Primary squamous cell carcinoma of the rectum in a patient on immunosuppressive therapy

Sir,

Primary squamous cell carcinoma of the rectum is a rare tumour.1–11 The diagnosis of squamous cell carcinoma rests on the exclusion of metastases from other organs, proximal extension of carcinoma arising from the anal canal and squamous-lined fistulous tracts. Here we report an uncommon presentation of rectal squamous cell carcinoma in a woman on long-term immunosuppressive therapy.
Our patient was a 44-year-old obese indigenous woman who presented with 3 weeks of fresh rectal bleeding and diarrhoea. She had end stage renal failure treated on peritoneal dialysis, non-insulin-dependent diabetes mellitus, hypertension, autoimmune thrombocytic purpura and systemic lupus erythematosus (SLE). The patient had been on immunosuppressive therapy for the latter two conditions for 16 years. There had been no gynaecological problems previously and this was later confirmed by consultation with gynaecologists. Rectal examination revealed a fixed circumferential growth 6 cm from the anal verge. There were no palpable inguinal lymph nodes. Colonoscopy confirmed the location of the tumour and biopsies taken revealed a moderately differentiated squamous cell carcinoma. A CT scan of the abdomen and pelvis and a chest X-ray revealed neither regional nor distant secondaries. A course of preoperative adjuvant therapy, consisting of 25 Gy in 5 fractions, was given over 1 week. One week later, the patient proceeded to a laparoscopic ultra-low anterior resection, with total mesorectal excision. The tumour was confirmed and the uterus and ovaries were confirmed to be normal. The growth was fixed to the right lateral pelvic floor and the rectal dissection had to be completed through a 6-cm suprapubic transverse incision. Bowel continuity was restored with a colonic J-pouch-anal anastomosis, covered with a temporary loop ileostomy. The patient was converted to haemodialysis after surgery; she has since progressed well and is awaiting closure of the ileostomy.

Gross examination showed a $3 \times 1.5 \times 1$ cm ulcerative tumour in the rectum. A well-differentiated squamous cell carcinoma was noted on microscopic examination (Fig. 1). The carcinoma invaded all the layers of the rectal wall into the perirectal fat. Perineural tumour infiltration was present. The twelve lymph nodes sampled in the specimen were free of carcinoma. Complete surgical excision was confirmed. The tumour cells were positive for p53 and p21 (Fig. 2, 3). p53 expression was located in the centre of the tumour cell nests whereas p21 staining was situated in the periphery of the tumour cell nests.

The origin of squamous cell carcinoma in the large intestine is largely unknown. A number of pathogenic origins for squamous cell carcinoma of the large intestine have been proposed. These include (1) proliferation of uncommitted stem cells following injury; (2) squamous metaplasia of normal glands from chronic irritation with later malignant change, established adenocarcinoma or adenoma with invasion; and (3) malignant change of displaced embryonic nests as noted in the association of colonic duplication in two cases.

The first theory seems to be the most logical explanation of the squamous cell carcinoma as it is supported by the coexistence of the colorectal squamous cell carcinoma and some predisposing diseases. The glandular epithelium, which has been destroyed by repeated deleterious influences, loses the ability to differentiate in the normal pathway. For instance, some cases of intestinal squamous cell carcinoma have been associated with mucosal injury like chronic ulcerative colitis. Also, *Entamoeba histolytica* have been found in patients with squamous cell carcinoma of the rectum. The mechanism may be mechanical irritation, chronic inflammation or transportation of carcinogenic viruses by the parasites. In addition, a
few cases have been reported in homosexual men. The pathogenesis can be explained by a similar mechanism. Interestingly, Sotlar and colleagues demonstrated human papillomavirus type 16 in a man with primary squamous cell carcinoma of the rectum.

In the present case, the pathogenesis is likely to be related to the oncogenic effect of chronic renal failure and long-term use of immunosuppressive therapy. Carcinogenic viruses or the direct carcinogenic effect of the immunosuppressive therapy may account for the activation of uncommitted stem cells in the pathogenesis of the squamous cell carcinoma.

Inactivation of p53 and p16 tumour suppressor genes is crucial in carcinogenesis of a variety of malignancies. Aberrant expression of these genes, as examined by immunohistochemistry, marks the transformation from a low-grade to a high-grade tumour in some sites. There is no previous study of these genetic changes in squamous cell carcinoma of the rectum. In this study, we noted the expression of p53 and p16 in the squamous cell carcinoma, proving that these genes were involved in the pathogenesis of the carcinoma. The spatial difference in the expression of these markers in the carcinoma suggests that p53 and p16 were common in different stages of carcinogenesis.

Review of the patient characteristics reported in the literature revealed that primary rectal squamous cell carcinoma occurs more often in females (male to female ratio approximately 1:2). Like rectal adenocarcinoma, squamous cell carcinoma of the rectum occurs mostly in patients of advanced age. The mean age of diagnosis of primary squamous cell carcinoma of rectum was 54 (range 33–93). Only five reported patients were younger than 40 years, and they were females. Three of these five patients had ulcerative colitis. Our reported patient is amongst the few younger patients noted in the literature. The presence of predisposing factors at a young age in this patient could account for the early development of squamous cell carcinoma of the rectum.

The clinical presentation of primary rectal squamous cell carcinoma does not differ significantly from that of typical rectal adenocarcinoma and includes abdominal pain, bleeding per rectum, change in bowel habits, anorexia or weight loss. On the other hand, the prognosis of these tumours seems to be worse than that of adenocarcinoma because of delayed diagnosis. In the present report, the patient also had an extensive tumour at presentation. Surgical resection is the most important treatment. Adjuvant radiotherapy and chemotherapy may be useful in advanced cases.

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