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CASE REPORT

Is acute dyspnea related to oxaliplatin administration?

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Abstract

The standard adjuvant treatment of colon cancer is fluorouracil plus leucovorin. Oxaliplatin improves the efficacy of this combination in patients with stage Ⅲ colon cancer and moreover its toxicity is well tolerable. We describe a rare clinical case of acute dyspnoea probably related to oxaliplatin at one month from the end of the adjuvant treatment. A 74-year-old man developed a locally advanced sigmoid carcinoma (pT3N1M0). A port a cath attached to an open-ended catheter was implanted in order to administer primary chemotherapy safely according to the FOLFOX4 schedule. One month following the end of the 6th cycle, the patient referred a persistent cough and moderate dyspnoea. Chest radiography displayed a change in the lung interstitium, chest CT scan confirmed this aspect of adult respiratory distress syndrome, spirometry reported a decreased carbon monoxide diffusion capacity. Antibiotic and corticosteroids were administered for 10 d, then a repeated chest X ray evidenced a progressive pulmonary infiltration. A transbronchial biopsy and cytology did not show an infective process, a CT scan reported radiological abnormalities including linear and nodular densities which were becoming confluents. Antimicotic and antiviral drugs did not evidence any benefit. The antiviral therapy was stopped and high dose metilprednisolone was started. The patient died of pulmonary distress after 10 d.

Key words: Acute dyspnea; Oxaliplatin; Colon cancer

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INTRODUCTION

For almost 15 years, adjuvant chemotherapy has been known to improve disease-free survival (DFS) and overall survival (OS) in colon cancer patients. The pivotal study of Moertel *et al* in 1990[1], demonstrated that OS and DFS are improved after 12 mo of treatment with bolus 5-fluorouracil (5-FU) and levamisole, which has led to the First National Cancer Institute (NCI) consensus recommendation for stage Ⅲ colon cancer[2]. Subsequent studies conducted in the 1990s have established 6 to 8 mo of adjuvant therapy with bolus 5-FU plus leucovorin (LV) as standard of care. The positive results of the international multi-center study of oxaliplatin/5-fluorouracil/leucovorin in the adjuvant treatment of colon cancer (MOSAIC) trial[3] enrolling both stage Ⅱ and Ⅲ patients, have led to US Food and Drug Administration approval of oxaliplatin plus 5-FU/LV (FOLFOX4) for patients with stage Ⅲ colon cancer in November 2004[4], which followed the European approval as adjuvant treatment of stage Ⅲ (Dukes C) colon cancer after complete resection of the primary tumour in September 2004. The US Food and Drug Administration approval is based on the demonstration of the statistical superiority of FOLFOX4 to infusional plus bolus 5-FU/LV (LV5FU2 regimen) on 3- and 4-year DFS in the stage Ⅲ subgroup of patients in the MOSAIC trial[3-5]. Vomiting is observed in about 47% of cases, granulocytopenia in about 79% of cases and thrombocytopenia in 77% of cases, paresthesia in about 92% of cases and increased enzymes in about 57%, respectively. Other types of toxicities are of low grade.

CASE REPORT

We describe a rare clinical case of acute dyspnoea at one month from the end of adjuvant treatment.

A 74-year old man developed a locally advanced sigmoid carcinoma (pT3N1M0). A port a cath attached to an open-ended catheter, was implanted in order to administer primary chemotherapy safely according to the FOLFOX4 schedule (oxaliplatin 85 mg/m^2 d 1, 5-FU 400 mg/m^2 d 1, 2 administered as bolus, 5-FU 600 mg/m^2 d 1, 2 administered by 22 h continuous infusion and LV 100 mg/m^2 administered by 2 h infusion, every 2 wk). The 6-mo administration went without acute complications (except for a grade 1 thrombocytopenia and neutropenia). One month following the end of the 6th cycle, the patient

referred a persistent cough and moderate dyspnoea. Chest radiography documented a change in the lung interstitium, chest CT scan confirmed this aspect of adult respiratory distress syndrome, spirometry reported a decreased carbon monoxide diffusion capacity. Antibiotic and corticosteroids were administered for 10 d; a repeated chest X ray evidenced a progressive pulmonary infiltration. The patient was urgently admitted to our hospital for increasing fever and dyspnoea. Transbronchial biopsy and cytology did not show an infective process, CT scan reported radiological abnormalities including linear and nodular densities which were becoming confluent. Antimicotic and antiviral drugs did not evidence any benefit. For a respiratory complication the patient was admitted to the Intensive Care Unit. The antiviral therapy was stopped and high dose metilprednisolone was started. The patient died of pulmonary distress after 10 d.

DISCUSSION

To our knowledge, this is one of the very few reports on such a phenomenon in patients with colorectal cancer (CRC) during FOLFOX4 chemotherapy. Rare cases of acute interstitial lung disease and of pulmonary fibrosis have been reported after oxaliplatin, including obliterated bronchiolitis with organized pneumopathy or interstitial pneumonia-like lung disease. The MOSAIC adjuvant trial has not reported such toxicity[3].

In our clinical case, the interstitial aspect of lung fibrosis appeared to be rapidly evolutionary, showing no improvement 7 d after steroid therapy.

Since the use of oxaliplatin chemotherapy has increased dramatically in the past 2 years in CRC patients, and because of the lack of clinical data in literature, we strongly recommend accurate basal pulmonary analysis with spirometry, especially in elderly patients, to evaluate the respiratory reserve and careful monitoring of any respiratory distress which may occur in patients during or at the end of oxaliplatin chemotherapy. Clinicians should be aware of the potential of lung toxicity caused by novel antineoplastic agents.

REFERENCES

1 **Moertel CG**, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Goodman PJ, Ungerleider JS, Emerson WA, Tormey DC, Glick JH. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *N Engl J Med* 1990; **322**: 352-358

2 **NIH consensus conference**. Adjuvant therapy for patients with colon and rectal cancer. *JAMA* 1990; **264**: 1444-1450

3 **André T**, Boni C, Mounedji-Boudiaf L, Navarro M, Tabernero J, Hickish T, Topham C, Zaninelli M, Clingan P, Bridgewater J, Tabah-Fisch I, de Gramont A. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med* 2004; **350**: 2343-2351

4 **Ibrahim A**, Hirschfeld S, Cohen MH, Griebel DJ, Williams GA, Pazdur R. FDA drug approval summaries: oxaliplatin. *Oncologist* 2004; **9**: 8-12

5 **André T**, Tournigand C, Achille E, Tubiana-Mathieu N, Lledo G, Raoul Y, Carola E, Flesch M, Muron T, Boutan-Laroze A, Guérin Meyer V, Boaziz C, Maigre M, Ganem G, Mousseau M, Mounedji-Boudiaf L, de Gramont A. [Adjuvant treatment of colon cancer MOSAIC study's main results]. *Bull Cancer* 2006; **93** Suppl 1: S5-S9

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