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【 CASE REPORT 】

Anisakiasis in the Small Intestine with Excessive Bleeding That Was Difficult to Diagnose Endoscopically

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Abstract:
Anisakiasis involves the stomach in most cases and occurs rarely in the small intestine. Anisakiasis in the small intestine is associated with abdominal pain and obstruction and is rarely associated with intestinal bleeding. Unlike in the stomach, anisakiasis in the small intestine is difficult to diagnose anatomically. The patient in this case study developed hypovolemic shock due to excessive bleeding and underwent emergency surgery. With the recent increase in the consumption of raw fish around the world, this report provides an important finding of bleeding in the small intestine due to an unknown cause.

Key words: anisakiasis, hypovolemic shock, intestinal bleeding, intestinal resection

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Introduction

Bleeding in the small intestine contributes to 2-10% of all cases of intestinal bleeding (1, 2). Bleeding in the small intestine in patients between the ages of 41 and 64 years has been attributed to the presence of vascular lesions (35%), tumors in the small intestine (31%), non-specific causes (10%), and ulcers (9%) (1). There are 2,000-3,000 annual cases of anisakiasis in Japan. In addition, with the increasing popularity of Japanese cuisine, the incidence of anisakiasis has become more frequent outside of Japan due to the increased consumption of raw fish (3-5). In general, anisakiasis in the small intestine is associated with various symptoms, such as abdominal pain and obstruction, while only 2% of these cases are associated with intestinal bleeding (6). The diagnosis of anisakiasis in the small intestine based on anatomical findings is extremely challenging. Thus, it is important to obtain information on the dietary history of a patient.

We herein report a valuable case of anisakiasis in the small intestine with hypovolemic shock that was difficult to diagnose endoscopically. The patient required emergency surgery and recovered. To our knowledge, there have been no reports of anisakiasis in the small intestine that was associated with hypovolemic shock.

Case Report

The patient was a 54-year-old man with no medical history of note. He noted a large amount of blood in his stool two days after consuming sushi (raw fish). He also temporarily lost consciousness and developed a cold sweat, and he was admitted to our emergency department.

On a physical examination, his abdomen was flat with mild tenderness but no guarding. His blood pressure was low (74/52 mmHg), and blood tests indicated anemia with a hemoglobin (Hgb) level of 10.0 g/dL. Computed tomography (CT) showed multiple diverticula in the ascending colon, but the primary site of bleeding was unclear. Emergency lower gastrointestinal endoscopy was performed, showing a large pool of blood in the colon. Diverticular hemorrhaging from the ascending colon was suspected; however, the primary site of bleeding could not be determined.

Since his hemodynamic condition was stable following transfusion, conservative treatment was initiated. However, he had a large amount of blood in his stool again the next

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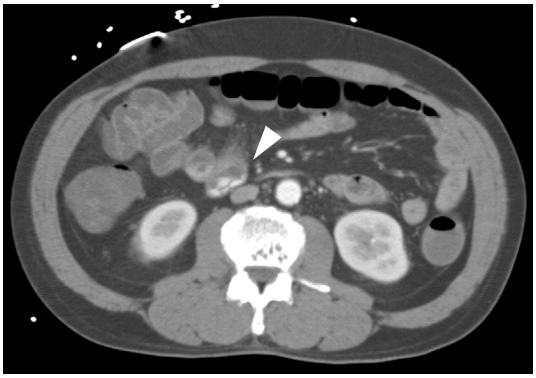

Figure 1. **Leakage of contrast is seen in the ileum on the second emergency computed tomography examination. This location was determined to be the primary site of bleeding (arrowhead).**

Figure 3. **An ulcer raised by approximately 3 cm is identified in the ileum (arrowhead). Anisakis larvae were not found.**

day. This suggested the possibility of bleeding from the small intestine, and anterograde and retrograde single-balloon enteroscopy (SBE) was performed urgently. The primary site of bleeding could not be identified even with SBE, and the deepest points of reach were marked for both routes with India ink. Since bleeding could have occurred in the small intestine between the marked points, capsule endoscopy (CE) was performed while the patient remained on transfusion. After 12 hours, he had a large amount of blood in his stool for the third time, with the Hgb level decreasing to 4.5 g/dL. The CE findings were affected by the low visibility due to the large pool of blood. He underwent another CT examination to identify the primary site of bleeding. Contrast enhancement was identified in the small intestine, suggesting that the small intestine was the primary site of bleeding (Fig. 1).

Given that it was difficult to identify the site of bleeding endoscopically and the bleeding could not be stopped, emergency surgery was performed. Intraoperatively, an ulcerated, raised nodule was found between the marked deepest points of reach for anterograde and retrograde SBE. This was determined to be the primary site of bleeding, and 20 cm of the ileum 300 cm from the ligament of Treitz were resected (Fig. 2). An ulcer that was raised by approximately 3 cm was identified in the resected specimen (Fig. 3). Necrotic granulation tissue with massive infiltration of eosinophils

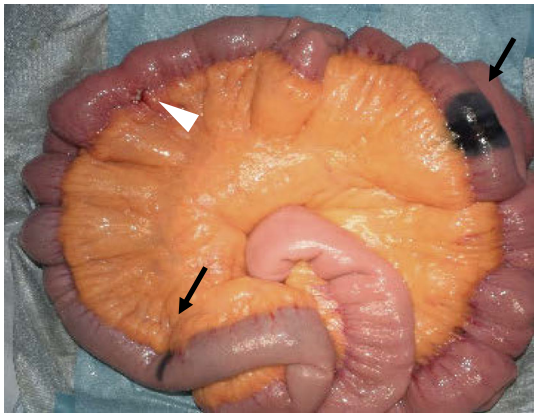

Figure 2. **The deepest points of reach in anterograde and retrograde single balloon enteroscopy are marked with India ink (arrow). A raised ulcer is found between the marked points, suggesting that this was the primary site of bleeding (arrowhead).**

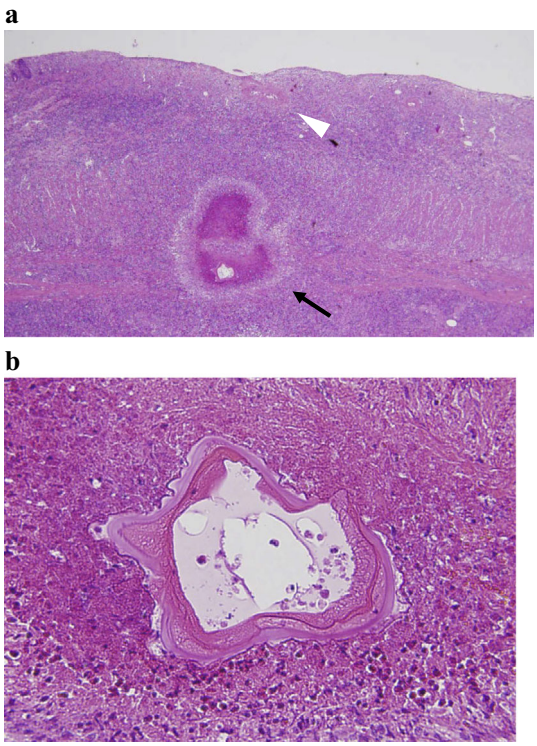

Figure 4. **a: Hematoxylin and Eosin (H&E) staining, ×100. The ulcer has formed beyond the muscularis mucosae, and the vessels are exposed (arrowhead). Massive infiltration of inflammatory cells is found from the submucosa to the muscular layer, and necrotic granulation tissue is found in the center. The necrotic tissue shows a cuticular structure (arrow). b: H&E staining, ×400. High-magnification image of the cuticular structure. There are no Anisakis larvae inside the structure.**

and lymphocytes was found from the submucosa to the muscular layer, and the tissue had a cuticular structure characteristic of nematodes, such as Anisakis (Fig. 4). The Anisakis larvae had likely been removed spontaneously by the repeated examinations and excessive bleeding. He tested

positive for anti-Anisakis IgE antibody (1.45 Ua/mL, normal range: <0.34 Ua/mL) two weeks after his symptoms developed. This finding, along with the postoperative pathological data and the clinical course of the patient, suggested that he had anisakiasis. He recovered postoperatively and was discharged on postoperative day 4.

Discussion

Bleeding in the small intestine is mainly caused by erosions, ulcers, vascular malformations, diverticula, and inflammatory bowel disease (7). Annually, about 20,000 cases of anisakiasis are reported around the world; of these cases, 90% involve the stomach, and only 4-5% involve the small intestine (2, 6, 8). The low incidence of anisakiasis in the small intestine may be attributed to the fact that Anisakis migration from the stomach into the small intestine occurs rarely and that Anisakis can easily be found endoscopically in the stomach (9).

Anisakiasis in the small intestine is associated with various symptoms, such as abdominal pain and obstruction (10-14). Specifically, they include intestinal obstruction (50.7%), perforation (8%), and intestinal bleeding (2%), with only about 7% of these cases treated surgically, like the patient in the present report (15). Studies have reported that the time from the consumption of raw fish to the development of abdominal pain is 12-24 hours for gastric anisakiasis and 5-7 days for intestinal anisakiasis (3, 4, 9, 16). Symptoms associated with intestinal anisakiasis, such as intestinal edema and obstruction, are often mistakenly considered non-specific abdominal pain (5, 10, 14). In the present case, emergency surgery was performed because the patient had an ulcer with exposed vessels in the ileum and eventually developed hypovolemic shock with a large amount of blood in his stool. Angiography was difficult due to intermittent massive bleeding and unstable condition.

The resected specimen suggested that Anisakis contributed to blood in his stool. Because Anisakis larvae had invaded the gut wall, the infiltration of inflammatory cells formed the ulcer. The rupture of exposed blood vessels at the ulcer caused massive bleeding. The primary site of bleeding was deep in the small intestine, making it difficult to diagnose the patient endoscopically. Ooka et al. reported that SBE is superior to CE for identifying the primary site of bleeding, with 73.6% and 47.5% of cases identified, respectively (7). In the present case, it was not possible to identify the location despite multiple endoscopic examinations; this may be because the primary site of bleeding was in the small intestine between the deepest points of reach for both the anterograde and retrograde routes, and the visibility was significantly reduced due to the large amount of blood in the stool. However the entire small intestine can only be examined in 16.7% of cases with SBE (17); in this case, it was possible to identify contrast enhancement in the small intestine due to bleeding on a repeat CT examination. When the site of bleeding deep in the small intestine cannot be identified with various examinations, a repeat CT examination might be useful for identifying the bleeding site. Chang et al. reported that the sensitivity for CT in diagnosing obscure acute gastrointestinal bleeding was 81% in patients who needed transfusion (18). However, emergency operation should be considered when it is difficult to identify the site of bleeding with a repeat CT examination.

Anisakiasis in the small intestine is difficult to diagnose; it is therefore important to obtain information on the recent dietary history of a patient (15, 16). If a patient has a recent history of consuming raw sea fish such as salmon and mackerel, examinations should be performed to detect the presence of anti-Anisakis antibody in paired serum, as well as the presence of Anisakis larvae by endoscopy. The present patient did not show an increase in the amount of anti-Anisakis IgE antibody in paired serum, with a level of 1.34 Ua/mL 6 weeks after the development of symptoms. While it is difficult to rule out the possibility of an infection that was already present, the dietary history of the patient and the pathological findings, including significant infiltration of inflammatory cells, edema, formation of granulation, and cuticular structure characteristic of nematodes such as Anisakis and Gnathostoma, were consistent with a diagnosis of anisakiasis (19). Filauro et al. reported a case of anisakiasis diagnosed based on a history of raw fish consumption and pathological findings of granulation, with neither the presence of Anisakis larvae nor anti-Anisakis antibody detected in paired serum (20). In the present study, anisakiasis was suspected based on the dietary history of the patient and the pathological findings of a cuticular structure characteristic of nematodes such as Anisakis; the Anisakis larvae had likely been removed spontaneously by the repeated examinations and excessive bleeding. Yoon et al. reported that the production of anti-Anisakis antibody may be insufficient with a short incubation period (12). Since the patient developed symptoms only two days after consuming raw fish, the incubation period may have been too short to allow the production of a detectable amount of antibody.

There are 2,000-3,000 annual cases of anisakiasis reported in Japan. With the increasing popularity of Japanese cuisine, the incidence of anisakiasis has become more frequent outside of Japan due to the increased consumption of raw fish (3-5). In Japan, gastric infection primarily occurs, whereas intestinal disease is more common in Europe (20, 21). While anisakiasis in the small intestine is rare, excessive bleeding may occur in some cases, as seen in the present study. In countries where the consumption of raw fish is common, anisakiasis in the small intestine should be considered when examining a patient who presents with bleeding deep in the small intestine due to an unknown cause.

Conclusion

We herein report a valuable case of anisakiasis in the small intestine in a patient who had a large amount of blood in his stool two days after consuming sushi (raw fish).

While anisakiasis in the small intestine is rare, excessive bleeding may occur in some cases. With the recent increase in the consumption of raw fish around the world, this report provides an important finding of bleeding in the small intestine due to an unknown cause.

The authors state that they have no Conflict of Interest (COI).

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