

Calculation of half-life of carcinoembryonic antigen after lung tumour resection: a case report

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Calculation of half-life of carcinoembryonic antigen after lung tumour resection: a case report. J. Verhelst, E. Vanden Broecke, J. Van Meerbeeck, W. De Backer, P. Blockx, P. Vermeire.

ABSTRACT: Since little is known about carcinoembryonic antigen (CEA) half-life in humans, we followed changes in CEA levels after curative resection of a small bronchial adenocarcinoma in a 54 yr old man with an unusually high preoperative serum CEA level of 1,199 ng·ml⁻¹. Serum CEA followed a four phase curve with an initial increase, attributed to release of CEA from the tumour, a rapid fall during four days (CEA half-life 3.2 days), a slower exponential decay to normal levels during almost three months (CEA half-life 11 days) and eventually maintenance of normal levels for 14 months. These results are consistent with data from animal experiments and a single report on CEA half-life in humans, but CEA half-life seems longer in man than in animals. This observation also suggests that a very high serum CEA level should not in itself preclude curative surgical resection of a primary bronchogenic carcinoma. *Eur Respir J.*, 1991, 4, 374-376.

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Little is known about the half-life of carcinoembryonic antigen (CEA) in humans despite long-term experience with its diagnostic use since the molecule was first discovered in 1965 [1].

Animal experiments demonstrated that CEA, a heterogeneous glycoprotein with a molecular weight of about 200,000, is cleared predominantly by the liver and its half-life in different animal species varies between 3-150 min [2-5]. In man, repeated measurements of CEA level after curative tumour resection represent the only way for measuring CEA half-life.

Unfortunately, most patients with resectable tumours have normal or only slightly elevated CEA levels, making precise calculations difficult and subject to high variability [6]. An unusually high CEA plasma level in a patient with a small lung tumour undergoing curative resection permitted us to calculate CEA half-life over a wide range of concentrations.

Case report

A 54 yr old male, heavy smoker, was admitted with right-sided thoracic pain of 3 wks duration and a round lesion of 4 cm diameter in the right upper lobe on chest radiography. On bronchoscopy a tumour was visualized distally in the anterior segmental bronchus of this lobe;

biopsy yielded an adenocarcinoma. Computerized tomography (CT) scan of the chest followed by mediastinoscopy did not show mediastinal invasion, whereas bone scintigraphy and abdominal echography failed to show any distant metastasis (T₂ N₀ M₀). However, a surprisingly high serum CEA of 1,199 ng·ml⁻¹ was found (Pharmacia, CEA RIA 100, normal <6 ng·ml⁻¹). Neurone-specific enolase was normal. Liver and renal function tests were within the normal range.

A thorough search to exclude tumour in other organ systems, including gastroscopy, barium enema, cystoscopy, CT scans of abdomen and brain, remained negative. The patient also had normal pulmonary function tests. He underwent a right upper lobectomy, which confirmed preoperative staging. On light microscopy the tumour was moderately differentiated and showed intense immunostaining for CEA. The patient has made an excellent postoperative recovery. The changes in CEA levels are shown in figure 1. Serum CEA increased from 1,199 ng·ml⁻¹ 5 days before to 1,614 ng·ml⁻¹ one day after operation. Subsequently, the serum levels followed a two-phase decrement: after an initial rapid fall to 52% of the initial titre during the first 4 days (CEA half-life of 3.2 days), a much slower nearly mono-exponential decay (CEA half-life of 11 days) was seen. After 83 days normal CEA levels (5.6 ng·ml⁻¹) were reached and maintained until 14 months after the

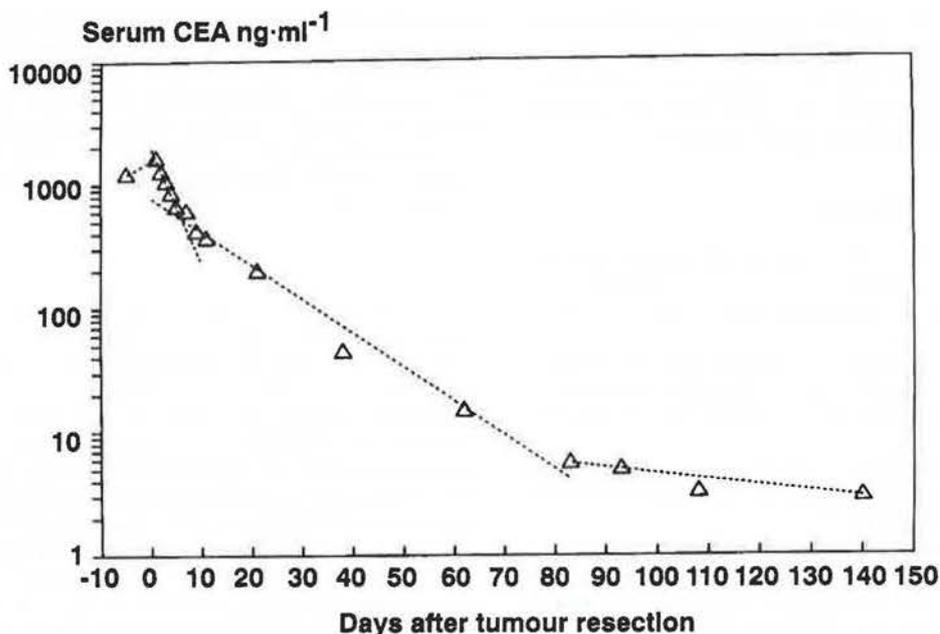


Fig. 1. - Changes in serum carcinoembryonic antigen (CEA) following curative resection of a small bronchial adenocarcinoma. After a moderate increase (day -5 to 1), a rapid fall is seen (day 1 to 4), followed by a slower exponential decline (day 4 to 83) and finally normal levels from day 83.

operation, the patient still being in good health without signs or tumour recurrence or metastasis.

Discussion

Calculation of CEA half-life in man is interesting and may be of clinical relevance, since CEA is widely used as a monitor for the effectiveness of tumour treatments, such as chemotherapy; a better understanding of the kinetics of circulating CEA is believed to enhance the ability to interpret sequential plasma CEA levels in patients and to predict tumour behaviour [7, 8].

The description of plasma CEA half-life in our patient is similar to the findings of LOKICH *et al.* [7], who also described a two-phase decline in serum CEA after excision of a single liver metastasis in 4 patients with colonic carcinoma: an initial rapid decay to 11–37% of basal values immediately after tumour removal was followed by a logarithmic decline with a CEA half-life of 2.8–8.6 days. However, the results from our patient may be more reliable for estimating this half-life, since there were no metastases and the initial CEA level was higher (1,199 ng·ml⁻¹ versus between 29.6–300 ng·ml⁻¹ in the patients of Lokich *et al.*).

We are not aware of other reports providing a precise description of CEA clearance in humans. Most available data stem from experiments in which human CEA was injected into animals. However, comparisons and extrapolations should be done with caution, since one could envisage that the kinetics of exogenous CEA injected into animals differ from those of the endogenously produced substance. MARTIN and HALPERN [2] found a mono-exponential CEA clearance pattern in

mice following intravenous injection of the substance, extracted from the serum of a cancer patient with high CEA levels. This pattern closely resembles the second-phase decline in serum CEA in our patient and in the patients of Lokich *et al.*, it may therefore represent the clearance of CEA present in serum following active secretion from the tumour ("secretory" CEA). By contrast, injection into animals of CEA, directly extracted from the tumour, shows a much faster multi-exponential clearance [3–5]. This could be explained by many CEA molecules inside tumour cells being biochemically different from "secretory CEA" because they contain a variable and smaller number of carbohydrate components. Since a reduction in carbohydrate components make CEA molecules less resistant to degradation, they are cleared at a rate inversely related to their carbohydrate content [4]. By analogy, we therefore suggest that the rapid initial fall of CEA in our patient could have resulted from rapid clearance of "non-secretory" CEA directly released from the tumour during the operation [9].

CEA half-life in our patient was much longer than that reported in animals (3 min in monkeys, 5 min in rats, 28 min in rabbits and 150 min in mice [2–5]), but similar CEA half-life values have been found after resection of single liver metastases in four patients with colonic carcinoma [7], suggesting major species differences in CEA clearance. Again differences in kinetics between exogenous and endogenous CEA may lead to different half-lives. In addition, also between humans differences in type of CEA and liver clearing capacity [10] may contribute to variability in CEA half-life.

In conclusion, at least from this unusual patient with bronchial adenocarcinoma, CEA half-life seems longer

in man than in some animal species and it basically follows a mono-exponential clearance pattern. From the presently available follow-up data, our study also indicates that a very high serum CEA level should not in itself preclude curative surgical resection.

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Calcul de la demi-vie de l'antigène carcino-embryonnaire après résection d'une tumeur pulmonaire: observation clinique. J. Verhelst, E. Vanden Broecke, J. Van Meerbeeck, W. De Backer, P. Blockx, P. Vermeire.

RÉSUMÉ: Comme l'on connaît peu de choses au sujet de la demi-vie de l'antigène carcino-embryonnaire chez l'homme, nous avons suivi les modifications du taux de CEA après résection curative d'un petit adénocarcinome bronchique, chez un homme de 54 ans qui avait un taux de CEA sérique pré-opératoire particulièrement élevé de 1,199 ng·ml⁻¹. Le CEA sérique a suivi une courbe en quatre phases, avec augmentation initiale attribuée à la libération de CEA par la tumeur, une chute rapide pendant quatre jours (demi-vie du CEA: 3.2 jours), une diminution exponentielle plus lente jusqu'à des niveaux normaux pendant environ trois mois (demi-vie du CEA: 11 jours), et persistance de niveaux normaux pendant 14 mois. Ces résultats sont cohérents avec les données provenant d'expérimentations animales et d'un article isolé sur la demi-vie du CEA chez l'homme, mais la demi-vie du CEA semble plus longue chez l'homme que chez l'animal. Cette observation suggère également qu'un taux très élevé de CEA sérique ne devrait pas, en lui-même, empêcher une résection chirurgicale curative d'un carcinome bronchique primitif.

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