the ileostomy to the contralateral abdominal wall. Ostomy care providers should be aware of the clinical presentation of ostomy-associated malignancy to ensure thorough evaluation and prompt referral for surgical management are provided.

Keywords: malignancy, ileostomy, lymphoma, squamous cell, adenocarcinoma

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Malignancy associated with a long-standing ileostomy is a rare event. Of the four primary small bowel malignancies (adenocarcinoma, lymphoma, carcinoid, and leimyosarcoma/stromal cell tumors), adenocarcinoma and lymphoma are the most common. Peristomal small bowel cancers tend to arise in a setting of preexisting disease such as Crohn’s, celiac sprue, and familial polyposis, which may predispose the small bowel epithelium to malignant transformation. Immunoproliferative small bowel disease and celiac sprue are well-known to increase the incidence of small bowel lymphoma. It has been postulated the mucosal environment associated with a long-standing stoma may favor malignant transformation; the milieu of altered intestinal flora and chronic exposure to bile acids are the proposed inciting agents. Patients with inflammatory bowel disease also may have an increased risk of intestinal lymphoma; a large population-based series estimated the relative risk between 0.4 and 2.4. This risk may be associated with long-term use of azathioprine or 6-mercaptopurine. Importantly, all types of ileostomy-associated malignancy have an insidious presentation marked by peristomal skin changes unresponsive to conservative measures. The wound, ostomy, continence (WOC) nurse plays a pivotal role in making the diagnosis, because these patients most commonly present to their ostomy care nurse as the first step in management.

Lymphoma. There have been two previously reported cases of lymphoma arising from an ileostomy, although malignancy associated with a long-standing ileostomy has been...
well described. Levecq et al reported a high-grade B-cell lymphoma arising in an ileostomy after only 2 years in a patient with indeterminant colitis and transfusion-related acquired immune deficiency syndrome. Pranesh reported a case of a B-cell non-Hodgkin lymphoma in an ileostomy arising 20 years after total proctocolectomy for ulcerative colitis.

Given the paucity of cases of ileostomy-associated lymphoma, treatment is extrapolated from sporadic lymphoma occurring in the small intestine, which can be either primary or secondary, as a consequence of systemic lymphoid malignancy. Previous literature reviews of gastrointestinal lymphomas estimate that primary small intestinal lymphoma accounts for 25% to 30% of all small bowel malignancies, with the gastrointestinal tract the most common site of primary extranodal lymphoma. Virtually all of these neoplasms are non-Hodgkin lymphomas and, apart from T-cell lymphomas arising in the setting of celiac sprue, most are of a B-cell origin. The tumors arise from the mucosa-associated lymphoid tissue of the small bowel. Evaluation of these tumors requires a high index of suspicion. In the authors’ experience, traditional diagnostic techniques such as endoscopy, sonography, and axial imaging may not yield conclusive results. The uptake of 18-F fluorodeoxyglucose on positron emission tomography is a useful means of diagnosing intestinal lymphoma.

The American Society of Clinical Oncology (ASCO) consensus considers the Musshoff modification of Ann Arbor Staging, which takes into account depth of tumor invasion and its effect on prognosis, the most widely accepted staging system for primary gastrointestinal lymphoma. Treatment is based on the stage of the disease (see Table 1), with a combination of surgery and polychemotherapy reserved for patients with Stage I and II disease; however, this strategy has the potential for significant radiation enteritis to surrounding small and large intestine and is utilized in select patients only. Response to therapy is correlated with stage of disease. The overall 5-year survival rate is 59% to 75%. Patients with Stage I and II disease have a 5-year survival approaching 82%, while patients with disseminated disease fare worse.

Recent retrospective case series and cohort studies suggest a regimen of chemotherapy alone with dose-intensified doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone is superior to cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) plus involved-field radiotherapy for the treatment of localized lymphoma.

**Squamous cell carcinoma.** Although exceedingly rare, squamous cell carcinoma at the mucocutaneous junction of an ileostomy has been reported in five instances as a late complication of end ileostomy following total proctectomy and once following ileal urinary conduit following cystoprostatectomy. No large series exist, but of the previously reported cases, the mean age at diagnosis was 72.5 with the earliest occurrence 26 years following creation of ileostomy, suggesting a chronic pathologic process. In addition, most cases report long-standing peristomal skin irritation with associated granulation, ulceration, stricture requiring revision of the ileostomy, or chronic bacterial infection of an ileal urinary conduit before squamous cell carcinoma developed.

All reports revealed well-differentiated squamous cell carcinoma arising at the mucocutaneous junction. Management involved multidisciplinary teams and relied on wide local excision to the level of the fascia and restiting of the ileostomy in four cases, local excision and ileostomy reconstruction in another, and palliative radiotherapy in another.

**Adenocarcinoma.** Adenocarcinoma arising in abnormally placed small intestinal mucosa (ileal anal pouch, ileostomy,
and ileal conduit) has been increasingly reported. The latent period between ileostomy formation and the development of adenocarcinoma ranged from 3 to 51 years. The mechanism of this increased risk is not entirely clear, but the "colonization" that occurs in the epithelium may predispose it to the metaplasia-dysplasia sequence. The change in bacteriology associated with a chronic ileostomy was first reported by Gorbach et al and has a putative role in the increased risk of malignant transformation. Chronic physical and chemical irritation also may be a risk factor.

Treatment of small bowel adenocarcinoma relies on aggressive surgical resection often followed by adjuvant chemotherapy. Due to the rarity of the condition, data regarding adjuvant therapy for primary small bowel adenocarcinoma are limited. Therapy modalities are extrapolated from other primary GI cancers. A multicenter phase II clinical trial of chemotherapy (fluorouracil [5FU]) and radiation in duodenal and periampullary carcinoma showed no significant survival benefit as adjuvant therapy. Recent advances in adjuvant chemotherapy protocols including folinic acid, fluorouracil, and oxaliplatin (FOLFOX); folinic acid, fluorouracil, and irinotecan (FOLFIRI); and other platinum-based therapy with or without irinotecan have shown promise in treating unresectable GI adenocarcinoma. However, these adjuvant therapies are not well studied in primary small bowel malignancies.

Prognosis is based on the status of the surgical margins, presence of extramural venous spread, lymph node status, tumor differentiation, and depth of tumor invasion. Five- and 10-year survival rates are reported to be 52% and 47%, respectively.

Due to the rarity of these tumors, two additional cases of rare primary gastrointestinal tumors arising in close proximity to small bowel ostomy sites are presented.

Case Reports

Case 1. Mr. H is 85 years old. He underwent a total proctocolectomy with end ileostomy in 1951 for medically refractory ulcerative colitis. He reported no difficulty with ostomy management over the ensuing years. He had no significant change in health status. He subsequently returned to his stoma care nurse 44 years later with new complaints of skin irritation, friability, and a persistent rash around the ostomy. He was found to have small bowel mucosal friability and a peristomal mass causing stenosis of the ileostomy aperture. A computed tomography (CT) scan of the chest, abdomen, and pelvis was obtained (see Figure 1) and demonstrated a large mass in the terminal ileum at the level of the ileostomy, without fixation to the surrounding small bowel, retroperitoneum, or abdominal wall. The mass was resected en bloc with the ileostomy, the surrounding skin, and associated abdominal wall musculature. The ileostomy was repositioned to the left lower quadrant. The resultant defect was closed with Alloderm (LifeCell Co, Bridgewater, NJ). Negative pressure wound therapy (VAC Therapy®, KCI, San Antonio, TX) was applied intraoperatively. Pathology results were consistent with a malignant large cell lymphoma arising from the ileostomy. Margins were free of disease, and zero out of seven lymph nodes were involved. Mr. H had no further ostomy-related complaints after surgery and was well at the time of most recent follow-up.

Case 2. Mr. B is a 63-year-old with a distant history of ulcerative colitis; he underwent a total proctocolectomy and end-ileostomy in 1992. He presented to a colorectal surgery clinic 21 years after surgery complaining of a gray-tan lesion of gradual onset at the skin around his ileostomy site. The lesion arose in the context of chronic skin irritation and difficulty with pouching of the ileostomy due to body habitus; he had experienced many years of these pouching and skin issues. The lesion was promptly recognized by his stoma care nurse, and he was referred to his colorectal surgeons for full-thickness punch biopsies in multiple areas of the developing mass. Histopathologic examination of these specimens revealed neoplastic proliferation with features diagnostic of invasive, well-differentiated squamous cell carcinoma. Irregular tongues of neoplastic squamous epithelium were seen invading stromal tissue as well as marked cytologic atypia with occasional mitotic figures (see Figure 2). A preoperative CT scan of the chest, abdomen, and pelvis was performed to exclude metastatic disease.

Mr. B underwent exploratory laparotomy with wide local excision of the abdominal wall, including ileostomy site, distal ileum and squamous cell carcinoma, and repositioning of the ileostomy to the contralateral abdominal wall.

The pathologic specimen from the final operation included the 5.1 cm x 4.9 cm gray-tan nodular to papillary fungating mass abutting the mucosa of the ileostomy. Histopathologic features...
examination was consistent with well-differentiated squamous cell carcinoma arising at the mucocutaneous junction. Adjacent intestinal mucosa were positive for focal ulceration and reactive changes. Circumferential and proximal margins, as well as a single small bowel lymph node, were negative for carcinoma. Mr. B recovered well from surgery and had no tumor recurrence at his 6-month follow-up.

**Conclusion**

Primary malignancy of the small bowel arising at the site of a stoma is a rare complication of a long-standing ileostomy. These patients most often present with complaints of chronic skin irritation at the stoma site, ulcerating or fungating masses, or stenosis of the ostomy. In this study, two patients represent additional cases of primary ileostomy associated malignancies: One patient presented with new skin changes and induration after many asymptomatic years; this patient was diagnosed with lymphoma. A second patient presented with ulceration representing squamous cell carcinoma. Although ostomy placement is critical to future skin care, it is imperative that any nonhealing wounds and chronic skin irritation be evaluated by an experienced professional. It is unclear how much time is necessary for malignant complications following chronic ostomy. It is important for the patient, WOC nurse, and the primary care physicians to recognize these signs promptly and refer the patient for additional work up. Any peristomal lesions persistent and unresponsive to conservative therapies should be referred for biopsy.

**References**


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**Figure 2.** Case 2: a) fungating peristomal mass; and b) H&E stain from biopsy specimen showing focal keratinization and well differentiated squamous cell carcinoma.
ILEOSTOMY-RELATED MALIGNANCY