Long-term Inflammatory Stimulation Caused by Trauma May Lead to Jejunum Intestinal Stromal Tumor: A Case Report

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Case Report

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Abstract

Background: Gastrointestinal stromal tumor (GIST) is the most common stromal tumor of the gastrointestinal tract and it is considered to be an aggressive tumor with potentially malignant tendency. GIST is a tumor derived from mesenchymal tissue of the gastrointestinal tract or rarely of intraperitoneal soft tissue. Stem cajal cells from the muscular layer of the digestive tract are the precursor cells of GIST, which are pacemaker cells that cause the intestinal peristalsis and contract. The etiology of GIST is mainly caused by mutations in the KIT or PDGFRA oncogene. Although some papers reported that inflammation can cause tumor formation, it has not been reported that inflammation can cause GIST formation.

Case presentation: A 64-year-old male patient was evaluated for recurrent dull pain and discomfort in the left upper abdomen. He had a history of abdominal trauma approximately six years prior. During this period, abdominal pain and fever were intermittent recurrent attacked. Intraoperative jejunum tumors were found to have inflammatory packages. Postoperative pathological examinations showed that the tumor envelope was intact and a large amount of inflammatory cells were seen around the tumor cells. Histopathology of the resected masses was positive for CD117 and Dog-1, and the patient was diagnosed as jejunum GIST.

Conclusion: We reported a case of gastrointestinal stromal tumor that may be caused by repeated stimulation of chronic inflammation that caused by trauma. Early detection and timely removal of the inducement of repeated chronic inflammation can effectively prevent the occurrence of GIST.

Background

The incidence of gastrointestinal stromal tumors (GIST) accounts for approximately 2% of all gastrointestinal tumors, GIST occurs in 10–20 cases per million people, of which 20–30% have malignant features, and GIST is originated from Cajal interstitial cells or common precursor cells in the tendon plexus of the gastrointestinal tract, both of which express type III tyrosine kinase receptors [1]. Activating mutations of membrane receptor KIT or platelet-derived growth factor A (PDGFRA) lead to uncontrolled cell growth and gastrointestinal stromal tumor formation [2]. GIST became the first reliable target tumor for tyrosine kinase inhibitor treatment [3]. GIST shows unpredictable malignant potential and tends to recurrence and the possibility of distant metastasis[4].Most cases of GIST are sporadic and have no obvious risk factors, although the incidence is increased in the context of some special tumor syndromes, such as familial GIST, Carney 's triad, Carney-Stratakis syndrome, Type 1 neurofibromatosis. The molecular events that led to GIST were sporadic [1]. Therefore, it is of great significance to explore the pathogenesis of GIST, and to our knowledge,there is no literature report on the relationship between inflammation and GIST. This case reported a case of gastrointestinal stromal tumor that may be caused by repeated stimulation of chronic inflammation that caused by trauma.

Case Presentation

A 64-year-old male patient came to our hospital because of recurrent dull pain and discomfort in the left upper abdomen for six years. The patient has no family history of tumor. Six years prior, the patient suffered from abdominal pain in the injured area due to a bull bump in his left upper abdomen. Abdominal pain relieved after two days of bed rest at home after injury, no special treatment. Afterwards, dull pain and discomfort appeared repeatedly in the injured area. When the pain worsens, it is often accompanied with low-grade fever. The symptoms were relieved by oral non-steroidal anti-inflammatory drugs at home. In the past 10 days, the abdominal pain worsened and came to the hospital.

On admission examination, the temperature was 38.3°C, the pulse 98 beats per minute, and the blood pressure 128/84 mmHg. Abdominal examination: flat abdomen, no gastrointestinal and peristaltic waves, a mass of about 4.5 ·5.0 cm in size can be palpable under the ribs of the left upper abdomen, hard, clear boundary, poor mobility, local tenderness, no tenderness and muscle tension, liver and spleen not palpable on palpation, there is no percussion pain in the liver and kidney area. Blood routine: WBC $11.04 \cdot 10^9/L$, N 0.87, HGB 112 g/L, no other obvious abnormalities.

Abdominal computed tomography (CT) scan showed a solid cystic mass of 4.4 ·4.9 cm in the upper left middle and upper abdomen, mainly cystic, with a partition inside, the solid part of the enhanced scan and the partition were significantly enhanced, and the tumor and the surrounding bowel were unclear. A small amount of gas density shadow is seen, the density of the surrounding fat interstices increases and a small amount of flocculent density shadow was seen (Fig. 1a).

Patient underwent abdominal tumor resection. Intra-operatively, there was a huge cystic solid mass in the upper left upper abdomen, located in the upper part of the jejunum, was hard in quality, and was closely connected to the middle mesangium, omentum and middle part of the jejunum, small intestine dilation and edema at the lesion site, and no abnormalities in the rest of the intestine. Tumor on the opposite side of the small intestine with omentum wrapping around (Fig. 1b); The maximum diameter of the tumor is 4.8 cm, postoperative anatomy of the tumor (Fig. 1c): the green circle is the intestinal wall tissue, the red circle is the small intestine perforation site, and the black circle is the inflammation around the perforation, the blue circle is the tumor tissue.

Microscopic examination revealed that the tumors were arranged in a spindle shape (Fig. 2a and 2b) and surrounded by a large number of chronic inflammatory cells (Fig. 2c). The results of immunohistochemistry showed the following antibody expression: CD117(++)(Fig. 3a), Dog-1(++)(Fig. 3b), CD34(++)(Fig. 3c), Bcl-2(+), SDH(+++), Vimentin(+), CD99(-), CgA(-), CD56(-), Desmin(-), S100(-), CK(-), SMA(-), STAT6(-), Syn(-) and Ki-67(+ 20%)(Fig. 3d). The mitotic figures were greater than 5/50 high power fields. The patient was diagnosed with jejunal GIST and was treated with oral imatinib(400 mg/d) after the operation. The patient was followed up for 1 year without tumor recurrence.

Discussion And Conclusions

Gastrointestinal stromal tumor (GIST) is a clinically heterogeneous disease with highly variable malignant potential. GIST can occur throughout the gastrointestinal tract, most of it in activating mutations of KIT or platelet-derived growth factor A (PDGFRA) genes, and it was mainly diagnosed by cell morphology and immunohistochemistry [1]. In this case, a large number of spindle cells were seen in the tumor (Fig. 2), and immunohistochemistry showed that CD117 and Dog-1 were positive (Fig. 3a and 3b). CgA and CD56 were negative, excluding neurogenic tumors, Desmin and S-100 were negative, excluding smooth muscle tumors[5]. Therefore, this case was diagnosed as GIST in jejunum. However, in this case, chronic inflammation and GIST appeared in the same site. To clarify their relationship is very helpful for the diagnosis and treatment of the disease and the prevention of GIST. There were three possibilities for their relationship: i) inflammation caused GIST; ii) GIST caused inflammation; iii) GIST and inflammation coexist alone.

i). This study supported GIST caused by repeated stimulation of chronic inflammation. This patient developed intermittent abdominal pain and fever after abdominal trauma, and the recurrence occurred within six years, which was relieved by oral non-steroidal anti-inflammatory drugs at home. While gastrointestinal stromal tumors caused obvious symptoms at 5 cm-10cm[6, 7]. Combined with the long duration of symptoms in this case, abdominal pain and fever can only be caused by repeated stimulation of inflammation caused by perforation after trauma; CT of the admitted abdomen revealed a solid cystic mass in the upper and middle abdomen, mainly cystic, with separation seen inside, and the solid part and separation of the enhanced scan were significantly enhanced. The boundary between the mass and the surrounding intestine was unclear, and a small amount of air density was seen in the surrounding area. Fat interstitial density increased and a small amount of flocculent density shadow was seen (Fig. 1a). During surgery, the tumor envelope on the contralateral side of the small intestine mesentery was intact, with omentum wrapping around it (Fig. 1b); The general anatomy of the isolated tumor (Fig. 1c) showed that the tumor envelope was intact, and perforation, inflammatory tissue, and a little pus can be seen at the edge of the tumor, combined with the patient's injury history, it is considered that the inflamed tissue contains GIST, and the small amount of gas is considered to be caused by intestinal perforation. Although there are reports in the literature that GIST can have rare clinical symptoms such as intestinal obstruction, perforation or rupture, abscess and intestinal fistula, etc., it is reported that GIST with the above-mentioned symptoms usually has a tumor diameter greater than 5 cm, even greater than 10 cm[6, 7]. And necrosis of small intestine GIST is generally central liquefaction necrosis [8]; Therefore, it is considered that inflammation stimulus and perforation accompanied with formation of abscess cavity after injury, and speculated that the chronic inflammation of the tumor edge is caused by infection caused by trauma. HE staining of postoperative sections showed tumor cells (Fig. 2b) and a large number of inflammatory cells (Fig. 2c); Recent studies reported that inflammation caused KIT or PDGFRA gene mutations[9, 10], Lisa W. Witten et al.[9] reported that miR-155 overexpression played an important role in inflammation and found that the KIT gene was mutated; Huss S et al.[10] reported that inflammatory fibrous polyps often accompany PDGFRA exons 12 and 18 Mutations, and the membrane receptor KIT or PDGFRA mutations can lead to uncontrolled cell growth and stromal tumor formation [2]. Therefore, this case report believes that trauma caused inflammation, which can lead to mutations in KIT

or PDGFRA genes, and further led to the formation of gastrointestinal stromal tumors. The general anatomy of the tumor (Fig. 1c) showed that the tumor capsule was intact, with a little pus and inflammatory tissue at the edge of the perforation. Therefore, it is considered that inflammation irritation and perforation accompanied with abscess formation after injury. The above speculates that the chronic inflammation of the tumor margin is caused by infection caused by trauma.

ii). Does GIST cause inflammation? The most common symptoms of GIST are bleeding into the intestine or abdominal cavity, anemia, and abdominal pain, other symptoms include indigestion, nausea or vomiting, constipation or diarrhea, frequent urination, and fatigue [1]. There are reports in the literature that GIST can have rare manifestations such as intestinal obstruction, perforation or rupture, abscess and intestinal fistula [11, 12]. However, if it is inflammation caused by GIST, such as abscess formation, it is usually acute and often accompanied by tumor central necrosis and rupture [8]. This patient has been suffering from intermittent abdominal pain and fever for 6 years, and the pathological examination of the capsule is intact. The tumor has no signs of necrosis or ulceration. A large number of inflammatory packages are seen on the edge of the tumor, suggesting that chronic inflammation is caused by repeated stimulation. For example, Chen et al.[12] and Misawa S et al. [13] reported the appearance of necrotic ulcers or abscesses in GIST. The tumor was large and had acute inflammation symptoms, which was inconsistent with the persistence of repeated chronic inflammation in this case. The above view does not support the formation of inflammation caused by GIST.

iii). If GIST occurs and chronic inflammation caused by trauma independently of each other, they usually occur in different locations. but this case occurs in the same location, although studies have reported the possibility of GIST and inflammation being parallel to each other[14]. Theodoropoulos GE et al. [15]reported that a patient with ulcerative colitis was diagnosed with GIST after surgery due to jejunoileum intussusception, but another study found that patients with inflammatory bowel disease (IBD) had an increased risk of cancer, especially it is for patients taking immunosuppressive agents[16]. Most cancers occur in the site of inflammation and have experienced the sequence of inflammation-dysplasia-cancer [17, 18]. Many studies [18, 19]reported that some inflammatory factors can change the tumor microenvironment and promote tumor survival. Cavnar MJ. [20]found that depletion of tumor-associated macrophages with similar functions to type I macrophages can increase tumor size in GIST mice. The above view does not support the independent occurrence of chronic inflammation and GIST, and it supports the possibility that chronic inflammation may cause GIST to be generated by repeated long-term stimulation of chronic inflammation.

For the treatment of GIST, surgery is the first treatment option. Tyrosine kinase inhibitors such as imatinib are used for neoadjuvant treatment of potentially resectable tumors and high-risk tumors after surgery, or as palliative treatment. The prognosis of the patient depends on the size of the tumor, the mitotic image, and the preservation of the pseudocapsule. In this case, the diameter of the tumor was 4.8 cm, and the mitotic figure > 5/50 HPF was defined as a medium-to-high prognosis risk factor. Imatinib was taken orally after the operation, and no recurrence was found after one year of follow-up.

In summary, we reported a case of intestinal perforation caused by trauma, which resulted in abscess formation accompanied by long-term chronic inflammation. GIST is mainly formed by activating mutations of the membrane receptor KIT or PDGFRA [2]. We speculate that long-term chronic inflammation can lead to activating mutations of membrane receptor KIT or PDGFRA, which in turn leads to the formation of GIST. Early detection and timely removal of the inducement of repeated chronic inflammation caused by trauma can effectively prevent the occurrence of GIST.

Abbreviations

GIST gastrointestinal stromal tumor

PDGFRA platelet-derived growth factor A

CT computed tomography

IBD inflammatory bowel disease

Declarations

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Authors' contributions

ZJM and WKM involved in drafting manuscript or revising it critically, DCF performed the histopathological diagnosis and the immunohistochemistry. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The case report was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (Zunyi, China). Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

a CT of the abdomen showed a solid cystic mass of 4.4 cm × 4.9 cm in the upper left middle and upper abdomen. The mass was mainly cystic, with a separation seen inside. The solid part and separation of the enhanced scan were obviously enhanced. The tumor and the surrounding bowel were not separated clear, there was a small amount of gas density shadow inside, the density of the surrounding fat gap increases and a small amount of flocculent density shadow was seen. b During the operation, a tumor on the opposite side of the mesentery was seen, with a large omentum wrapping around. c Postoperative dissection of the tumor: the intestinal wall tissue indicated by the green circle, the small intestine perforation indicated by the red circle, the inflammation tissue around the perforation indicated by the black circle, and the tumor tissue indicated by the blue circle.

Figure 2

HE staining image. a Gastrointestinal stromal tumor and surrounding tissues (magnification $\times 100$). b Gastrointestinal stromal tumor tissues (magnification $\times 400$) ; c Chronic inflammation tissues, with a large number of inflammatory cells, indicated by green arrows (magnification $\times 400$).

Figure 3

The results of immunohistochemical image showed the following antibody expression in GIST. a CD117 positive expression (magnification × 100). b DOG1 positive expression (magnification × 100). c CD34 positive expression (magnification × 100). d Ki-67 positive expression was above 20% (magnification × 400).