

## Colonic Perforation Secondary to Taxol Therapy: An Unusual Presentation

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Dear Editors,

In December 2005 a 52-year-old woman presented with a FIGO stage III ovarian carcinoma which was treated primarily with optimal surgical cytoreduction and left-sided hemicolectomy due to colonic involvement. Postoperatively combination-chemotherapy was started: taxol 175 mg/m<sup>2</sup> and carboplatin dosed to an AUC of 6.0 intravenously every 3 weeks. A significant decrease of the tumor marker CA 125 was observed during the first cycles: from 980 U/ml initially to 55 U/ml after the third cycle (normal value: less than 35 U/ml). Treatment was tolerated fairly well.

In March 2006 she was admitted at the surgical department because of an acute abdomen. The day prior to the admission the fourth chemotherapy cycle had been administered without complications. A few hours before admission she developed a sudden abdominal pain with nausea and vomiting. Temperature was 37.6 °C. Peripheral blood revealed a normal white blood count ( $6.1 \times 10^9/l$ ). Immediate laparotomy revealed an acute peritonitis, extensive adhesions and a 4 mm wide defect in the sigmoid. Peritoneal carcinomatosis was present. Exploration showed a limited local transmural ischemic necrosis next to the perforation. Because of extensive adhesions we performed a closure of the perforation by suturing the edges of the defect. Thereafter the abdomen was washed out with saline and closed normally. Apart from a minor wound infection recovery was uneventful. On the basis of the clinical and operative findings the perforation was considered to be a complication of taxol therapy.

Colonic perforation as a serious side-effect of taxol has been reported previously [1–3]. The incidence has been estimated to be 2.5% in patients receiving taxol for the first time [3]. Most patients need surgical treatment, although in some cases conservative approach might be successful [3]. In general it is correlated to a necrotizing enterocolitis during neutropenia.

Our patient, however, was not neutropenic or feverish on the day of admission, since she received the cytostatics just one day prior to admission. Usually this complication is seen 7–14 days after a chemotherapy course [3, 4]. So this sequela in our patient is rather unusual and unexpected.

Although infrequent, this is a serious complication with a mortality-rate of 48% when treated medically and 21% when treated surgically [4]. This serious event might occur even following the first cycle. In our case this event took place after the fourth cycle. Also in a taxane like docetaxel colonic perforation has been documented [4, 5].

The underlying pathogenetic mechanism is not fully understood. Many suggestions have been made lately; a possible role of a clostridium infection has been suggested in some cases [6]. It is also assumed that taxol affects the mucosal integrity of the intestines, leading to mucositis and necrosis. A synergistic interaction between the compromised bowel and the taxol-induced mitotic arrest is considered to be an additional causal factor. Furthermore, several other mechanisms have been proposed secondary to cytostatic therapy, such as thrombogenesis, blood shunting, induction of intestinal dysmotility and altered immunological defenses [7]. A possible contribution of corticosteroids to intestinal injury cannot be fully excluded. Our patient received dexamethasone 20 mg twice, the evening before and on the day of chemotherapy in order to prevent fluid retention. This drug might impair the macrophage function and promote bacterial invasion. After recovery of our patient cytostatic treatment was resumed with a combination of carboplatin and cyclophosphamide.

We would like to emphasize that in any patient treated with taxol chemotherapy, and presenting with signs of an acute abdomen, a therapy-associated intestinal perforation should be considered, even in the absence of neutropenic fever shortly after a taxol containing chemotherapy course.

## References

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