Case Report
Collision tumor of carcinoma and lymphoma in the cecum: case report and review of literature

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Abstract: Collision tumors that occur in the gastrointestinal tract, especially the intestine, are rare, and collisions of carcinoma and lymphoma are even more rare. We report a case of collision tumor with adenocarcinoma and non-Hodgkin’s diffuse large B-cell lymphoma in the cecum of an elderly male patient. Literature was reviewed to explore the clinicopathologic features, differential diagnosis, treatment, and prognosis of collision tumors with carcinoma and lymphoma involving the gastrointestinal tract, to enhance the understanding of this rare tumor, and improve diagnosis and treatment.

Keywords: Collision tumor, diffuse large B-cell, lymphoma, carcinoma, gastrointestinal tract

Introduction
Collision tumor is a rare occurrence where two different tumors occur in the same organ [1].

Adenocarcinoma is the most common malignant tumor of the gastrointestinal tract, while lymphoma is relatively rare and accounts for only 1%-4% of all malignant tumors of the gastrointestinal tract [2]. A collision tumor with both components is extremely rare, especially in the intestine [1, 3].

The earliest such tumor that we can find was the collision of adenocarcinoma and pleomorphic malignant lymphoma reported by Coppola et al. in 1969 [1]. In recent years, a collision of adenocarcinoma with low-grade lymphoma in the intestine, and collision of lymphoepithelioid carcinoma with low-grade lymphoma in the stomach have been reported occasionally [3, 4]. The latest report was three years ago. The treatment of collision tumors is mainly surgical resection combined with radiotherapy and chemotherapy [5].

Here we report a case of collision tumor in the cecum, composed of adenocarcinoma and non-Hodgkin’s diffuse large B-cell lymphoma. 22 cases of collision tumor of carcinoma and lymphoma from 1969 to now were found in the PubMed database. Diagnosis and treatment are discussed.

Case report
A 77-year-old man presented to the outpatient department of Gastrointestinal Surgery of the Affiliated Yantai Yuhuangding Hospital of Qingdao University with right lower quadrant pain for more than 3 months. There was no obvious inducement for the patient to have persistent moderate blunt pain in the right abdomen, and radiation pain in the right waist, which had nothing to do with body position. The patient had intermittent episodes with these above symptoms, and had 1 stool/day, yellow and watery. The patient denied symptoms such as nausea, vomiting, belching, bloating, loss of appetite, dizziness, or fatigue. Diet and sleep were acceptable, and there was no obvious change in weight. Physical examination revealed abdominal distension, soft abdominal muscles, and no tenderness or rebound tenderness. CT showed that the intestinal wall of the ascending colon was irregularly thickened and rough. Enhanced scan showed obvious enhancement. A mass of soft tissue density shadow with a cross-section of about 5.5×3.9 cm was seen around it, and the enhanced scan show-
Blood cell count showed that the lymphocyte percentage was 14.1% (normal threshold was 20-50%), the absolute value of lymphocytes was 0.89×10^9/L (normal threshold was 1.1-3.2×10^9/L), and the absolute value of monocytes was 0.61×10^9/L (normal threshold was 0.1-0.6×10^9/L). Remaining indicators were in the normal range. The patient underwent a right hemicolectomy, followed by chemotherapy for diffuse large B-cell lymphoma lymphoma. The patient was followed up for 4 months without recurrence or metastasis.

Pathologic findings

Received in formalin was a section of intestine with omentum (part of ileum, cecum, and part of ascending colon). The lengths of the three portions were respectively 4 cm, 6 cm, and 13 cm; and the circumferences were 5 cm, 6 cm, and 6 cm. An ulcerative mass with a size of 6×5×4 cm was seen on the cecal mucosa adjacent to ileocecal valve. The cut surface was gray and soft, fish-like, with a clear boundary. The appendix was 3 cm long, 0.8 cm in diameter, and the volume of the omentum was 17×8×2 cm.

Microscopy showed that the tumor was composed of two components. They were adjacent to each other but relatively independent, with almost no cross-growth. One component was a typical moderately differentiated adenocarcinoma of the colon, which invaded the subserous layer, and an intravascular cancer embolus could be seen locally. The other component was distributed from the subserous layer to the serosa. Microscopically, the cells with medium to large size and relatively uniform morphology grew diffusely, with frequent mitosis and obvious cell atypia (Figure 2). Immunohistochemistry showed that the cells were positive for CD20, bcl-6, MUM-1, and bcl-2 (Figure 3), and about 10% weakly positive for c-myc. Ki67 proliferation index was about 80%. Cells were negative for CD10, CD3, and cyclin D1. In situ hybridization showed EBER was negative. IgH gene rearrangement study showed that the B-cell rearrangement was positive (PCR+ Fragment Analysis) (Table 1 and Figure 4). The final diagnosis was non-Hodgkin's diffuse large B-cell lymphoma (non-germinal central origin). No carcinoma metastasis or lymphoma involvement were found in 14 mesenteric lymph nodes.

Discussion

Collision tumors of carcinoma and lymphoma in the gastrointestinal tract are extremely rare, especially in the intestine [4]. Through the analysis of this case and literature review (see Table 2 for specific details of all cases) [1-21], it was found that this type of tumor mostly occurs in middle-aged and elderly men (male:female =10.5:1, with an average age of 66 years). All patients who had tumor in the intestines were male, and all of them were over 60 years old. Almost all patients were treated for gastrointestinal symptoms such as abdominal pain, nausea, and vomiting. Imaging examination was indistinguishable from simple carcinoma or lymphoma. Laboratory tests were also nonspecific.

The tumor in the current case occurred in the ileocecal area. Other instances of this tumor mostly occurred near the ileocecum, which may be due to the rich and active proliferation of lymphoid tissue there. However, when the tu-
Figure 2. A. Interface of carcinoma and lymphoma (H&E 4×); B. The carcinoma component is moderately differentiated adenocarcinoma (H&E 10×); C and D. Medium to large lymphoma cells with relatively uniform morphology grew diffusely, with frequent mitosis and obvious cell atypia (H&E 10× and 40×).

Figure 3. A. Cytokeratin is positive in the adenocarcinoma; B. CD20 is diffusely positive in the lymphoma; C and D. bcl-2 and bcl-6 are positive in the lymphoma.
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mor occurs in the stomach, unlike adenocarcinoma, which tends to occur on the small curvature of the gastric antrum, there is no particularly preferred location. Sometimes the tumors are solitary in the entire stomach, and sometimes they are multiple. The specimen in this case was regarded as ordinary ulcerative cancer. Grossly this type of tumor is an almost ulcerative or irregular mass, and the sections are gray-white, soft to medium. It is indistinguishable from simple cancer or lymphoma.

Through literature review, we found that the histologic morphology of tumors could be roughly divided into three types: the most common type is where carcinoma and lymphoma are in the same tumor and the two types of tumor cells are mixed and grow crosswise. The second is with carcinoma and lymphoma are in the same tumor, but the two tumor types are not mixed and grow relatively independently (our case belongs to this type). Third, the two tumor components are in separate tumors respectively, and the two tumors are adjacent or close to each other (whether the latter is a real collision tumor remains to be discussed) [22]. In the literature we reviewed, when the tumor occurs in the intestine, all the carcinoma components are moderately-differentiated adenocarcinoma; most of the lymphoma components are low-grade B-cell lymphomas, such as follicular lymphoma (FL) [2], or mucosa-associated extranodal marginal zone lymphoma (MALT) [11]. A few are diffuse large B-cell lymphoma (DLBCL) [9], and some are peripheral T-cell lymphoma (non-specific) (PTCL) [14]. Since collision tumors of carcinoma and lymphoma in the intestinal tract are so rare, the pathogenesis of this kind of tumor in the intestine is still unclear. Some reports suggest that excessive lymphoid reaction (such as immune reaction) in adenocarcinoma would lead to malignant transformation of lymphoid tissue [14]. It was also believed that patients with lymphoma were more likely to suffer from adenocarcinoma due to lack of immune surveillance. The most common carcinoma component of gastric cancer is poorly differentiated adenocarcinoma (partly signet ring cell carcinoma), followed by well and moderately differentiated adenocarcinoma. Very few are lymphoepithelioma-like carcinoma. Most of the lymphoma components are MALT, some are DLBCL, and few are HL. Shotaro et al. believed that Helicobacter pylori (HP) infection was related to the occurrence of carcinoma and lymphoma in the collision tumors of the stomach [22]. In such lesions, lymphoma may occur before cancer, and HP infection is more closely related to the prognosis of cancer [22].

In this case, the pathologist noticed only the moderately differentiated adenocarcinoma and missed the component of lymphoma, and mistakenly thought it was all poorly differentiated adenocarcinoma. In the diagnosis of collision tumors, the most important thing is to avoid a missed diagnosis. When the lymphoma component is low-grade lymphoma, it may be missed as a reactive lymphoid proliferation. When the lymphoma component is high-grade lymphoma, it may be missed as poorly differentiated cancer. When the lymphoma component is predominant, diffuse poorly differentiated carcinoma may be called as lymphoma cells. Therefore, especially in gastrointestinal biopsies, if we encounter carcinoma with diffuse hyperplasia of lymphoid tissue in the background, or the tumor cells are poorly differentiated, we must be vigilant and perform immunohistochemistry for epithelial and lymphoid markers to avoid a missed diagnosis. Further classification of each tumor component still requires the use of immunohistochemistry and genetic testing.

This patient received chemotherapy for diffuse large B-cell lymphoma after surgery, and had no recurrence or metastasis for two months. Due to the short follow-up time, we cannot ju-
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Figure 4. Fragment analysis graph.
## Table 2. Specific data for all cases

<table>
<thead>
<tr>
<th>No.</th>
<th>Year</th>
<th>Age (years)/Sex</th>
<th>Location</th>
<th>Collision component</th>
<th>Lymph node metastasis/involvement</th>
<th>Gene</th>
<th>Treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2014</td>
<td>81/M</td>
<td>Sigmoid colon, spleen</td>
<td>MDA</td>
<td>Low-grade B-cell lymphoma</td>
<td>+</td>
<td>+</td>
<td>K-ras(+), B-raf(+)</td>
</tr>
<tr>
<td>2</td>
<td>2011</td>
<td>86/M</td>
<td>Caecum, Ascending colon</td>
<td>MDA</td>
<td>DLBCL</td>
<td>NA</td>
<td>NA</td>
<td>EBER(+)</td>
</tr>
<tr>
<td>3</td>
<td>2010</td>
<td>62/M</td>
<td>Caecum, Duodenum</td>
<td>MDA</td>
<td>FL</td>
<td>-</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>2010</td>
<td>67/M</td>
<td>Ascending colon, Terminal ileum</td>
<td>MDA</td>
<td>MALT, FL</td>
<td>-</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>2003</td>
<td>73/M</td>
<td>Rectum, Terminal ileum</td>
<td>MDA</td>
<td>PTCL (unspezified)</td>
<td>NA</td>
<td>NA</td>
<td>IgH rearrangement(+)</td>
</tr>
<tr>
<td>6</td>
<td>2017</td>
<td>65/M</td>
<td>Gastrocorpus, lesser curvature</td>
<td>LLC</td>
<td>DLBCL</td>
<td>NA</td>
<td>NA</td>
<td>EBER(+) in carcinoma</td>
</tr>
<tr>
<td>7</td>
<td>2016</td>
<td>71/M</td>
<td>Gastrocorpus, greater curvature</td>
<td>MDA</td>
<td>DLBCL</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>2014</td>
<td>53/M</td>
<td>Almost full stomach</td>
<td>SRCC</td>
<td>MALT</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>9</td>
<td>2012</td>
<td>72/M</td>
<td>Fundus</td>
<td>Adenocarcinoma</td>
<td>HL</td>
<td>-</td>
<td>+</td>
<td>EBER(+) in lymphoma</td>
</tr>
<tr>
<td>10</td>
<td>2010</td>
<td>80/M</td>
<td>Anastomosis</td>
<td>Adenocarcinoma</td>
<td>DLBCL</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>11</td>
<td>2010</td>
<td>65/M</td>
<td>Upper part of the stomach</td>
<td>LLC</td>
<td>MALT</td>
<td>NA</td>
<td>NA</td>
<td>EBER(+) in carcinoma, IgH rearrangement(+)</td>
</tr>
<tr>
<td>12</td>
<td>2007</td>
<td>63/F</td>
<td>Almost full stomach</td>
<td>PDA, SRCC</td>
<td>MALT with DLBCL component</td>
<td>+</td>
<td>+</td>
<td>API2-MALT1(+)</td>
</tr>
<tr>
<td>13</td>
<td>2005</td>
<td>40/F</td>
<td>Stomach and other organs</td>
<td>SRCC</td>
<td>MALT</td>
<td>+</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>14</td>
<td>2001</td>
<td>66/M</td>
<td>Lesser curvature of the stomach</td>
<td>PDA</td>
<td>B-cell malignant lymphoma</td>
<td>+</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>15</td>
<td>2001</td>
<td>47/M</td>
<td>Gastrocorpus</td>
<td>PDA</td>
<td>MALT</td>
<td>+</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>16</td>
<td>1996</td>
<td>71/M</td>
<td>Fornix extend to the cardioesophageal junction</td>
<td>PDA</td>
<td>DLBCL</td>
<td>-</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>17</td>
<td>1989</td>
<td>61/M</td>
<td>Stomach</td>
<td>Adenocarcinoma</td>
<td>Diffuse lymphoma, large-cell type</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>18</td>
<td>1985</td>
<td>74/M</td>
<td>Antrum</td>
<td>WDA</td>
<td>Malignant lymphoma of the mixed type</td>
<td>-</td>
<td>-</td>
<td>NA</td>
</tr>
</tbody>
</table>

### Collision tumor of carcinoma and lymphoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Year</th>
<th>Sex</th>
<th>Location</th>
<th>Stage</th>
<th>Histology</th>
<th>Type</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>1974</td>
<td>65/M</td>
<td>Almost full stomach</td>
<td>PDA</td>
<td>A malignant lymphoma, largely of the histiocytic variety</td>
<td>-</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>21</td>
<td>1974</td>
<td>72/M</td>
<td>Almost full stomach</td>
<td>PDA</td>
<td>Histiocytic type of malignant lymphoma</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>22</td>
<td>1969</td>
<td>45/M</td>
<td>Lesser curvature, liver, spleen, lung</td>
<td>WDA</td>
<td>Pleomorphic lymphoma</td>
<td>+</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>current</td>
<td>2020</td>
<td>77/M</td>
<td>Caecum</td>
<td>MDA</td>
<td>DLBCL</td>
<td>-</td>
<td>-</td>
<td>EBER(-), IgH rearrangement (+)</td>
</tr>
</tbody>
</table>

MDA: Moderately differentiated adenocarcinoma; PDA: Poorly differentiated adenocarcinoma; WDA: Well differentiated adenocarcinoma; NA: Not available (Not mentioned in the article); n: Cancer and lymphoma are not in the same tumor; NRM: No recurrence and metastasis; LLC: Lymphoepithelioma-like carcinoma; SRCC: signet-ring cell carcinoma.
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dge whether the current treatment was effective for a long time or caused other harm. However, through a comprehensive analysis of the literature [1-21], we found that the treatment of collision tumors requires simultaneous treatment of the two tumor components, mainly surgical resection combined with radiotherapy and chemotherapy. For the adenocarcinoma component, if it is well-differentiated, there is no need to perform radiotherapy and chemotherapy for cancer after resection. If it is a cancer with lymph node metastasis or even distant metastasis, adjuvant radiotherapy and chemotherapy can be carried out after surgery if the physical condition allows. For lymphoma components, the corresponding chemotherapy regimen is added according to the different types of lymphoma.

Two patients of the 23 cases had liver metastasis (one with adenocarcinoma component metastasis, the other unknown), and 6 patients died. The liver is the most common site of gastrointestinal cancer metastasis [2, 8]. After the resection of poorly differentiated or advanced gastrointestinal cancer, if not supplemented by radiotherapy and chemotherapy, it may relapse or metastasize [2]. 6 deceased patients had the 4 following conditions: high-grade cancer or lymphoma; the tumor was found to be in a state of spread; radiotherapy and chemotherapy could not be carried out after surgical resection due to individual reasons; and missed diagnosis of lymphoma components [1, 9, 12, 13, 15, 21]. Therefore, it is inferred that the prognosis of patients with collision tumor depends on the highest grade and stage of the two collision components, and is also closely related to comprehensive and appropriate treatment [15, 21].

In sum, due to the rarity of collision tumors with carcinoma and lymphoma in gastrointestinal tract, the pathogenesis and optimal treatment still need further exploration. In the daily pathologic diagnosis, we should be aware of this kind of tumor and avoid missed diagnosis and misdiagnosis.

Disclosure of conflict of interest

None.

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