

Case Report

Carcinoembryonic antigen; lack of clinical utility in a case of metastatic colorectal carcinoma

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Carcinoembryonic antigen (CEA) is a glycoprotein tumour marker that had been in clinical use for more than three decades in colorectal carcinoma (Ca). Issues of lack of sensitivity and specificity has limited its' use in screening and diagnosis of colorectal carcinoma but is commonly applied in the therapeutic monitoring and prognostication of colorectal carcinoma. However some studies have called for caution in the it's' use routinely as the major tool for monitoring disease progression in colorectal carcinoma. This case report of a 33 year-old male with metastatic colorectal carcinoma shows the inapplicability of plasma CEA evaluation on the monitoring of therapeutic response to chemotherapy. This case report highlights the need for clinicians to be conscious of the ineffectiveness and sometimes misleading results than can occur with CEA as a monitoring tool in colorectal carcinoma.

Keywords: Tumour marker, carcinoembryonic antigen, colorectal carcinoma.

INTRODUCTION

Carcinoembryonic antigen (CEA) is one of the oldest tumour markers applied principally in colorectal carcinoma (Ca) (Duffy et al., 2007). It is biochemically a glycoprotein which basically functions in cell adhesion mechanisms.(Thompson, 1991). Active production of CEA occurs during fetal life with subsequent decline after birth such that plasma levels are many folds less in adult life. Because of the latter and the fact that CEA concentrations in healthy tissues are about 60-fold less than in malignant conditions, CEA assumes an attractive biomarker tool for colorectal Ca. Tumour markers have putatively being used for screening, diagnosis, staging and monitoring of cancers.(Al-Shuneigat et al., 2011). However their lack of specificity and sensitivity limits their use in screening and diagnosis (Takekazu et al., 1999). CEA, as other tumour markers, is not exempt from these drawbacks of poor sensitivity and specificity and as such is not recommended for screening nor diagnosis. Its' clinical application in the context of colorectal Ca is majorly for monitoring of therapy and prognostication(Gershon et al., 2006) though it is noteworthy that some studies have also shown the usefulness of CEA in the detection of liver metastasis(Duffy, 2001). Under current guidelines, CEA is to be assayed preoperatively or prior to chemotherapy, and in addition if it felt clinically that it will assist in staging and surgical planning (Gershon et al., 2006). Subsequently it is measured during active treatment for example post-operatively or in the course of

chemotherapy usually at 1-3 month intervals.

It is important however to point out that apart from colorectal ca, certain benign conditions such as smoking, infections, inflammatory bowel disease, pancreatitis, cirrhosis of the liver, biliary obstruction can also cause elevated CEA (Perkins et al., 2003).

Case Report

A 33-year-old male with background schizophrenia presented with weakness, easy fatigability, palpitations, and breathlessness of three months' duration. History showed poor nutritional intake over the course of the past two years, characterized by alternating periods of prolonged poor appetite and occasional desire and fair intake of junk foods. Over this period the patient had lost about a quarter of his body weight. There was a history of occasional abdominal discomfort but nil associated constipation, vomiting, haematochezia nor melaena.

There was no associated cough, night sweats nor chest pains. No history of peripheral oedema, orthopnea nor abdominal swelling was gotten. He was a non-smoker and the fifth of six siblings who had to stop his educational pursuits due to the onset of psychiatric illness about twelve years earlier.

At the time of presentation, the patient was in relatively stable mental state and volunteered the bulk of the history, only being assisted occasionally by a relative. He

had been off antipsychotics for about six months prior to presentation.

Physical examination showed a febrile (39°C) emaciated young man with severe pallor. He was physically weak but was well oriented in time, place and person. There was neither associated jaundice nor cyanosis. Vital signs were as follows;

- Pulse(radial) 112bpm(regular, low volume)
- BP 98/60mmHg (supine)
- respiratory rate 26/min

Further examination showed pitting feet oedema, vague abdominal tenderness but nil masses palpable per abdomen. A provisional diagnosis of anaemic heart failure was made. Nutritional anaemia was suspected as the most probable cause. Other differential diagnoses included aplastic anaemia, human immunodeficiency virus (HIV) infection, myelodysplastic syndrome, and were to be ruled out.

Background acute malaria was kept in view.

Summary of initial laboratory investigation results were as follows;

- ⊙ FBC; HB 4g/dl, WBC (relative lymphocytosis 60%), normal platelet count
- ⊙ Peripheral blood film shows normocytic RBCs
- ⊙ Malaria parasite: ++
- ⊙ Retroviral screening: negative
- ⊙ Stool M/C/S: E. histolytica cysts, nil ova
- ⊙ B. marrow aspiration; hypercellular marrow, reversed myeloid/erythroid (M/E) ratio, E series-normoblastic, M series- sequential maturation, adequate megakaryocytes.

Hospital course

He was admitted and being managed by the hematology unit of the hospital, which was a tertiary level care health facility. Patient was treated for malaria and commenced on treatment for anaemic heart failure.

A total of five blood transfusions were given during this first hospital admission. The management of the patient was tailored into seeking out a haematologic cause of the anaemic heart failure.

Three (3) months into this hospital stay, an abdomino-pelvic ultrasound (U/S) showed a 'mass shadow' in the caecal region. Barium studies were requested and after two unsuccessful attempts, a double contrast barium enema study showed filling defects in caecal and sigmoidal regions.

At this juncture the surgeons were invited to take over the patient's management as colorectal carcinoma became a differential diagnosis. However due to an onset of an industrial dispute in the healthcare facility, the patient had to be transferred to another tertiary level hospital.

CEA evaluation was done and yielded a value of 2.8µg/L (Reference interval; 0-4µg/L).

Exploratory laparotomy was undertaken and a diagnosis of inoperable metastatic colorectal carcinoma was made ('frozen pelvis-like appearance'). Intra-operatively it was difficult to ascertain the site of origin within the large gut and there were apparent metastasis involving the bladder, the sheaths of the iliac vessels and other contiguous tissues within the lower abdomen and pelvis. The liver appeared morphologically unaffected. No frozen section was done but two biopsy specimens of suspected lymph nodes were taken intra-operatively, ileocolic (transverse colon) bypass was undertaken in order to ensure continuous bowel passage of materials.

Histology showed that the biopsy specimens were not lymph nodes but mesenteric tissue and findings were pleomorphic cells with scantily interspersed mucin and reactive hyperplasia.

In view of the unspecific nature of the biopsy specimens from the surgery, a clear-cut histological diagnosis was difficult. However given the clinical findings buttressed by the operative findings and available limited histological features as corollaries, patient was diagnosed as a case of *adenocarcinoma* of the colon.

Patient was commenced on chemotherapy using 5-fluorouracil and leucovorin with a view to monitoring the tumour mass radiologically and if shrinkage was observed with time, a re-operation attempt to de-bulk the tumour would be done.

Three other CEA measurements were undertaken post-operatively at one month intervals. This was to be a form of a guide to monitor tumour progression. Values were 2.9µg/L, 2.7µg/L and 3.0µg/L respectively. (Figure 1).

The patient had additional transfusions of three (3) units of blood spanning the period from operation to 3 months post-op. In the course of the hospital stay, the patient had bladder involvement with fistulae and consequent urinary faecoliths.

There was poor response to management with clinical deterioration resulting in subsequent coma and death five (5) months after laparotomy.

DISCUSSION

CEA though an ineffective tool for diagnosis, has found application in prognostication and monitoring of progression of colorectal ca especially in the course of therapy (Bruinvels et al., 1994; Makela et al., 1995). However this clinical utility is predicated on taking a baseline value prior to commencement of therapy. As would be expected, colorectal ca causes elevated levels of CEA which on initial assessment forms the baseline to juxtapose further evaluations which are helpful in treatment options.

In managing metastatic colorectal cancer, changes in chemotherapy regimens are often considered when there is evidence of progressive disease.

This case is an illustration of the ineffectiveness of CEA

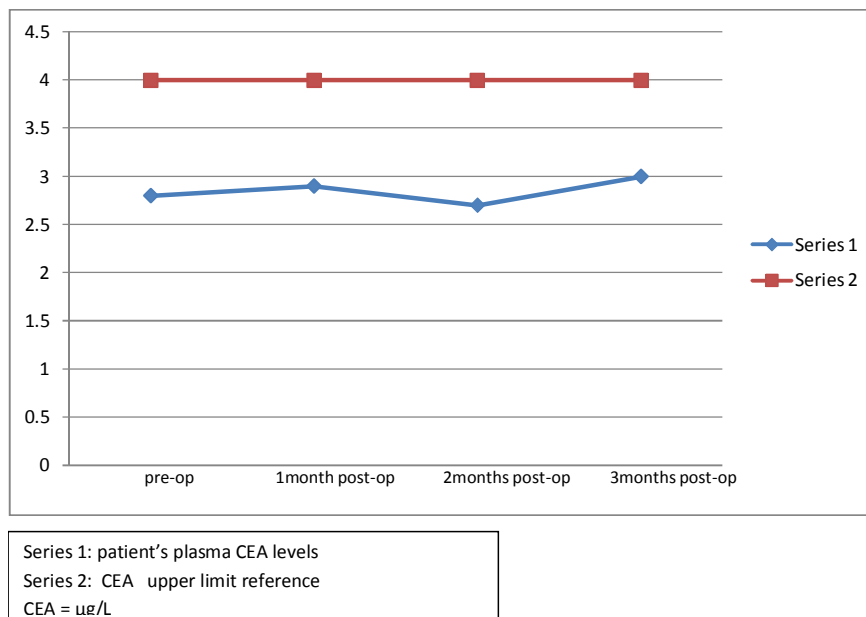


Figure 1. Graph of CEA patterns over three months

as a tumour marker for the aforementioned uses in colorectal Ca. Firstly, at onset, the CEA level was within reference interval despite extensive metastatic disease which was at least stage IIIC, which surgery subsequently confirmed. This is not rare in that some studies had noted that sometimes tumors may not cause an abnormal blood CEA level, even in advanced disease (Kapiteijn et al., 1991, Grossmann et al., 2007). As such this puts off any possible usefulness of the plasma CEA as an indication of positive chemotherapeutic outcome.

Secondly, in the course of treatment of this case, despite worsening disease progression, the CEA levels remained within reference interval. This may not be unconnected to the fact that the liver inexplicably in this case, was relatively spared as seen in surgery and such sparing might have continued even with disease deterioration. Studies have shown that oftentimes in the absence of associated liver metastasis, CEA levels will not be elevated even in the presence of advanced disease(Wang et al., 1994; Moura et al., 2001)and conversely in the presence of distant lung metastasis it could be also not be elevated(Fakhri, 2008).

In addition it has been shown that poorly differentiated colorectal tumours may not produce CEA(ASCO, 1996). As such it is evident that CEA sensitivity and specificity is both tumour dependent and metastatic site dependent. Given that the biopsy specimens were not truly representative, it is difficult to conclude if the issue of tumour dependent CEA sensitivity contributed to the findings here.

Another drawback with use of CEA in monitoring colorectal Ca therapy is that a CEA surge can occur

following chemotherapy especially in regimens that include oxaliplatin (Wen and Wells, 2006) . This surge can give a false impression of worsening disease. However this did not apply to this case because oxaliplatin was not part of the regimen.

In view of conflicting evidence, American Society of Clinical Oncology (ASCO) does not recommend the routine use of CEA alone in monitoring treatment response in patients with colorectal cancer.(Bast et al., 2001). So some authorities posit that CEA monitoring should not be performed alone but should be combined with other methods such as radiologic evaluations.

CONCLUSION

This case report highlights the deficiency of the utility of CEA as a potential tool for monitoring of therapy and possible prognostication of colorectal carcinoma which can sometimes occur. It is important that clinicians are aware of this possibility in order not to unwittingly draw false conclusions.

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