Case Report

Successful Imatinib Treatment of an Abdominal Compartment Syndrome due to Huge Gastrointestinal Stromal Tumour

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Keywords

Abdominal compartment syndrome · GIST · Imatinib · Intensive care

Abstract

Gastrointestinal stromal tumours (GISTs) are the most common digestive mesenchymal tumours, whose prognosis has been revolutionised by targeted therapies such as oral imatinib. Abdomen compartment syndrome (ACS) is associated with mortality superior to 50% in adults. ACS has never been reported to date in patients with GIST. Specific anti-cancer treatment in critically ill patients in intensive care unit (ICU) remains a matter of debate given the high mortality rate. Here, we report the case of a 58-year-old woman with ACS related to a 40-cm huge GIST and multi-organ failure requiring mechanical ventilation, vasopressive support and haemodialysis. She was treated in emergency with imatinib *via* the naso-gastric tube (day 1), then at day 3 by decompressive laparotomy and

“open abdomen” without any tumour removal. Imaging after 11 days imatinib showed objective tumour response. Because of improvement of multi-organ dysfunctions, the laparotomy was closed at day 14, and the resuscitation procedures were progressively stopped. After discharge from hospital, she survived nearly two years. This is the first case of successful treatment of cancer-associated ACS by targeted therapy and decompressive laparotomy. Imatinib in critically ill patients with GIST may be successful even in presence of multi-organ failure.

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Introduction

Abdominal compartment syndrome (ACS) is defined by systemic dysfunction associated with sustained increased intra-abdominal pressure (IAP) more than 20 mm Hg [1]. Mortality is higher than 90% without treatment and early detection is crucial for obtaining the best therapeutic results. Primary and secondary ACSs are triggered by a condition located in and out of the abdomino-pelvic cavity respectively. The main consequences of ACS include hemodynamic, respiratory and renal dysfunctions. When ACS is due to intra-abdominal tumor, the only effective treatment is abdominal decompression with surgical resection. However, the prognosis is very poor and ~50% of adult patients die in acute phase [2].

Gastrointestinal stromal tumors (GISTs) are the most common digestive mesenchymal tumours [3]. They mainly develop in stomach (60%) and jejunum/ileum (30%), but can occur anywhere along the gastrointestinal tract and peritoneum. The most frequent metastatic sites are liver and peritoneum. GISTs are characterised by activating gain-of-function mutations of *KIT* or *PDGFRA* oncogenes. The successful development of targeted therapies directed against *KIT* and *PDGFRA* receptors (imatinib, sunitinib, regorafenib) has revolutionized the treatment of advanced stages. The main abdominal complications of GIST are bleeding, intestinal obstruction, rupture, and peritonitis. To our knowledge, a GIST-associated ACS has never been reported in literature.

We present here a case of patient with huge GIST with ACS successfully treated in intensive care unit (ICU) by both decompressive laparotomy and imatinib without any initial tumor resection.

Case Presentation

A 59-year-old woman, without particular history, consulted her general practitioner in December 2016 after one week with asthenia, abdominal pain and increase of abdominal perimeter. The thoraco-abdomino-pelvic (TAP) computed tomography (CT)-scan showed a huge abdominal solid mass of likely mesenteric origin. She was transferred to our institution on December 25, 2016.

Clinically, her weight was stable and WHO performance status (PS) was equal to 1. The physical examination found an increase of abdominal volume without obvious palpable mass. The laboratory tests showed inflammatory syndrome, moderate anicteric cholestasis, and elevated lactate dehydrogenase. A new CT-scan revealed the intra-abdominal mass of 26 × 21 × 41 cm, occupying the whole abdominal cavity, heterogeneous before and after iodine injection, associated with low abundance ascite (Fig. 1A). Gastric endoscopy-ultrasound-guided tumor biopsies revealed tumour cells with morphological and immunohistochemical criteria evoking GIST. The diagnosis was confirmed by the presence of a *KIT* exon 11 mutation.

Nine days after hospitalization, the patient displayed acute respiratory failure with hypercapnia and hypoxemia, justifying her transfer to our ICU and mechanic ventilation. The ratio of partial pressure arterial oxygen and fraction of inspired oxygen (P/F ratio) was 190 with 70% FiO₂, positive end-expiratory pressure (PEEP) at 10, and thoraco-pulmonary compliance was 30 mL/cm H₂O. A few hours after, hemodynamic instability and acute renal failure occurred, requiring vasopressive support and establishment of hemodialysis. The IAP measured using intravesical catheter was high, equal to 22 mm Hg evoking ACS. Imatinib was immediately started *via* the nasogastric tube at high dose of 800 mg/day (day 1, D1). Despite initiation of other therapeutic measures of intra-abdominal hypertension, the IAP increased to 25 mm Hg at D3 and organ dysfunctions were getting worse, leading to practice an emergency decompressive laparotomy *via* a transversal incision. After surgery, the “open abdomen” was left open and managed with a Vacuum-Assisted Closure (VAC)-type dressing (Fig. 2). The IAP rapidly decreased to 7 mm Hg. However, evolution was marked by hemorrhagic ascites requiring transfusion and albumin perfusion, and by acute pulmonary edema with weight gain of 15 Kg in one week. A CT-scan done at D12 imatinib treatment showed a decrease of the tumor size (22x20x36 cm) and density (13 Hounsfield Units, HU; Fig. 1B), suggesting efficiency of imatinib.

Then, the multi-organ dysfunctions improved. The laparotomy was closed (skin plan only) at D14, and the resuscitation procedures were progressively stopped: in all, the patient stayed 11 days with open abdomen, and received 28 days of mechanic ventilation, 19 days of non-invasive ventilation, 15 days of hemodialysis, and 8 days of vasopressive support. After 8 weeks in the ICU, she was transferred into the Department of Medical Oncology. A CT-scan showed further tumor regression (Fig. 1C) in size (21 × 19 × 35 cm) and density (10 HU). The clinical status continued to improve. The patient was discharged home on March 2017 with a standard imatinib dose (400 mg/d), 11 weeks after hospital admission. During several successive follow-up visits, she fared very well with a PS equal to 0. On CT-scan, the tumor regression continued on June and October 2017 (Fig. 1D). On November 2017, after 10 months of imatinib, the disease progressed and imatinib dose was increased to 800 mg/d. However, after 3 months, the disease worsened: imatinib was relayed by sunitinib during 5 months, then by regorafenib. On November 2018, the patient died from further disease progression, nearly two years after initial diagnosis.

Discussion

Since the 2000s, ACS is recognized as a well-defined clinical entity [1]. Primary ACS may be due to decreased abdominal wall compliance after abdominal surgery for example, to increased intra-luminal contents in case of ileus or gastric distension for example, or to increased intra-abdominal contents in case of acute pancreatitis, intra-abdominal infection, intra-abdominal or retroperitoneal tumors for example. In our case, the cause was a huge 40-cm GIST, the origin of which could not be clearly defined, either peritoneal or digestive with huge peritoneal metastasis. To our knowledge, this is the first case of GIST-associated ACS reported in literature. The other cancer-associated ACS published in the English literature include Wilm's tumor, neuroblastoma, benign and malignant ovarian tumors, prostate and rectal cancers, rhabdomyosarcoma, and Burkitt lymphoma [4–10].

The diagnosis was based on the detection of increased IAP combined with appearance of multi-organ failure, renal, hemodynamic, and respiratory. IAP was measured using the trans-vesical method that is the standard method [1]. Despite initiation of adequate medical

treatment, the situation worsened, and decompressive laparotomy was required. Such surgical procedure, crucial in case of failure of conservative medical treatment, reduces the mortality by between 16 and 37% [11]. During laparotomy, the peritoneal cavity is opened and left open: “open abdomen” presents several clinical challenges, and diverse solutions preventing complications have been developed, including the method of wound aspiration by creating negative pressure that we used. This method allows to eliminate secretions, protects the viscera and avoids the lateral musculo-aponeurotic retraction. Our patient did not experience severe complication during the 11 days of “open abdomen” and the bedside dressing changes in the ICU, as previously reported [12]. The aim of decompressive laparotomy in ACS is both to release the IAP and to treat the underlying disease. In our case, and by contrast to the other cancer-associated ACS reported in literature [4, 5, 7–10], no surgical removal of tumor was done because of the huge tumor size. The specific treatment was based on imatinib tablets taken *via* the naso-gastric tube during the mechanic ventilation. In emergency and before having the tumor mutational status, we gave a double dose of imatinib to increase the probability of tumor response in the eventuality of *KIT* exon 9 mutation [13]. Treatment was quickly efficient, both clinically with improvement of ACS and radiologically on CT-scan done at D11. Efficiency was favored by the presence of a *KIT* exon 11 mutation, known to be sensitive to imatinib [3]. Thanks to decrease in tumor size and density, the ACS was resolved and the abdomen could be closed 11 days after laparotomy. To our knowledge, such successful treatment of cancer-associated ACS by targeted therapy has never been described. There is one similar recent report of ACS successfully treated with chemotherapy for a Burkitt lymphoma [6]. During the course, the 42-year patient required mechanical ventilation and developed several organ failures. After laparotomy, abdomen was left open, and the patient received systemic R-CHOP chemotherapy, allowing tumor response, weaning from vasopressor and respiratory support, and of abdomen closure 18 days after laparotomy.

In conclusion, we report the first case of successful treatment of cancer-associated ACS by targeted therapy and decompressive laparotomy without any tumor removal. At a time when the prognosis of critically ill cancer patients has improved over the past decades and specific anticancer treatments such as chemotherapy and targeted therapy are under assessment in the ICU [14, 15], our case underlines that efficient oral target therapy for a life-threatening malignancy-related complication may be life-saving even in presence of multi-organ dysfunction.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure Statement

The authors declare that they have no competing interests.

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None.

Author Contributions

Conceptualization: FB. Data collection and interpretation: all authors. Manuscript writing: AB, DM and FB. Approval of the article: all authors.

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Fig. 1. CT-scan aspects of GIST before and during imatinib treatment. Transversal (up), and coronal (bottom) planes of TAP CT-scan at four successive times. Before imatinib treatment (December 26, 2016): see the huge mass with necrotic center occupying the whole peritoneal cavity from diaphragm to pelvis. Tumor density is 45 HU (Hounsfield Units). Almost no viscera is visible. After 12 days imatinib (January 16, 2017), objective tumor response is visible in term of size and density. The tumor response further improved after 8 weeks imatinib (March 7, 2017), and was maximal after 10 months (October 3, 2017).

Fig. 2. “Open abdomen” after decompressive laparotomy. Photographs taken during the ICU hospitalization. The tumor is visible through the transversal incision. After surgery, the “open abdomen” was managed with a Vacuum-Assisted Closure (VAC)-type dressing and bedside dressing changes in the ICU.