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**Differences in examination results of small anastomotic fistula after radical gastrectomy with afterward treatments: A case report**

Lu CY *et al.* Examinations and treatments of EJF

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**Abstract****BACKGROUND**

Gastrografen swallow, methylthioninium chloride test, and computed tomography (CT) are the main methods for postoperative anastomotic fistula detection. Correct selection and application of examinations and therapies are significant for the early diagnosis and treatment of small anastomotic fistulas after radical gastrectomy, which are conducive to postoperative recovery.

**CASE SUMMARY**

A 44-year-old woman underwent radical total gastrectomy for laparoscopic gastric cancer. The patient developed a fever after surgery. The methylthioninium chloride test and early CT suggested no anastomotic fistula, but gastrografen swallow and late CT showed the opposite result. The fistula was successfully closed using an endoscopic clip. The methylthioninium chloride test, gastrografen, and CT performed on different postoperative dates for small esophagojejunostomy fistulas are different. The size of the anastomotic fistula is an important factor for the success of endoscopic treatment.

**CONCLUSION**

The advantages and limitations of the diagnosis of different examinations of small esophagojejunosomy fistulas are noteworthy. The size of the leakage of the anastomosis is an important basis for selecting the repair method.

**Key Words:** Laparoscopic; Gastrectomy; Anastomotic leak; Methylthioninium chloride; Gastrografin; Esophagojejunal anastomotic fistula; Case report

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**Core Tip:** Gastrointestinal anastomotic fistula is one of the major complications after gastrointestinal anastomosis. The early diagnosis of small anastomotic fistulas and the choice of treatment are particularly important. We reported a case of a gastrointestinal anastomotic fistula that was not easily diagnosed at an early stage and discussed the advantages and limitations of the current main methods of examination in the context of medical imaging. In addition, we discussed the appropriate treatment for different anastomotic fistulas.

## **INTRODUCTION**

Esophagojejunal anastomotic fistula (EJF) is a major complication of radical gastrectomy. Mediastinal and lung infections are often seen in patients with EJF, which seriously endanger the health of patients<sup>[1]</sup>. The reported rates of the EJF after radical gastrectomy vary from 0% to 5.8%, with 0% to 5.8% after laparoscopic, 0% to 3.4% after robotic surgery, and 0% to 5.8% after open surgery<sup>[2-6]</sup>. The mortality rate was 26.32%<sup>[7]</sup>. Gastrografin swallow, methylthioninium chloride test, and computed tomography (CT) are currently the main means of postoperative anastomotic fistula detection at present. The treatment of anastomotic fistula mainly includes endoscopic clamping, stent placement, tissue sealant filling, and surgical re-operation if necessary<sup>[8]</sup>. Correct

selection and application of examinations and therapies are significant for the early diagnosis and treatment of small anastomotic fistulas after radical gastrectomy, which are conducive to postoperative recovery.

Based on the diagnosis and treatment process of a patient with anastomotic fistula after radical gastrectomy for gastric cancer, we discuss the main diagnosis and treatment methods of anastomotic fistulas in depth, which is conducive to the timely diagnosis and accurate treatment of postoperative anastomotic fistula.

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## **CASE PRESENTATION**

### ***Chief complaints***

A 44-year-old woman presented to the Department of Gastrointestinal Surgery of our hospital complaining of upper epigastric pain.

### ***History of present illness***

Patient's symptoms started 2 months ago, usually between meals. Acid burps or acid belching can occasionally occur. Antacids usually resolve her symptoms. Gastroscopy and biopsy were performed 10 days ago, and gastroscopy revealed a stage A1 gastric ulcer with bleeding. In addition, biopsy showed abnormal cell proliferation and infiltration between the inherent glands of the gastric mucosa, which indicated a poorly differentiated adenocarcinoma (Figure 1). A contrast-enhanced abdomen CT scan showed local thickening of the gastric wall along the greater curvature of the gastric body, enlarged small lymph nodes around the stomach, and multiple enlarged lymph nodes enlarged in the mesentery.

The patient underwent laparoscopic radical gastrectomy (total gastrectomy Roux-en-Y anastomotic regional lymph node dissection) + jejunostomy + cholecystectomy + splenic hilar lymph node dissection. Side-to-side anastomosis between the oesophagus and jejunum was performed. She developed a persistent fever after surgery, which meant she started having a fever on the postoperative day 1 and was unable to reduce it to a normal temperature on her own.

### ***History of past illness***

The patient had a free previous medical history.

### ***Personal and family history***

The patient had no personal or family history related to gastric cancer and anastomotic fistula.

### ***Physical examination***

Physical examination revealed mild tenderness in the upper abdomen without rebound pain. She developed a persistent fever after surgery, which cannot be completely cured by physical cooling and the use of antibiotics (Figure 2).

### ***Laboratory examinations***

A severe leukocytosis  $25.69 \times 10^9/L$  appeared on postoperative day 1, with predominant neutrophils (90.20%), which indicated a possible bacterial infection. A similar situation persisted until postoperative day 4, which was the third day after Cefoperazone Sodium and Sulbactam Sodium was given to the patient. Since then, blood analysis has consistently revealed a mild leukocytosis. Ciprofloxacin was applied on postoperative day 15, after which the infection indicators dropped to normal.

### ***Imaging examinations***

On postoperative day 4, CT showed dilatation of the esophagus, duodenum, and jejunum with effusion. A small amount of ascites was found around the spleen, and pleural effusion was observed. On postoperative day 6, after the patient received oral methylthioninium chloride, there was no blue fluid draining from the tube. The CT and oral methylthioninium chloride results suggest that the anastomosis appears to be well closed (Figure 3A). However, despite the use of various anti-inflammatory treatments over the following few days, the patient's symptoms were not relieved. Therefore, CT

was performed again on the postoperative day 13, and showed that the anastomotic site at the lower end of the oesophagus was thickened and blurred, and the right parastinastinal cystoid air cavity was connected to the anastomotic site (Figure 3B).

#### ***Further diagnostic work-up***

Gastrografen swallow on postoperative day 13 was used to confirm the diagnosis of anastomotic fistula (Figure 4A).

#### ***Microbiological identification of the causative agent***

Sputum culture was performed on postoperative day 9. The *Ralstonia mannitolilytica* infection was reported on postoperative day 14, which was sensitive for Ciprofloxacin.

#### **FINAL DIAGNOSIS**

The possibility of anastomotic fistula was highly considered.

#### **TREATMENT**

After ciprofloxacin had controlled the infection, endoscopic metal clip therapy was performed on postoperative day 23 to clamp the anastomotic fistula. And meglumine diatrizoate esophagogram showed no anastomotic fistula (Figure 4B).

#### **OUTCOME AND FOLLOW-UP**

After the application of antibiotics and clamping of the anastomotic fistula, the infection of the patient was gradually controlled on the postoperative day 24. Since then, anastomotic fistulas related signs did not appear again.

#### **DISCUSSION**

A 44-year-old woman developed a persistent fever after laparoscopic radical total gastrectomy for gastric cancer. The methylthioninium chloride test and early CT suggested no anastomotic fistula; however, gastrografen swallow and late CT showed

the opposite result. The fistula was successfully closed using an endoscopic clip. The methylthioninium chloride test, gastrografin, and CT performed on different postoperative dates for small esophagojejunostomy fistulas are different. The size of the anastomotic fistula is an important factor for the success of endoscopic treatment.

The reported rates of the EJJ after radical gastrectomy vary from 0% to 5.8%<sup>[2-6]</sup>, and with a mortality rate of 26.32%<sup>[7]</sup>, which is one of the main causes of postoperative sepsis<sup>[9]</sup>. EJJ usually occurs near the suture line. Cardiovascular disease, age, smoking, malnutrition, operative hormones, local blood supply, and inflammatory reactions to suture materials are the risk factors for anastomotic fistulas<sup>[6]</sup>. However, the effect of tumour stage and the timing of lymph node dissection on the incidence of anastomotic fistula remains controversial<sup>[10,11]</sup>. Anastomotic fistulas can be classified based on the time of onset, clinical presentation, site of anastomotic fistula, radio-appearance, and mixed factors<sup>[12]</sup> (Table 1), which are critical for selecting diagnosis and treatment.

There is no gold standard for the diagnosing anastomotic fistulas. The most common manifestations of intraperitoneal complications of anastomotic fistula include signs of sepsis and laboratory signs (leukocytosis and elevated C-reactive protein levels) postoperative 7 to 10<sup>[13]</sup>. In this case, the persistent postoperative fever suggested a possible anastomotic fistula. To detect anastomotic fistula, air leak testing and transgastric methylthioninium chloride injection were used during the surgery, but Sethi *et al* believed that intraoperative leak testing has no correlation with leak due to laparoscopic sleeve gastrectomy<sup>[14]</sup>. Postoperative examination of the anastomotic fistula is important. Gastrografin swallow, methylthioninium chloride test, and CT are the main means of postoperative anastomotic fistula detection at present<sup>[15,16]</sup>. Many studies have shown that postoperative gastrografin swallow and methylthioninium chloride test were effective in confirming clinical evidence of anastomotic fistula<sup>[15]</sup>. The methylthioninium chloride test was performed on the postoperative day 6 and showed a negative result, while the result of gastrografin swallow on postoperative day 22 was positive. Although the sensitivity of gastrografin swallow was higher than that of the methylthioninium chloride test, it had a high false-negative rate<sup>[16]</sup>. Some studies found



that CT had more advantages in diagnosing anastomotic fistulas than gastrografin swallow and methylthioninium chloride test<sup>[17]</sup>. Oral contrast agents may also be used to increase the sensitivity to CT<sup>[18]</sup>. Factors associated with the CT-based diagnosis of anastomotic fistula include mediastinal fluid, mediastinal air, wall discontinuity, and fistula. However, isolated mediastinal gas can be observed in patients without any leakage, which is a common finding after surgery and the diagnostic value of CT in different postoperative periods for anastomotic fistulas is also different<sup>[17]</sup>. In this case, CT was performed on postoperative days 4 and 14. Notably, the examination result indicated anastomotic leakage on postoperative day 14. Although some studies have discussed the CT-based diagnostic score for anastomotic fistula and the diagnostic value of radiographic image details, such as the differences in the number of bubbles around the anastomosis and the mediastinal space, CT cannot completely replace other diagnostic methods<sup>[17,19]</sup>.

The treatment of anastomotic fistulas mainly includes endoscopic clamping, stent placement, and tissue sealant filling. The use of fibrin to promote the healing of anastomotic fistulas had a good clinical effect, while other researchers believed that it was only due to the mechanical sealing<sup>[20,21]</sup>. The actual therapeutic gold standard for postoperative oesophageal anastomotic fistulas is stent implantation<sup>[22]</sup>. Endoscopic clipping is another treatment for postoperative anastomotic fistula, which is suitable for anastomotic fistulas with small circumferences and ineffective conservative treatment. <sup>3</sup> Two types of clips, through-the-scope clip (TTSC) and over-the-scope clip (OTSC), were used for endoscopic clipping. Anastomotic fistulas less than 10 mm in diameter are recommended to be clipped using a single TTSC<sup>[23]</sup>. Meanwhile, TTSCs and OTSCs have a high clipping success rate in anastomotic fistulas with a diameter of 10 to 20 mm<sup>[24,25]</sup>. Due to the limitation of the clip arm width and grasping force, TTSC is only applicable to anastomotic fistulas of less than 20 mm in diameter with healthy non-everted regular edges<sup>[26]</sup>. However, OTSCs have high clinical success rates for large anastomotic fistulas of up to 30 mm in diameter<sup>[24]</sup>. Anastomotic fistulas larger than 30mm in diameter are difficult to be clipped by endoscopy<sup>[27]</sup>. Endoscopic vacuum



therapy (EVT) was introduced 10 years ago to treat anastomotic fistulas, and it has a higher closure rate than stent implantation<sup>[28]</sup>. Anastomotic fistula associated with fluid collection is a common indication for EVT, and EVT has a higher cure rate than stents for this type of anastomotic fistulas<sup>[27,29]</sup>. However, EVT requires frequent replacement of endoscopic devices, which means a higher risk for recurrent sedation. Hence, the correct choice of repair method is helpful in avoiding repeated surgeries. The European Society of Gastrointestinal Endoscopy (ESGE) recommends to consider endoscopic closure based on the type and size of the anastomotic fistula, the presence and characteristics of leaking fluid, the general situation of the patient, and the endoscopy expertise available at the center<sup>[27]</sup>.

## **CONCLUSION**

Early diagnosis of the small anastomotic fistulas is particularly important for the patient prognosis. Current studies suggest that the sensitivity of CT is higher than that of Gastrografin swallow and methylthioninium chloride tests; however, it cannot be used as the gold standard for the diagnosis of anastomotic fistula. Accurate diagnosis of anastomotic fistula should be combined with clinical manifestations and appropriate examination methods should be selected to avoid false results. The selection of anastomotic fistula repair should be conducted according to the ESGE recommendations. Endoscopic therapy, including stent placement, endoscopic clipping, and vacuum therapy, is preferred for patients with stable leakage and without peritonitis.

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