

RESEARCH COMMUNICATION

Efficacy of Carcinogenic Embryonic Antigen in Differential Diagnosis of Diseases of Pancreas and Liver - A Comparative Study in a Tertiary Care Hospital of Western Nepal

Ankush Mittal^{1*}, Shamim Mohammad Farooqui², Samuel Pyrtuh³, Bibek Poudel¹, Brijesh Sathian⁵, Shambhu Kumar Yadav¹

Abstract

Objective: The objective of our present study was to assess the efficacy of carcinoembryonic antigen (CEA) for differentiating and diagnosis of pancreatic and liver diseases in Pokhara valley. **Materials and methods:** A hospital based retrospective study was carried out using data retrieved from the register maintained in the Department of Biochemistry of the Manipal Teaching Hospital, Pokhara, Nepal between 1st January, 2011 and 31st October, 2011. Estimation of CEA was performed by ELISA reader for all cases. Approval for the study was obtained from the institutional research ethical committee. **Results:** Of the 771 subjects, 208 (27%), 60(7.8%), 240(31.1%), 54(7.0%), 75(9.7%), 59(7.7%), 75(9.7%) cases were of active chronic hepatitis, cryptogenic cirrhosis, alcoholic cirrhosis, primary biliary cirrhosis, hepatoma, acute or chronic pancreatitis, carcinoma of pancreas respectively. The majority of cases (104) of active chronic hepatitis had CEA levels <5ng/ml(50%). CEA levels were found to be increased in cases of alcoholic cirrhosis with maximum number of cases (106) in range of 10 to 20 ng/ml (44%). There were no cases having more than 20ng/ml of CEA in primary biliary cirrhosis and acute or chronic pancreatitis. In cases of pancreatic cancer, maximum number of cases (35) were having CEA >20ng/ml(47%). **Conclusion:** High levels of CEA are associated with advanced stage of disease. CEA can thus provide an important improvement in the diagnosis by differentiating pancreatic cancer especially from chronic pancreatitis when there is a high suspicion of malignancy. Increased CEA levels may also signify progression from benign to malignant transformation in the liver.

Keywords: Carcinogenic embryonic antigen - pancreatic carcinoma - pancreatitis - cirrhosis of liver - Western Nepal

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Introduction

Acute pancreatitis is categorized into interstitial edematous pancreatitis and a hemorrhagic necrotizing pancreatitis (Haas et al., 2002). The interstitial edematous pancreatitis is considered by edema (exudation) of the pancreatic interstitium and a hemorrhagic necrotizing pancreatitis is regarded as autodigestion of a minor or major portion of the pancreas and peripancreatic tissues (Huis et al., 2001). Eighty percent of acute pancreatitis are accredited to biliary and alcoholic origin and can lead to recurrent acute pancreatitis and pancreatic cancer (Whitcomb, 2004).

Worldwide, 213,000 deaths occur each year due to pancreatic cancer. Men and women have an approximately at equal risk of getting pancreatic cancer. The major risk factors of pancreatic cancer are alcoholism, cigarette smoking, age, race, gender, religious background, chronic pancreatitis, diabetes and peptic ulcer surgery (Fraumeni, 1975). Clinical symptoms to a certain extent are unspecific for pancreatic cancer ensuing in a large number of

abdominal and extra abdominal diseases that have to be considered regarding the differential diagnosis.

Carcinoembryonic antigen (CEA) represent a family of glycoproteins released into the body fluids. The release of CEA differs according to their tissue of origin and elevated circulating levels of CEA could be useful for early diagnosis, differentiating and management of pancreatic and liver disorders (Nakahara et al., 1987). Elevated CEA plasma levels have been demonstrated in acute or chronic pancreatitis, carcinoma of pancreas, acute viral hepatitis, cryptogenic alcoholic cirrhosis, chronic active hepatitis, chronic persistent hepatitis, extrahepatic biliary obstruction, primary biliary cirrhosis and hepatoma (Gerber et al., 1978).

The three commonest risk factors for chronic liver diseases are excessive alcohol consumption, blood borne viruses, in particular hepatitis B and C, and obesity (Shrestha, 1992). In Nepal, easy availability, cultural acceptability and high social tolerance accentuates the danger of alcohol abuse. Production, sale, and consumption of alcohol is ever on the increase, leading to

¹Department of Biochemistry, ²Intern Department, ³Department of Anatomy, ⁴Department of Community Medicine, Manipal College of Medical Sciences, Pokhara, Nepal *For correspondence: drmittala@gmail.com

a much higher prevalence rate of alcoholic liver disease in Nepal (Mishra et al., 2009). Higher incidence of liver diseases in Nepal can lead to greater chances of developing pancreatic cancer. The aim of our present study is to assess the efficacy of CEA for differentiating and diagnosis of pancreatic and liver diseases in Pokhara valley.

Materials and Methods

It was a hospital based retrospective study carried out using data retrieved from the register maintained in the Department of Biochemistry of the Manipal Teaching Hospital, Pokhara, Nepal between 1st January, 2009 and 31st October, 2011.

Inclusion Criteria: A total number of 771 patients suffering from pancreatic and liver disorders with normal and elevated CEA were included.

Exclusion Criteria: Those patients whose CEA levels were found to be normal and elevated based on the history of patients suffering from any other cause apart from liver and pancreatic disorders. Also patients who were on treatment based on CEA elevation were also excluded as drugs could interfere in the CEA levels and also in assay. Approval for the study was obtained from the institutional research ethical committee. Estimation of CEA was performed by ELISA reader for all cases. The standard procedure was followed as per manufacturer's instructions for ELISA (Zamcheck et al., 1981). Analysis was done using descriptive statistics and testing of hypothesis. ANOVA was used to find out the statistical significance between the groups. The data was analyzed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version.

Results

Of the 771 subjects, 208 (27%), 60(7.8%), 240(31.1%), 54(7.0%), 75(9.7%), 59(7.7%), 75(9.7%) cases were of active chronic hepatitis, cryptogenic cirrhosis, alcoholic cirrhosis primary biliary cirrhosis, hepatoma, acute or chronic pancreatitis, carcinoma of pancreas respectively.

Table 1 illustrates the total number of cases for each liver and pancreatic disease. Total cases of each disease were subdivided according to the levels of CEA. The CEA levels were categorized into four groups i.e. 5 to 10ng/ml, 10 to 20ng/ml, >20 ng/ml. Majority of cases (104) of active chronic hepatitis were having CEA levels <5ng/ml(50%). CEA levels were found to be increased in cases of alcoholic cirrhosis with maximum number of cases(106) in range of 10 to 20 ng/ml(44%). There were no cases having more than 20ng/ml of CEA in primary biliary cirrhosis and acute or chronic pancreatitis. In cases of pancreatic cancer, maximum number of cases(35) were having CEA >20ng/ml(47%).

Table 2 represents the mean values of CEA of liver and pancreatic diseases. The mean values of CEA having range of 10 to 20 ng/ml (18.48±SD1.2) and >20ng/ml (31.49±SD8.58) in cases of carcinoma of pancreas were found to increased when compared with the mean values of other pancreatic and liver diseases. The mean

Table 1. Percentage of Cases with Different Levels of CEA in Various Pancreatic and Liver Disorders

| Total no. of cases | No. of cases with serum level (ng/ml) | | | |
|-----------------------------------|---------------------------------------|----------|-----------|----------|
| | <5 | 5 to 10 | 10 to 20 | >20 |
| Active chronic hepatitis: 208 | 104 (50%) | 58 (28%) | 30 (14%) | 16 (8%) |
| Cryptogenic cirrhosis: 60 | 11 (18%) | 19 (32%) | 21 (35%) | 9 (15%) |
| Alcoholic cirrhosis: 240 | 48 (20%) | 53 (22%) | 106 (44%) | 33 (14%) |
| Primary biliary cirrhosis: 54 | 38 (70%) | 10 (19%) | 6 (11%) | 0 (0%) |
| Hepatoma: 75 | 10 (13%) | 31 (41%) | 26 (35%) | 8 (11%) |
| Acute or chronic pancreatitis: 59 | 40 (68%) | 12 (20%) | 7 (12%) | 0 (0%) |
| Carcinoma of pancreas: 75 | 12 (16%) | 18 (24%) | 10 (13%) | 35 (47%) |

Table 2: Comparison of Mean Values of CEA in Pancreatic and Liver Diseases

| | Serum levels of CEA : Mean± SD | | | | p Value |
|--------------------------------|--------------------------------|-------------------|----------------------|----------------------|----------|
| | <5 | 5 to 10 | 10 to 20 | >20 | |
| Active chronic hepatitis: | 2.9±1.5 (2.7, 3.2) | 6.7±1.4 (6.3,7.1) | 15.0±1.4 (14.4,15.6) | 22.9±1.4 (22.1,23.6) | 0.0001** |
| Cryptogenic cirrhosis: | 2.6±1.7 (1.4,3.7) | 7.9±1.5 (7.2,8.6) | 15.8±3.0 (14.4,17.1) | 26.1±2.8 (23.9,28.3) | 0.0001** |
| Alcoholic cirrhosis: | 3.5±1.4 (3.1,3.9) | 7.0±1.7 (6.6,7.5) | 17.1±2.6 (16.6,17.7) | 26.2±4.0 (24.8,27.7) | 0.0001** |
| Primary biliary cirrhosis: | 1.9±1.4 (1.4,2.4) | 5.9±1.1 (5.1,6.7) | 13.0±1.0 (11.8,13.8) | NC | 0.0001** |
| Hepatoma | 1.5±1.2 (0.7,2.4) | 5.7±0.5 (5.5,5.9) | 13.4±2.5 (12.4,14.4) | 23.1±1.3 (22.1,24.1) | 0.0001** |
| Acute or chronic pancreatitis: | 1.6±1.0 (1.3,2.0) | 6.1±1.0 (5.6,6.6) | 11.8±1.1 (10.7,12.8) | NC | 0.0001** |
| Carcinoma of pancreas: | 4.3±0.4 (4.0,4.5) | 8.6±1.0 (8.1,9.1) | 18.5±1.2 (17.6,19.4) | 31.5±8.6 (28.6,34.4) | 0.0001** |

values of CEA for all ranges in cases of cryptogenic and alcoholic cirrhosis were almost similar. In cases of primary biliary cirrhosis, maximum elevation of CEA was upto 12.80 ± SD0.94. In the same way, in cases of acute or chronic pancreatitis, the utmost elevation was upto only 11.76±SD1.14. There was significant difference in highest mean values of CEA in pancreatic cancer cases and cases of acute and chronic pancreatitis.

Discussion

CEA symbolizes a family of complex immunoreactive glycoprotein with branched oligosaccharide chains linked to a polypeptide chain having a molecular weight of 180 kDa, found in serum or plasma (Oikawa et al., 1987). Pancreatic cancer and acute or chronic pancreatitis share several of their etiological and pathological features.

Inflammatory variations usually ensue in association with a primary carcinoma, while an augmented occurrence of pancreatic carcinoma has been testified in connotation with long-standing chronic pancreatitis. The differential identification among pancreatic cancer and acute or chronic pancreatitis is indispensable as the treatment and prognosis of these two diseases is diverse (Evans et al., 1997). Our present study revealed that CEA was found to be increased in 47% of patients with pancreatic cancer exhibited values > 20 ng/ml with the mean values of 31.49 ± 8.58 ng/ml compared to healthy subjects. The increased activity of cyclic-AMP in pancreatic cancer cells stimulate the synthesis and release of carcinoembryonic antigen, a membrane-associated glycoprotein antigen (Sack et al., 1988). In our current study, due to the benign causes such as chronic pancreatitis, maximum elevation of CEA was only within the range of 10 to 20 ng/ml with the mean values of 11.76 ± 1.14 ng/ml. Carcinoma of the pancreas is not readily differentiable from pancreatitis on the basis of CEA levels, but higher levels are more indicative and strongly suggestive of underlying malignancy. The findings of the current study conformed to the reports from the study conducted by Nakaizumi et al. (1999). Like most other tumor markers, CEA is useful for monitoring and differentiating disease but not for diagnosis or detection. The present study reveals that the highest percentage of cases with levels of CEA was in between 10 to 20 ng/ml among those who had cryptogenic cirrhosis (35%) and alcoholic cirrhosis (44%). In normal liver tissue, CEA accumulates in the apical cytoplasm and along the luminal surface of bile duct epithelial cells and is excreted by bile ducts. The rise in CEA levels in diseased liver are due to increased production or release of CEA by the damaged liver, decreased hepatic metabolism, or diminished excretion of CEA of extrahepatic origin (Piantino et al., 1981). Furthermore, the patients suffering from primary biliary cirrhosis did not have CEA values more than 20 ng/ml indicating non malignant origin. The above outcomes corresponded with the verdicts of Maestranzi et al. (1998) that the magnitude of the CEA level correlates with the severity of the liver disease. Therefore, CEA was a useful indicator for differentiating pancreatic cancer from chronic pancreatitis and also most useful in assessing different type of liver diseases but cannot be a conclusive factor for the diagnosis.

In conclusion, high levels of CEA are associated with advanced stage of the disease. CEA can provide an important improvement in the diagnosis by differentiating pancreatic cancer especially chronic pancreatitis in whom there is a high suspicion of malignancy. CEA elevations accompany both benign and malignant diseases of liver. Increased CEA levels signifies the progression from benign to malignant transformation.

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