



Tako-tsubo syndrome after intraperitoneal hyperthermic chemotherapy (HIPEC) with cisplatin: an unusual complication of cytoreductive surgery plus HIPEC

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Dear Sir

Extensive cytoreduction surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) has been proven to be useful in the radical treatment of peritoneal carcinomatosis by primary tumors of the peritoneum and metastases from ovarian, colon, and gastric carcinoma. In addition to the complications of surgery, adverse events also appear secondary to the toxicity of intraperitoneal chemotherapy. Different patterns of toxicity associated to HIPEC have been described. We present the case of a 72-year-old woman with primary peritoneal carcinomatosis, treated with cytoreductive surgery plus HIPEC, who developed a Tako-tsubo syndrome during intraperitoneal administration of cisplatin.

The patient was a 72-year-old woman with a history of hypertension, diabetes mellitus and obstructive sleep apnea syndrome. She had no previous cardiological history. She was diagnosed with primary peritoneal carcinomatosis as a result of progressive abdominal distension and imaging test findings. An abdominal CT scan showed moderate ascites with abnormal distribution and tumor spread by the peritoneum and Douglas, with normal-sized ovaries. A percutaneous omentum biopsy confirmed the diagnosis of high-grade serous carcinoma consistent with primary peritoneal carcinoma. Tumor markers levels were elevated for Ca 125 (394 U/ml) and HE4 (1500 pM/l). CEA and AFP levels were

normal. The patient received neoadjuvant treatment with 5 cycles of carboplatin AUC5-paclitaxel 175 mg/m² with partial response to treatment. She underwent cytoreduction surgery and HIPEC, showing a PCI of 22, with tumor disease spread by all quadrants except the left hemidiaphragm. Complete peritonectomy was performed, including greater omentum, pelviperitonectomy, and bilateral pelvic lymphadenectomy. HIPEC was administered at the end of the surgery using an open technique with cisplatin (75 mg/m²), at 42.2 °C for 60 min. During the completion of HIPEC, the patient had an episode of hypotension, ST segment elevation on ECG, and troponin T increase to 680 pg/ml (normal levels < 14 pg/ml). In the recovery room, an echocardiography showed hypokinesia of the apical segments with adequate contractility of the basal segments. After a good initial recovery and awaiting a coronary angiography, the patient presented a sudden death on the 8th postoperative day.

To our knowledge, this is the first report of Tako-tsubo syndrome related to the intraperitoneal administration of cisplatin using the HIPEC technique.

Tako-tsubo syndrome is characterized by the presence of a transient systolic dysfunction of the left ventricular apex, with electrocardiographic abnormalities mimicking myocardial infarction, in the absence of obstructive coronary disease [1]. Although its etiology is unknown, it has been related to the presence of acute physical or emotional stress and may be caused by diffuse catecholamine-induced microvascular spasm or dysfunction, resulting in myocardial stunning. Stress cardiomyopathy is much more common in women than men and occurs predominantly in older adults. Some studies support the existence of polymorphism of estrogen receptors that make the cardiovascular system more susceptible to adrenergic substances [2].

Although less frequent, some cases have been reported during aggressive surgeries, such as liver transplantation, associated with surgical stress and hypovolemia [3]. In

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our case, it is possible that surgical stress associated with hemodynamic changes developed during the HIPEC phase, played a major role in the appearance of Tako-tsubo syndrome. During cytoreduction surgery, there is a significant loss of volume secondary to blood loss and visceral exposure during a long operative time. Hemodynamic changes may occur due to peripheral vasodilation during the hyperthermia in the administration of intraperitoneal chemotherapy. Furthermore, cytoreductive surgery plus HIPEC increases proinflammatory cytokines levels that produce vasodilation and vascular permeabilization, interfering with hemodynamic stability.

Some cytostatics such as capecitabine, 5-fluoruracil and trastuzumab have been associated with stress cardiomyopathy [4]. Cisplatin is an alkylating agent and is the most widely used drug in HIPEC for ovarian cancer with peritoneal metastases. Intravenous cisplatin has a known cardiotoxicity, although no case of Tako-tsubo has been described after its intraperitoneal administration [5].

The main limitation of this report is the impossibility of having data from a coronariography since the patient died suddenly, before it could be performed, on the 8th postoperative day.

Compliance with ethical standards

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