Spontaneous hemoperitoneum in recurrent jejunal gastrointestinal stromal tumor after imatinib therapy

Dear Editor,

Spontaneous hemoperitoneum from recurrent metastatic gastrointestinal stromal tumor (GIST) has been seldom reported in the literature, and the appropriate management is not conclusive. Herein we present a case of recurrent jejunal GIST after complete resection. After 2 years of tyrosine kinase inhibitor (TKI) therapy, abdominal distension, anemia, and presentation of Cullen’s sign (Fig. 1) developed. Exploratory laparotomy revealed a massive hemoperitoneum and a large amount of necrotic fragile tumors.

In patients with inoperable GIST receiving imatinib, the median time to progression is approximately 2 years. By reducing the tumor burden, resection of the residual GIST might delay or prevent the development of resistant cloning and, theoretically, prolong the time to disease progression. The median time to best response is 3.5 months, and there is little chance of tumor shrinkage after 9 months [1]. Some researchers have proposed surgical intervention should be taken into consideration after 3–9 months of TKI therapy if the disease appears grossly resectable [2]. In our case, general progression of recurrent GIST during imatinib therapy revealed deterioration of antitumor effect, which may be due to acquired resistance from unproved additional mutation.

Tumor bleeding that required intensive treatment was reported to occur in less than 5% of GIST patients who underwent imatinib therapy [3]. The most important symptom suggestive of ruptured GIST is abdominal pain, particularly in association with anemia or hypovolemia [4]. To the best of our knowledge, this is the first case of spontaneous hemoperitoneum during imatinib therapy presenting with the unusual Cullen’s sign. Emergent surgery may be encountered in acute management of internal bleeding induced by imatinib. However, surgery may not be satisfactory under this circumstance. Some authors suggest that tumors become amenable to surgery with prior imatinib therapy, evolving necrosis and localized progression could benefit from surgery to avoid life-threatening complications. The genotype of c-kit mutation is a possible factor indicating the risk of tumor rupture or bleeding induced by imatinib, because the high responsiveness rapidly leads to tumor necrosis. In our case, the large amount of necrotic fragile tumors and lack of gross intact tumor structure found at operation seemed to exhibit a correlation between spontaneous hemoperitoneum and the antitumor effect of imatinib.

Missing the appropriate time of surgical intervention may lead to two consequences: (1) losing the opportunity to

Figure 1. Marked abdominal distension and presentation of Cullen’s sign (edema and bruising around the umbilicus) revealed the development of hemoperitoneum before the exploratory laparotomy. The insert shows great amounts of necrotic fragile tumors (about 1800 g) disseminated in the abdominal cavity and an evacuated massive spontaneous hemoperitoneum.

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reduce the tumor burden to eliminate the chance of developing secondary mutation that may result in acquired resistance; and (2) increasing the risk of tumor rupture from antitumor effect of imatinib or overgrowth of the GIST resulting in life-threatening complications and unfavorable emergent operation. We recommend surgery at 3—9 months after initiation of imatinib therapy, when the TKIs are most effective, for inoperable GIST if the tumor responds well to the target therapy and is grossly resectable. However, more frequent evaluation of the tumor receiving imatinib may be necessary for early detection of large volumes of tumor necrosis, which implies a high risk of tumor rupture and fatal spontaneous hemoperitoneum. To advance the timing of surgical resection may be the best policy in preventing this dangerous situation.

References


Tzu-Chieh Yin
Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Wen-Chieh Fan
Department of Surgery, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

Che-Jen Huang*
Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

*Corresponding author. Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, 100, Tzyou 1st Road, San-Ming District, Kaohsiung 807, Taiwan.
E-mail address: chjehu@kmu.edu.tw (C.-J. Huang)