CASE REPORTS

Stomal adenocarcinoma in Crohn's disease

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Abstract

Malignant change occurring at the site of a stoma in two patients with proved Crohn's disease is described. Patients with ulcerative colitis have an increased risk of colonic malignancy and Crohn's disease is also associated with both small and large bowel carcinoma. Most previous reports of stomal carcinoma have been associated with ulcerative colitis although Crohn's disease seems to carry a greater risk of associated small bowel carcinomas. This is the first report of stomal carcinoma complicating Crohn's disease. Epithelial dysplasia is associated with gastrointestinal carcinomas in both ulcerative colitis and Crohn's disease and a dysplasia-carcinoma sequence has been suggested as the origin of these tumours. In both our patients with stomal adenocarcinoma, dysplasia was identified in adjacent tissues, which suggests a similar mechanism. Malignant change should be suspected if epithelial dysplasia is discovered in a biopsy specimen from the mucosa of an ileostomy in Crohn's disease, and this risk is increased if the dysplasia is of a high grade.

Patient 1

In 1956, a 25 year old woman developed 'boils' on her face and body and diarrhoea. A diagnosis of pyoderma gangrenosum with colitis was established. She had recurrent episodes over the following nine years which required frequent hospital admissions and was given both oral and rectal steroids to control her symptoms. During 1964, her symptoms worsened and she developed recurrent mouth ulcers. Later in the year a further acute exacerbation failed to respond satisfactorily to medical treatment and she was referred for surgery. A small and large bowel resection was performed, removing six inches of diseased terminal ileum in continuity with the colon up to the mid-sigmoid region. An ileostomy and left iliac colostomy were fashioned. The remaining colon and rectum were subsequently resected four months later for continued colitis.

Review of the histological sections from both surgical specimens showed transmural disease, patchy involvement of the mucosa, non-caseating epithelioid granulomas with Langhan's giant cells, fissures, and neuromatous hyperplasia – all indicative of Crohn's disease. This complements the clinical findings of stomal ulceration and pyoderma gangrenosum.

She made a good recovery and remained well for the next 23 years until she presented again in October 1987. She then noticed a fleshy lump of tissue underneath the ileostomy spout which bled intermittently as the edge of the ileostomy bag flange rubbed against it. This was initially thought to be an 'ileostomy granuloma' and a large appliance flange was fitted, but the bleeding continued and a biopsy was arranged. A local excision of this nodule, which was now some 2.5 cm in diameter, was performed. Histology showed a moderately differentiated mucin secreting adenocarcinoma arising at the mucocutaneous junction of the ileostomy stoma (Figs 1 and 2). Study of the ileal mucosa in the vicinity of the stomal carcinoma showed high grade dysplasia in the crypts of Lieberkuhn.

A computed tomogram of the abdomen has been performed and failed to show metastatic spread in either the anterior abdominal wall or in the retroperitoneal lymph nodes. Eighteen months later she remains well with no clinical evidence of local or metastatic disease.

Patient 2

In 1945, a 24 year old man presented with a four month history of passing blood and slime per rectum. He was treated medically for the next two years, but suffered multiple exacerbations requiring admission to hospital and was referred for surgery. A caecostomy was performed through a gridiron incision and this functioned satisfactorily over the next six years, although he continued to pass blood and pus per rectum. He

Figure 1: Patient 1. Whole mount section through the tumour arising at the junction of skin (on the left) with ileostomy. Pools of mucin secreted by tumour are evident in the dermis. (Haematoxylin and eosin, original magnification $\times 4$.)

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Figure 2: Patient 1.
Infiltrating moderately
differentiated
adenocarcinoma.
(Haematoxylin and eosin,
original magnification
 $\times 750$.)

subsequently developed severe perianal involvement with recurrent ischiorectal abscesses and anal fistulae. In 1953, he was admitted with another severe exacerbation, passing profuse amounts of blood and pus per rectum with severe excoriation around the caecostomy site. Sigmoidoscopy showed rectal ulceration and a barium enema stricture formation throughout the colon and he underwent proctocolectomy. The colon was thickened and the mucosa was friable. There were two inflammatory masses where strictures had been seen and several anal fistulae which extended up to the rectum were laid open. The old caecostomy site was excised and the tissues closed in layers. A Brooke ileostomy was fashioned above this level.

Review of the histological blocks, originally reported as ulcerative colitis, showed severe inflammatory changes extending into the mesenteric fat with fissure formation and lymphoid hyperplasia affecting the submucosa and occasional ill defined epithelioid granuloma within the wall. This supports the diagnosis of Crohn's disease and is more in keeping with the clinical features of fistula formation and severe perianal disease.

Over the ensuing years the patient remained in good health apart from an intermittent discharge of pus and blood from the site of his original caecostomy wound. In 1977, he was admitted as

Figure 3: Patient 2.
Infiltrating moderately
differentiated
adenocarcinoma with mucin
secretion. (Haematoxylin
and eosin, original
magnification $\times 750$.)

Figure 4: Patient 2. Whole mount section through tumour
arising at the junction of the skin (on the left) with the stoma.
(Haematoxylin and eosin, original magnification $\times 4$.)

an emergency with a sudden haemorrhage from this wound site. He reported that there had been an increased offensive discharge with ulceration and swelling for the previous two weeks. There was a 5.0 cm fungating mass below the ileostomy which was initially thought to be a granuloma, but a biopsy specimen showed it to be a mucin-secreting adenocarcinoma (Fig 3). A wide excision was performed removing skin and muscle layers to the peritoneum. There was no evidence of metastatic disease at laparotomy. Histologically, the tumour was confined to the skin and subcutaneous fat (Fig 4). In 1978, he presented with a further subcutaneous mass below the previous excision which also proved to be recurrent tumour and a lymphangiogram showed iliac node involvement. He was subsequently treated with both radiotherapy and chemotherapy, but developed a fungating ulcer some 10.0 cm in diameter in the right iliac region. He died in 1980, three years after his initial presentation. Necropsy showed no other primary site of malignant disease or evidence of further Crohn's disease.

Review of the histology of the tumour mass confirmed it to be a mucin secreting adenocarcinoma of the colonic type with argentaffin cells and mucin secretion pattern consistent with colonic mucosal origin. Remnants of colonic mucosa were identified in the vicinity of the caecostomy site and showed high grade dysplasia. It would seem likely that remnants of colonic mucosa persisted at the caecostomy site which eventually gave rise to invasive adenocarcinoma.

Discussion

These two patients with Crohn's disease showed malignant change some 23 and 30 years after

formation of a stoma. In the first, adenocarcinoma developed at the mucocutaneous junction of a standard Brooke ileostomy and in the second, adenocarcinoma developed in a mucosal remnant after a caecostomy, once popular for the treatment of acute inflammatory bowel disease. While malignant change has been known for many years to be associated with ulcerative colitis,¹ the development of cancer in patients with Crohn's disease has only more recently been appreciated.²⁻⁴

Carcinoma of the ileostomy is rare, although it has recently been suggested that the incidence is increasing.⁵ The histological type is usually an adenocarcinoma, although squamous cell carcinoma has been described, associated with scarring after skin grafting, presumably a 'Marjolin's ulcer' effect.⁶ There tends to be a long latent period after the formation of the ileostomy, usually more than 25 years, although there have been reports of carcinoma occurring earlier.^{5,7} Previous reports have identified patients with either ulcerative colitis or polyposis coli as being at risk, although it is these patients who are more likely to have had ileostomies for a significant length of time.^{5,7-21} To date, Crohn's disease has not been associated with a risk of ileostomy carcinoma, although it is possible that cases have been previously misdiagnosed as ulcerative colitis.⁵

Malignancy developing in a caecostomy for ulcerative colitis has been reported once before,²² the stoma being formed for control of an acute exacerbation 31 years previously. Carcinoma is also known to develop in Crohn's fistulae^{23,24} as well as in defunctioned segments of active disease.²⁴ The second patient undoubtedly developed a fistula from a remnant of the caecostomy tract many years before developing the adenocarcinoma. A similar case of cancer developing from a mucosal remnant left after an ileostomy has also been reported.⁹

Carcinoma of the ileum has been associated with both inflammatory bowel disease and polyposis coli. On two occasions patients with ulcerative colitis have been reported to have ileal carcinomas; both also had severe longstanding colitis with premalignant changes in the colon and backwash ileitis.^{25,26} Polyposis coli is associated with carcinoma of the duodenum and ileum,²⁷ but there have been more reports of Crohn's disease associated with carcinoma of the ileum,²⁸ particularly if an exclusion bypass has been performed.²⁴

One reason that stomal carcinoma more commonly complicates ulcerative colitis than Crohn's is that ileostomies are more frequently fashioned for ulcerative colitis and polyposis, while such a procedure is relatively contraindicated in Crohn's disease. Different or additional aetiological factors may operate to produce malignant change in exposed mucosa of an ileostomy in comparison with the intraperitoneal ileum. Firstly, the exposed mucocutaneous junction of a stoma is subject to both physical and chemical injury from the stoma appliance, cleaning agents, adhesives, and creams used to protect the skin or, conversely, the skin may be inadequately protected and subject to long-term excoriation from the ileostomy effluent.

Secondly, the intestinal flora in patients with ileostomies is affected²⁹ and it is possible that a combination of these potential carcinogenic agents could, over a period of 20 years, induce malignant change.⁵

Epithelial dysplasia in a patient with ulcerative colitis is known to be associated with a high risk of colorectal carcinoma, and this has been utilised in cancer surveillance programmes.³⁰ Intestinal carcinoma associated with Crohn's disease has also been associated with similar dysplastic changes but this occurs only adjacent to the tumour and is less pronounced.² Despite the absence of more distant dysplasia, so essentially precluding its use as a surveillance marker, the consistent association of carcinoma with dysplasia in Crohn's indicates a dysplasia-carcinoma sequence origin for these tumours.^{2,31} Dysplasia was noted in the adjacent tissue of both patients with stomal carcinoma reported here, and this suggests that the origin of these cancers was similar. The presence of dysplasia in a biopsy specimen of an ileostomy in Crohn's disease would seem to be a useful indicator of a possible coexistent malignant lesion.

As in both our patients, the diagnosis is frequently delayed as these lesions are commonly thought to be granulomas and treated as such by cauterisation until recurrence occurs and a biopsy is performed. Review of the now 22 reported cases of ileostomy carcinoma suggests that overall the prognosis is favourable.^{5,7-21} The mean age of patients at presentation is 56 (range 39 to 79) years with a stoma having been present for a mean of 26 (range 3 to 38) years. By far the majority (17) occurred in patients who had been treated for ulcerative colitis, only three were in patients with polyposis coli and we report the only two cases in association with Crohn's disease. The long lead time suggests that the tumour is predominantly slow growing, only six patients have developed proved metastatic spread and all of these had moderate or poorly differentiated tumours. Four of these patients have died of carcinomatosis as a result of the stomal carcinoma, the remaining patients have apparently all been cured by local excision, although the length of follow up is inadequate in most reports and recurrent disease must have occurred in a proportion. Despite this, local excision is a successful treatment for these tumours, although the extent of the surgical excision varies between reports, some being more radical than others, requiring insertion of a mesh prosthesis to strengthen the resulting anterior abdominal wall defect. It is apparent from these results that the surgical treatment should include a wide local excision of the tissues of the anterior abdominal wall, with a limited resection of the ileum and refashioning of an ileostomy at a new site. Experience with our second patient also suggests that a careful excision of all mucosa is advisable when a stoma is refashioned or closed to prevent the future development of malignant change.

Epithelial hyperplasia, lymphoid nodules, and squamous metaplasia are all consequences of ileostomy irritation³² and are regularly seen in surgical outpatients and treated by cauterisation, biopsy rarely being performed. We suggest that

biopsy specimens be taken of all persistent lesions on stoma, particularly ileostomies, before cauterisation. The presence of epithelial dysplasia seems to be a useful histological precursor of malignant change. Follow up of all patients with ileostomies is advisable, with annual examination of the stoma without the appliance to detect mucosal abnormalities.

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