

LETTER TO THE EDITOR

REVERSIBLE SERUM CARCINOEMBRIOGENIC ANTIGEN (CEA) ELEVATION DUE TO ORLISTAT USE: A CASE REPORT

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Carcinoembriogenic antigen (CEA) is a serum marker commonly used as a clinical tool in the follow-up of patients with several types of tumor, particularly colorectal carcinoma. An elevation in CEA levels can precede clinical evidence of recurrence, but these levels can also increase in patients with nonmalignant pathologies. Nevertheless, an elevation in CEA levels is always associated with the introduction of extensive work-ups and typically generates significant patient anxiety. Orlistat is a medication commonly used as an adjunctive weight-control measure due to its ability to decrease the absorption of dietary triglycerides. Its predominant side-effects are related to its activity in the gastrointestinal tract. We report the case of a patient who developed a documented, reversible elevation in CEA with the use of this medication. The use of orlistat should be considered in the differential diagnosis of patients presenting unexplained elevations of CEA.

CASE REPORT

A 66-year-old female patient was submitted to a left hemicolectomy in January 2002 due to a T3N0M0 well-differentiated colon adenocarcinoma. At that time, no adjuvant treatment was recommended for the patient. One year later, during a routine follow-up examination, the patient was found to have elevated levels of CEA and a chest X-ray showing a 1.5-cm nodule in the right upper lung lobe. A CAT scan confirmed the presence of this nodule, which was consistent with a metastatic lesion. The patient was treated with capecitabine as a single agent, which resulted

in partial remission. A resection of the lung nodule was carried out in August 2003, and the pathologic examination confirmed the presence of a metastatic adenocarcinoma consistent with the primary colon cancer.

The patient remained free of any signs of recurrent disease, with a normal CEA (normal value ≤ 5.0 ng/dl) level, for several years after the aforementioned treatment. However, in January 2008, after having taken orlistat (120 mg, three times per day) for weight control for 6 months, the patient was found to have an elevated CEA level of 8.3 ng/dl (baseline 3.0 ng/dl). The test was repeated, and this result was confirmed. A thorough work-up, including a laboratory evaluation of renal, liver and thyroid function, as well as a positron emission tomography and a colonoscopy, were carried out and showed no abnormalities. Four weeks later a reanalysis of the patient's CEA level confirmed an elevated CEA level of similar magnitude.

In August 2008 the patient was advised to discontinue the use of orlistat. In September the patient's CEA level had returned to the normal range. The measurement was repeated monthly and has remained normal ever since, with the most recent test completed in January 2009, with a result of 3.1 ng/dl.

INTRODUCTION

CEA was first described as a colon cancer marker in 1965¹. Since that time, CEA has been demonstrated to be a valuable clinical tool in the follow-up of patients with colorectal carcinoma². Elevated levels of CEA can precede clinical evidence of tumor recurrence in up to 80% of patients, underscoring its usefulness in the management of colorectal cancer patients. It is well known that CEA is an immunoglobulin-like protein produced in the gastrointestinal mucosa whose level can increase in other malignant and nonmalignant pathologies. Therefore, in spite

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of its clear clinical utility, CEA is not as specific as initially hypothesized. Consequently, the correct interpretation of elevated CEA levels requires a careful clinical investigation to identify the reason for this abnormality.

Because of its low specificity, serum CEA levels should not be used for colon cancer screening³. Normal CEA values are between 2.5 ng/ml and 3.0 ng/ml for non-smokers and between 2.5 ng/ml and 5.0 ng/ml for smokers⁴.

Orlistat is widely used as an adjunct weight-control measure due to its ability to decrease the absorption of dietary triglycerides by inhibiting intestinal lipases. The predominant side-effects of orlistat are gastrointestinal in nature, including intestinal borborygmi, abdominal cramps, flatus, fecal incontinence, oily spotting and flatus with discharge.⁵ In a meta-analysis of nine clinical trials, these side-effects occurred in 15 to 30 percent of patients⁶. Less frequently, orlistat can induce moderate and adverse gastrointestinal effects, such as abdominal pain. A few cases of serious hepatic adverse effects (cholelithiasis, cholestatic

hepatitis and subacute liver failure) have also been reported.⁷

DISCUSSION

In this case report, a patient with an elevated level of CEA was identified during a routine follow-up examination. Interestingly, the CEA level returned to the normal range when orlistat use was discontinued. We hypothesized that such an observation could possibly be attributed to enteritis due to the presence of fatty stool in the bowel, the same explanation for the majority of orlistat's adverse effects.

To our knowledge, this is the first report to link the use of orlistat to the development of elevated CEA levels. Considering the number of patients who use this medication for weight control, it may be an important cause of false-positive CEA elevations. Based on this clinical observation, we believe that inquiring about the use of orlistat should be part of the evaluation of patients who present with unexplained elevations of CEA.

REFERENCES

1. Gold P, Freedman SO. Demonstration of Tumor-Specific Antigens in Human Colonic Carcinomata by Immunological Tolerance and Absorption Techniques. *J Exp Med*. 1965;121:439-62.
2. Mayer RJ, Garnick MB, Steele GD, Jr., Zamcheck N. Carcinoembryonic antigen (CEA) as a monitor of chemotherapy in disseminated colorectal cancer. *Cancer*. 1978;42:1428-33.
3. Macdonald JS. Carcinoembryonic antigen screening: pros and cons. *Semin Oncol*. 1999;26:556-60.
4. Fletcher RH. Carcinoembryonic antigen. *Ann Intern Med*. 1986;104:66-73.
5. Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes. A 1-year randomized double-blind study. *Diabetes Care*. 1998;21:1288-94.
6. Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for obesity and overweight. *Cochrane Database Syst Rev*. 2004;CD004094.
7. Filippatos TD, Derdemezis CS, Gazi IF, Nakou ES, Mikhailidis DP, Elisaf MS. Orlistat-associated adverse effects and drug interactions: a critical review. *Drug Saf*. 2008;31:53-65.