MULTIPLE COLON PERFORATION AS A FATAL COMPLICATION DURING TREATMENT OF METASTATIC MELANOMA WITH IPILIMUMAB – CASE REPORT

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Ipilimumab, an anticancer drug, is an anti-CTLA4 monoclonal antibody. It is used in treatment of disseminated melanoma. Therapy is associated with high risk of complications. One of the most serious, although one of the rarest is perforation of gastrointestinal tract. In this case report we describe a 52-year old male, with disseminated melanoma with unknown starting point, treated with anti-CTLA4 monoclonal antibody. After 3rd dose of drug administration, bloody diarrhea and acute abdominal pain occurred as a symptom of gastrointestinal perforation. A single perforation was sutured during laparotomy. Symptoms of acute abdomen returned after 10 days. Pus-faecal peritonitis, symptoms of necro-hemorrhagic colitis and multilocal perforation of the colon were found during relaparotomy. Pancolectomy with end ileostomy was performed. Few hours since relaparotomy patient died due to multiple organ failure.

The purpose of this case report is to draw attention to a risk of multilocal colon perforation in patient treated with ipilimumab.

Key words: melanoma, ipilimumab, anti-CTLA4, complications

Ipilimumab belongs to the group of cancer drugs which use the antigen-antibody reaction. The active drug substance is the anti-CTLA4 monoclonal antibody directed against the CD152 receptor located on the surface of T lymphocytes mediating the inhibition of lymphocyte T activation (1). The administration of ipilimumab promotes the activation of T lymphocytes towards proliferation. Thus, arising lymphocytic infiltrations in the vicinity of the tumor increase the chance of tumor cell apoptosis.

The efficacy of anti-CTLA4 was confirmed in case of patients with advanced melanoma, and introduced into the treatment of the above-mentioned disease. The recommended therapeutic schedule consists in the intravenous dosage of 3 mg/kg/ body weight, once every 3 weeks in four doses. Ipilimumab therapy might be responsible for the development of complications, such as reduction of appetite, nausea, vomiting, enteritis, diarrhea, rash presence, pruritis, fever, and others (1-5). The most severe complications, although rare, include gastrointestinal perforation, septic shock, Guillain-Barré syndrome, hepatic and renal failure. As a result, each of these complications lead to patient death. According to recent analysis of ongoing clinical trials with a dose of 10 mg/kg/body weight, one may come to the conclusion that increased drug doses increase the risk of complications (6, 7).

CASE REPORT

In November, 2011, a 52-year old man observed enlarged lymph nodes in his left
Multiple colon perforation as a fatal complication during treatment of metastatic melanoma with ipilimumab

The lymph nodes were collected for histopathological analysis, which supplemented by immunohistochemical analysis revealed the presence of melanoma metastases. The primary lesion was not found. Over time, peripheral lymphadenopathy was observed. The PET-CT examination performed in May, 2012 revealed the presence of generalized malignancy in the chest, abdomen, and pelvis. Neoplastic lymphadenopathy predominated, the liver was free of secondary lesions. In June, 2012 imaging examinations showed the presence of a metastatic lesion located in the VIII hepatic segment. The patient received ipilimumab therapy. Since treatment was held under a clinical trial regimen the dose of the drug was concealed. After the third dose of the drug the patient complained of hemorrhagic diarrhea. The patient developed an acute abdomen as a symptom of gastrointestinal perforation and ensuing peritonitis. Laparotomy was performed at the Department of Surgery, county hospital, with suturing of the perforated bowel. After stabilization of the general condition the patient was transferred to the Department of Surgical Oncology, Gdynia Oncology Center for the treatment of systemic therapy complications. Steroid therapy was initiated. Ipilimumab was not administered. Ten days after laparotomy the patient was transferred to the Department of Surgery, Gdynia Oncology Center with clinical symptoms of diffuse peritonitis, as a consequence of gastrointestinal perforation, and presence of left pleural cavity fluid. Ad hoc laboratory and imaging diagnostics confirmed the clinical diagnosis and the patients’ severe condition. Alkalosis dominated. Laboratory results were as follows: CRP – 41.4, hemoglobin – 10.5 g/dl, hematocrite – 35%. After decompression of the left pleural cavity, 800 ml of a serous-hemorrhagic content was obtained. Emergency laparotomy was performed demonstrating fecal-purulent peritonitis, necrotic colitis, and multifocal colon perforation. Colectomy was performed with end ileostomy. The patient was transferred to the ICU with symptoms of septic shock, where he died several hours later, due to multiorgan failure. The histopathological examination revealed the presence of multifocal deep ulcerations with the development of fissures penetrating into the muscular layer (fig. 1).

In 35% of patients treated by means of anti-CTLA4, one may observe the occurrence of complications. Death, due to gastrointestinal perforation is observed in less than 1% of patients (4). Despite the incidence of complications, including those that are life-threatening, such as multifocal colon perforation, ipilimumab remains a useful drug possibly prolonging the life of patients diagnosed with advanced melanoma (6, 7). Our observation confirmed the advisability of emergency clinical surveillance, considering a patient with colitis and perforation, as potential fatal complications during ipilimumab therapy.

REFERENCES