Anal Carcinoma in Patients with Crohn's Disease: Three Cases Report and Literature Review

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Abstract

**Background:** Anal cancer in patients with Crohn’s disease (CD) is rare, and the relationship between infliximab and anal cancer is not clear yet. The present study aimed to report three patients with CD complicated with anal cancer who used infliximab with their basic features.

**Case presentation:** Three cases were reported, including two females and one male, aged 29-56 years old. All of them developed perianal lesions during the period of Crohn’s disease. All three patients had used infliximab for Crohn’s disease before the diagnosis of anal cancer, except one patient who stopped using infliximab three times due to allergy; the other two patients had used infliximab until the diagnosis of anal cancer. Two patients had a good prognosis with early therapeutic intervention.

**Conclusion:** Based on the results, Chinese and Western patients with Crohn’s disease who developed anal carcinoma had similar features. Conventional perianal evaluation is important in patients with Crohn’s disease. The association between infliximab therapy and anal cancer has not been fully established and needs to be fully evaluated before the use of infliximab in Crohn’s disease.

**Keywords:** Anal cancer, Case report, Crohn’s disease, Infliximab

1. Background

Crohn’s disease (CD) is a chronic inflammatory granulomatous disease characterized by alternating periods of relapse and remission. Patients might present with abdominal pain, diarrhea, weight loss, and perianal involvement, such as fistula and abscess. Anal carcinoma is rare in the general population, accounting for 1%-2% of gastrointestinal tumors. Histologically, it is mainly squamous cell carcinoma (1). The risk of this cancer in patients with CD is 11 times higher than that in the general population (2). Nonetheless, anal carcinoma in patients with Crohn’s disease is quite rare, and scant attention has been paid to patients with CD who developed anal carcinoma, especially those who had accepted infliximab.

In this study, we aimed to report three patients with CD complicated with anal cancer with their basic features listed in Table 1.

3. Case presentation

Case 1 was a 31-year-old female with a 7-year history of CD. Previous budesonide, mesalamine, and other medications did not improve the symptom effectively. She was treated with infliximab; nonetheless, it stopped due to an allergy. After the diagnosis of CD, the perianal symptoms kept repeating, especially the anal fistula, anal fistula resection, incision, and suture hanging were performed. Lymph node biopsy pathology was performed due to the left swollen groin lymph node, and the pathologic result showed poorly differentiated mucinous adenocarcinoma. Enhanced computed tomography (CT) of the upper abdomen and pelvic cavity indicated CD with anal cancer, liver, bone, and lymph node metastasis (Figure 1). The patient received chemotherapy; moreover, radiofrequency therapy and capecitabine oral chemotherapy were performed after six cycles of chemotherapy. As a mass was found in the anal finger examination, targeted chemotherapy drugs were added for treatment. About 10 months after chemotherapy, anal cancer recurred and was accompanied by a large number of bloody ascites. Finally, cardiac arrest occurred due to hemorrhagic shock, and treatment was abandoned.

Case 2 was a 55-year-old female with a 13-year history of CD. Infliximab therapy was administered. Magnetic resonance imaging (MRI) showed the anal fistula (Figure 2). Anal fistula hanging operation had been performed twice before, and the perianal condition was stable after the operation. Postoperative pathological results demonstrated squamous cell carcinoma in situ. The patient received laparoscopic radical resection of anal cancer, ileocecal and terminal ileocecal resection, as well as sigmoid colostomy. The operation was successful and the postoperative recovery was good. Mesalamine
Table 1. Summary of clinical features of three patients with Crohn’s disease complicated with anal carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
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<tbody>
<tr>
<td>Age</td>
<td>31 years old</td>
<td>56 years old</td>
<td>29 years old</td>
</tr>
<tr>
<td>Gender</td>
<td>F</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Perianal lesions</td>
<td>Anal fistula</td>
<td>Complex anal fistula</td>
<td>Anal fistula</td>
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<tr>
<td>Pathological types of anal carcinoma</td>
<td>Mucous adenocarcinoma</td>
<td>Squamous cell carcinoma</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>The interval between Crohn’s disease and anal carcinoma</td>
<td>7 years</td>
<td>13 years</td>
<td>8 years</td>
</tr>
<tr>
<td>Anal carcinoma treatment</td>
<td>Chemotherapy + drug targeted therapy</td>
<td>surgery</td>
<td>Radiation therapy + chemotherapy</td>
</tr>
<tr>
<td>Outcome after treatment</td>
<td>Anal cancer recurred accompanied by massive bloody ascites. Dead of hemorrhagic shock occurred.</td>
<td>Follow up regularly and the condition was stable</td>
<td>Follow up regularly after treatment</td>
</tr>
<tr>
<td>Duration of infliximab use</td>
<td>47 months</td>
<td>11 months</td>
<td>30 months</td>
</tr>
</tbody>
</table>

Figure 1. Enhanced computed tomography of upper abdomen and pelvic cavity of case 1 showed liver, bone and lymph node metastasis. The MRI of anal canal of case 1 showed anal cancer.

Figure 2. The magnetic resonance imaging of anal canal of case 2 showed anal fistula and anal abscess.
was treated with CD after surgery, and the condition was stable with regular follow-ups.

Case 3 was a 29-year-old male with an 8-year history of CD with anal fistula. Oral mesalamine treatment was discontinued due to unstable effects. Later, the treatment was changed to infliximab treatment, and the treatment interval was adjusted according to the condition of the combination of azathioprine and infliximab dose. The perianal condition was repeated, and MRI indicated the anal fistula, as well as an abscess (Figure 3). The perianal condition was improved after the anal fistula suture hanging operation was once performed. Postoperative pathological results showed (perianal) keratinized squamous cell carcinoma with high to medium differentiation. The patient received radiotherapy: intensity-modulated field in pelvic tumor area (including anal mass and inguinal metastatic lymph nodes) 10MV-X SAD 100 DT 5400cGy/30F/ 41D. Chemotherapy with nedaplatin and capecitabine was performed regularly after the radiotherapy, and the condition is stable.

5. Discussion

From 2019-2020, three patients with CD combined with anal cancer were admitted and the incidence of CD combined with anal cancer in our hospital was 0.04% (3/8241), according to the number of CD patients in the hospital displayed in Figure 4. One patient died after multiple metastases due to a lack of timely diagnosis and treatment. The
other two patients were detected early and treated with surgery, radiotherapy, and chemotherapy, respectively, and obtained stable conditions after therapy. According to the previous study, the CD patients who developed anal cancer were predominantly female at a relatively young age with perianal lesions. The main type of carcinoma is squamous cell carcinoma and adenocarcinoma, and the outcome was basically good (2-11). The clinical characteristics were similar to those of the three cases in the present study.

Clinicians should devote attention to the perianal symptom of patients with CD. Chronic complex anal symptoms, especially the anal fistula, in patients with CD seemed to be an increased risk of anal cancer, and changes in symptoms were important warning signs of anal cancer (12,13). The MRI can be an effective way to detect anal cancer (8). Nonetheless, no study has proposed the optimal frequency and method for monitoring long-term anal or perianal CD (14), as well as standardized screening methods (6). The lack of routine perianal management could lead to the untimely diagnosis and treatment of anal carcinoma (12).

The mechanism of CD with anal cancer has not been fully elucidated, and possible mechanisms include local and systemic chronic inflammation, HPV infection, decreased defensin function, and drug-induced immunosuppression (7, 9, 10, 12, 14). In addition, all three patients included in this study used infliximab to treat CD. Infliximab was considered to suppress tumor necrosis factor so as to promote the growth of the tumor, control inflammation, and alleviate anus symptoms to delay the diagnosis of anal cancer (2, 3). Although experiments on animal models have illustrated that infliximab has a certain promoting effect on the occurrence of cancer (15), no link has been found between infliximab therapy and the occurrence of anal cancer in existing studies and cases (16-18). Nevertheless, it is recommended that patients with CD with the perianal disease be fully evaluated before the use of the infliximab therapy, and biopsy is the best (19).

6. Conclusion

Crohn's disease with anal cancer is uncommon. Conventional perianal evaluation is important in patients with Crohn's disease. Treatment includes surgery and radiation therapy combined with chemotherapy. The association of infliximab therapy with anal cancer has not been fully established and needs to be fully evaluated before the use of infliximab in Crohn's disease.

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Footnotes

Conflicts of Interest: None to declare.

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Ethical consideration: Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

References


