Received: 24 February 2022 | Accepted: 19 March 2022

DOI: 10.1002/cia2.12237

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

Invasive squamous cell carcinoma arising from long-lasting enterocutaneous fistula due to Crohn's disease

A 53-year-old woman with Crohn's disease (CD) diagnosed more than 30 years earlier was referred to us because of a 4 month history of abdominal tumors. She underwent a total colectomy, small intestinal resection, and an eternal enterostomy 24 years earlier and had two enterocutaneous fistulous tracts with repeated inflammation on the lower-right side of her abdomen for 13 years. She had been treated with 5-aminosalicylic acid for more than 15 years, but did not receive immunosuppressants or tumor necrosis factor alpha inhibitors. Physical examination revealed a 6×3.5 cm reddish ulcerative tumor on the lower-right side of her abdomen surrounded by brownish pigmentation with indurations (Figure 1A). Histopathological examination of the tumor revealed atypical squamous cell proliferation with marked keratinization (Figure 1B,C). Histological continuity between the epidermis and atypical cells was not observed, and immunostaining of the cells was negative for human papillomavirus. Computed tomography and positron emission tomography/computed tomography demonstrated a large mass involving the abdominal walls and enlargement of the inguinal and right external iliac lymph nodes (Figure 1D). Her serum squamous cell carcinoma (SCC) antigen level was also elevated (5.4 ng/ml; normal range, <2.5 ng/ml). The patients were then diagnosed with SCC arising from an enterocutaneous fistula (ECF) related to CD. She was treated with radiation therapy (30 Gy) for a skin tumor and bilateral inguinal lymph nodes, followed by chemotherapy with pepleomycin. Unfortunately, her disease slowly progressed and she died 5 months after her initial visit.

Crohn's disease is a chronic inflammatory bowel disorder characterized by transmural inflammation and fistula formation.[1] Perianal fistulas are common complications of the disease, and patients with anal and/or perianal CD have a high risk of perianal fistula-related

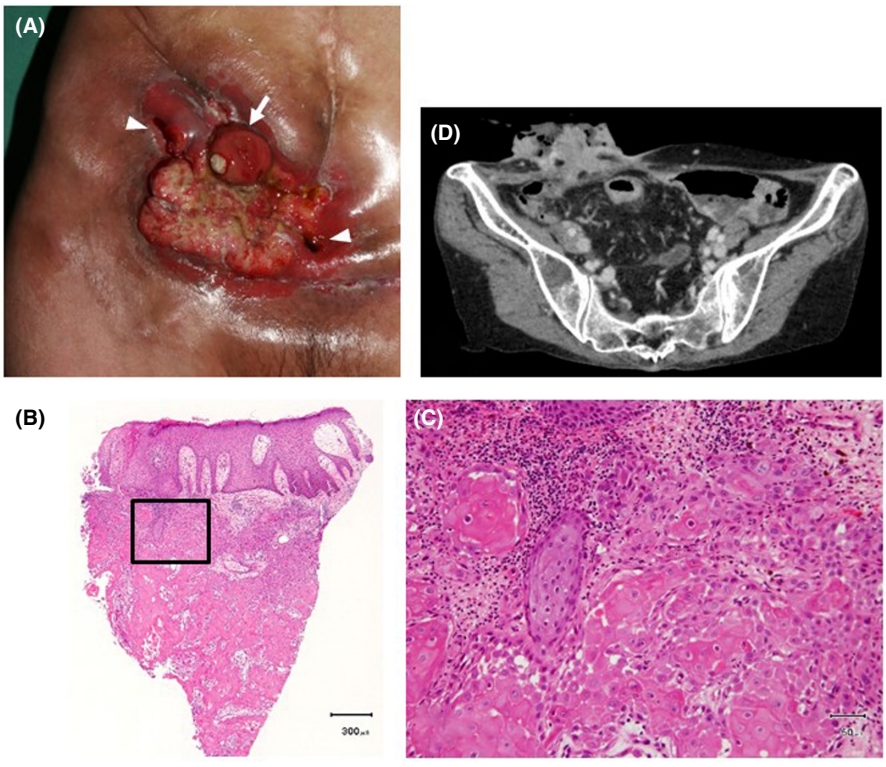

FIGURE 1 Clinical presentation, histological findings, and computed tomography findings. (A) reddish ulcerative tumors spreading on the lower abdomen. A stoma (arrow) and two enterocutaneous fistulas (arrowhead) are adjacent to the tumor. The tumor was surrounded by brownish induration. Histopathological analysis of a skin biopsy reveals atypical cell proliferation in the dermis with marked keratinization (B: ×40, C: ×200). (D) Axial computed tomography shows a large mass occupying the abdominal wall entering the abdominal cavity

cancer.[2] Fistula-related carcinoma develops in approximately 1% of patients with fistulizing perianal CD. More than half of these carcinomas are adenocarcinoma; most of the rest are SCC.

Compared with perianal fistulas, ECF is rare, but it is associated with significant morbidity and mortality due to various complications.[3] Late complications, such as late onset of malignancy, have been given little attention in the literature, with a limited number of patients with cancers arising from ECF and only one fistula-associated SCC patient, who was treated with long-lasting azathioprine followed by infliximab, being reported.[4] The causes of malignancies arising from chronic fistulas are unclear, but chronic inflammation and immunosuppression are considered mechanisms of carcinogenesis in CD patients. Chronic inflammation, a feature of CD, induces constant epithelial regeneration, ulceration, and high cell turnover rates, leading to dysplasia and subsequently carcinoma. Our patient was not treated with immunosuppressants or biologics; however, so it is likely that her chronic inflammation led to carcinogenesis.

The onset of malignancies arising from ECF in CD patients may increase in future because of the expanding use of immunosuppressants and/or biologics and improvements in the treatment of acute complications of ECF. Therefore, diagnosticians should be alert to early signs of fistula-associated malignancies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: The written informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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