Squamous cell carcinoma of the vulva in a young woman with Crohn's disease

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Summary

Background: Crohn's disease is a chronic inflammatory disorder of the gastrointestinal tract. Because Crohn's disease is transmural it may form fistulas to adjacent structures, including the perineum and vulva. *Case:* A 28-year-old white female with a history of Crohn's disease presented with a non-healing vulvar fistula. Biopsy revealed squamous cell carcinoma. *Conclusion:* Young women may develop squamous cell carcinoma associated with fistulae of Crohn's disease.

Key words: Squamous cell carcinoma; Vulva; Crohn's disease.

Introduction

Crohn's disease is chronic inflammatory disorder of the gastrointestinal tract. Because Crohn's disease is transmural it may form fistulas to adjacent structures, including the perineum and vulva. We report a case of squamous cell carcinoma arising in a Crohn's disease-associated fistula to the vulva.

Case Report

A 28-year-old white female was referred to our institution secondary to a vulvar biopsy consistent with invasive squamous cell carcinoma. The patient's past medical history was significant for Crohn's disease for which she had undergone resection of an anal fistula at 18 years of age followed by partial colectomy with ostomy and subsequent takedown with reanastomosis. Approximately two years prior to presentation, she reported developing two right-sided vulvar fistulas for which she received a six-week course of metronidazole and ciprofloxacin. She reported subsequent improvement in her symptoms for the following two years until she noticed a cyst-like structure on her right vulva at the site of a previous fistula that was becoming increasingly painful and swollen. After a six-week trial of metronidazole and ciprofloxacin without relief, a fistulagram and biopsy were performed. The fistulagram failed to show any abnormal communication. The biopsy results were reported as moderately differentiated, nonkeratinizing invasive squamous cell carcinoma.

The patient was referred to Roswell Park Cancer Institute. Upon exam, an ulcerated endophytic lesion approximately 3 cm in diameter was visualized. Upon further questioning, she denied any history of genital warts or smoking.

She admitted to a history of cervical dysplasia which was treated with a LEEP. She had received prednisone for her Crohn's disease six years prior for six months.

She underwent a right hemivulvectomy and right inguinal lymph node dissection without complications. Pathological examination of the vulvectomy specimen revealed poorly differentiated squamous cell carcinoma measuring 3 cm in width and 0.4 cm out of 0.8 cm in depth. Angiolymphatic invasion was present. The surgical margins were free of tumor. Eleven of 11 lymph nodes were negative for malignancy. She had an uneventful postoperative course and was discharged home in stable condition on postoperative day number three.

Discussion

Squamous cell carcinoma of the vulva is rare among young patients [1]. Women with Crohn's disease are at an increased risk of vulvar cancer. In their review of 1,227 patients with Crohn's disease, Greenstein *et al.* reported two patients with squamous cell cancer of the vulva which represented a 14.2 times increase over the expected incidence [2]. One of those carcinomas was associated with perianal involvement of Crohn's disease. Additionally, they observed three cases of squamous cell cancer of the anus, two of which arose in association with chronic perianal fistulas. Considering the association of fistula with the increased incidence of squamous cell cancer in Crohn's disease the investigators concluded "that the association is more than coincidental" and hypothesized that the lesions may result from chronic inflammation and intrinsic immunosuppression. The exact etiology of carcinoma arising in chronic fistulae is unsure. Church *et al.*, in their review of four cases of fistula-associated carcinoma cases, proposed that the carcinomas develop due to chronic epithelial irritation with resultant hyperplasia and subsequent transformation to carcinoma [3].

Due to its rarity it is difficult to determine the incidence of squamous cell carcinoma arising in a Crohn's disease fistula. In a survey conducted by Korelitz there were three reported cases of carcinoma occurring at the site of a fistula in 16,469 patients with Crohn's disease [4]. In their review of over 1,000 patients with Crohn's disease affecting the anus or rectum, Ky *et al.* noted a total of seven patients with carcinoma associated with anorectal fistulas, four with squamous cell carcinoma and three with adenocarcinoma [5].

A majority of the information regarding carcinoma arising in the fistulas of Crohn's disease is in the form of

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case reports and small series of patients [3, 5-10]. In their report of seven patients with carcinoma arising in anorectal fistulas, Ky *et al.* reported that the average age of diagnosis was 47 years [5]. However, the two women diagnosed with squamous cell carcinoma were 30 and 31 years old. Similar findings were reported by Korelitz who observed that the average age of carcinoma found in an anorectal fistula of Crohn's disease was 50 years old [7]. The three women diagnosed with squamous cell carcinoma were only 30, 31 and 38 years of age. Buchman *et al.* detailed the clinical course and diagnosis of squamous cell carcinoma associated with chronic perineal involvement of Crohn's disease in women aged 28 and 35 [8]. These observations highlight the relatively young age at which females affected with Crohn's disease fistulas and involvement of the perinieum can develop squamous cell carcinoma.

A high index of suspicion must be maintained in women with Crohn's disease with perineal involvement to avoid a delay in diagnosis. In discussing his nine patients with carcinoma arising in Crohn's disease fistulas, Korelitz reported that in "no case was the carcinoma suspected on initial examination or, in some cases, even after multiple examinations" [7]. The diagnosis of carcinoma may be missed by attributing the symptoms to benign pathology. Most often the presenting complaint is pain [3, 7, 8]. One must also be suspicious of bleeding and discharge related to a fistula [3, 10].

By being aware of the possibility of squamous cell cancer developing in young women in association with a Crohn's disease fistula, maintaining a high index of suspicion and a low threshold to biopsy worrisome lesions, it may be able to improve patients' outcome via an earlier stage at diagnosis and prompt initiation of treatment.

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