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A Descriptive Study of Hepatic Enzyme Profile in Metastatic Liver Disease

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ABSTRACT

This is a cross-sectional descriptive study, carried out in patients admitted to surgical and radiotherapy units of a Government Medical College. A total of 62 cases of liver metastasis, diagnosed clinically and radiologically with histopathological confirmation were included in the study. Out of 62 cases of metastatic liver disease, 40 cases were detected along with the primary, 11 cases were detected during the follow-up period. Alkaline phosphatase was found to be elevated above the cut off limit of 120 IU/L in 49 out of 62 patients ie, in 79% of cases. GGT was elevated in 38 out of 62 patients studied. It contributed to 61.3% of the cases with liver metastasis. An elevation of 5"nucleotidase was observed in 51.6% of cases studied. SGPT was found to be elevated in 43.5% of cases. From this cross-sectional study it can be concluded that the majority of liver metastasis occur from GI malignancies and they are mostly from colo-rectal malignancy and are usually adeno carcinoma. Enzyme estimation is a good indicator of metastatic liver disease. Enzymes especially serum alkaline phosphatase and gamma glutamyl transpeptidase are simple and useful indicators of hepatic metastasis.

KEYWORDS heptic enzymes, liver metastasis, alkaline phosphatase.

INTRODUCTION

The problem of metastatic liver disease is well known for its high incidence, problems with regard to its management and more over difficulty in early detection .The high incidence of metastases in liver are thought to be as a result of its dual blood supply, ie portal vein and hepatic artery, and histological filtering effect and biological prediliction of cancer cells - probably based on cell-cell interaction. [1]Surgical resection is a treatment having a "potential for cure" in patients with limited metastases from colo-rectal carcinoma for others, chemotherapy, radiotherapy and arterial embolization have only a palliative role. Difficulty in early detection is there, no laboratory test is sufficiently sensitive or specific to be exclusively used for evaluation of hepatic metastasis, widely used tests include liver enzyme estimation, tumor marker assay, radio-immuno localization, radiological studies like ultrasonogram and Computerized Tomography (CT) scan. Serum Liver enzyme levels are frequently elevated in patients with metastatic liver disease. However, the significance of ALP and other liver enzymes alone in terms of detecting hepatic metastasis or prognosis is not well established. Enzyme estimation is a simple examination for detection of liver secondaries. Many studies have demonstrated the usefulness of imaging and scintigraphy, many more used single enzyme estimation to detect hepatic metastasis but only limited studies are available using a battery of enzymes to screen for liver secondaries. Ours study is a humble venture in this regard using a battery of 4 enzymes to see the percentage positivity of enzymes in proven cases of hepatic secondaries and which enzymes are elevated maximally. Moreover the liver enzyme estimation is much cheaper than imaging studies. The ALP estimation also have prognostic significance. Screening for hepatic metastases in patients with cancer is best accomplished with the more sensitive and less expensive group of biochemical liver tests.

MATERIALS AND METHODS

The aim of the study was to determine the proportion of patients having elevated liver enzymes among those with hepatic metastasis diagnosed clinically and confirmed radiologically and histopatholagically. The patient variables namely age, sex, history regarding the primary malignancy and hepatic metastasis were taken in detail. . Levels of Liver enzymes which includes Serum Alkaline phosphatase (ALP), Serum Gamma-glutamyl transpeptidase (GGT), Serum Glutamate-Pyruvate Transaminase (SGPT), 5'nucleotidase (5-NT) were studied. The study was a cross-sectional study which was conducted in patients admitted to surgical and radiotherapy units of a Government Medical College. The study population included all patients admitted to surgical & radiotherapy units during the study period of 6 months from February 2014 to August 2014 with the diagnosis of hepatic metastasis from any primary tumor, the metastasis being detected either along with primary or in follow-up period after resection or treatment of primary malignancy. Those patients with liver disease, obstruction to biliary system, previous hepatic injury, bony metastasis from any primary and patients on antituberculous drug therapy or any hepatotoxic drugs were excluded from the study. The patient variables namely age, sex, history regarding the primary malignancy and hepatic metastasis were taken in detail. All these cases were examined clinically prior to the selection, diagnosis was made by abdominal ultrasonogram or CT scan and then confirmed by fine needle aspiration biopsy (FNAB) or needle biopsy. Levels of Liver enzymes which includes Serum Alkaline phosphatase (ALP), Serum Gamma-glutamyl transpeptidase (GGT), Serum Glutamate-Pyruvate Transaminase (SGPT), 5'nucleotidase (5-NT) were studied. The data collected is then analyzed in spss 16 and results obtained.

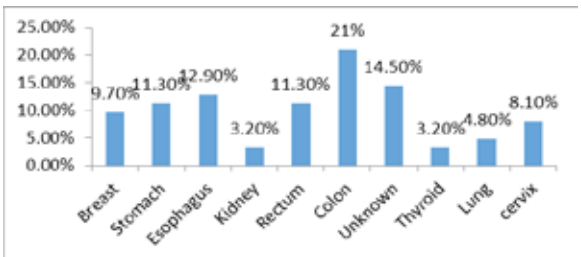
RESULTS

In the Medical college, during the period of this study,from

February 2014 to August 2014,we detected a total of 62 cases of liver metastasis, diagnosed clinically and radilogically with histopathological confirmation.

The incidence and distribution of the primary is as follows

GRAPH 1 DISTRIBUTION OF PRIMARY MALIGNANCIES



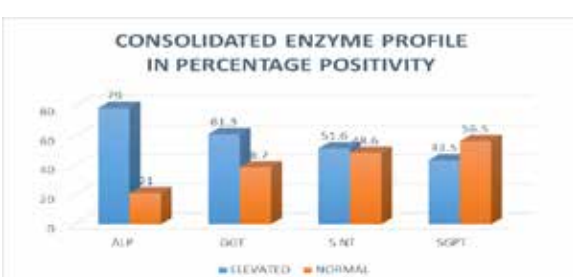
Out of 62 cases of metastatic liver disease, 40 cases were detected along with the primary, 11 cases were detected during the follow-up period. In 9 cases primary could not be identified.

The most common type of primary producing liver metastasis is colorectal carcinoma, accounting to 32.3% 0f liver metastasis (20 out of 62 cases). Secondaries from unknown primaries account for 14.5% of total liver secondaries, esophagus account for 13% of liver secondaries and breast, stomach and kidney account for 9.7%, 11.3% and 3.21%of liver secondaries respectively(see Graph-1).

ENZYME ANALYSIS

The patients were subjected to liver enzyme analysis using a test battery of 4 enzymes namelyAlkalinephosphatase(ALP),Gamaglutamyltranspeptidase(GGT), 5'Nucleotidase(5NT) and serum glutamate pyruvate transaminase(SGPT). Alkaline phosphatase was found to be elevated above the cut off limit of 120 IU/L in 49 out of 62 patients ie, in 79% of cases. It was not elevated in 13 of the patients with proven liver metastasis. GGT was elevated in 38 out of 62 patients studied above the cut off limit of 40IU/L. It contributed to 61.3% of the cases with liver metastasis(see graph. It was not elevated in 38.7% of cases. An elevation of 5"nucleotidase above 15 IU/L was observed in 51.6% of cases studied. 48.4% showed no elevation. SGPT was found to be elevated above 56IU/L in 43.5% of cases. Among the enzymes studied alkaline phosphatase was found to be elevated in maximum number of cases ie, 79% cases followed by GGT in 61.3%of cases(see Graph-2). SGOT and 5"nucleotidase did not show elevation much elevation in majority of cases. So ALP turns out to be the best biochemical tool to detect liver metastasis in combination with imaging modalities either CT or Ultrasonogram.

GRAPH-2 CONSOLIDATED ENZYME PROFILE



DISCUSSION

Liver enzymes can be divided into two categories those reflecting hepatocellular damage like aminotransferase and those reflecting obstruction.[2]. The study was a cross sectional study to look in to the hepatic enzyme profile of all patients with hepatic metastasis admitted during the period of 6 months mentioned above. Age group of patients ranged from 41 to 90 years, the mean age group was 49 to 68years. Biopsy from metastasis or intra-operative findings can be used as 'the gold standard' for the presence of liver metastases.[3] In our study patients with hepatic metastasis diagnosed radiologically and histopathologically were included, all those with bony metastasis, preexisting liver disease, and hepatitis were all excluded. Of 62 patients studied, 56 showed elevation of one or more of the 4 enzymes studied. Serum ALP was elevated in 49 of the 62 patients, which implies 79%positivity(see Graph-2). Alkaline phosphatase is a membrane-bound enzyme found in the bile canalicular pole of the hepatocyte. Elevated alkaline phosphatase levels are commonly seen in patients with biliary obstruction or diffuse liver metastases. Levels of alkaline phosphatase up to three times normal are nonspecific it can be considered as a serum marker of cholestasis.[4] In a previous study published in the Journal of Clinical Gastroenterology sited that patients with malignant biliary obstruction from a variety of cancers, including pancreatic cancer, gallbladder cancer, ampullary cancer, and lymphoma had elevation of ALP and it also described diffuse liver metastases as a cause of the extremely high elevation of alkaline phosphatase.[5] GGT elevation was noted in 38 patients among the 62 patients which implies 61.3% positivity in our study .In another previous study published in British journal of surgery ALP and GGT proved to be the most valuable biochemical tests as sensitivity of the other biochemical tests were very low. The specificity of ALP and GGT were respectively 78 and 68 per cent in the previous study.[5] 5'nucleotidase and SGPT were positive in 51.6% and 43.5% respectively. These results are at par with western literature which shows serum ALP as the most sensitive biochemical test to detect hepatic metastasis. In an article published in Archives of Surgery the most sensitive and specific estimations were for AP and GGT. The most sensitive and the most specific tests for the presence or absence of hepatic metastasis were measurements of alkaline phosphatase and gamma-glutamyltranspeptidase.[6] Tartter et al showed sensitivity of ALP to be 77% [7].Those with extensive bilobar metastasis showed marked elevation of more than one enzyme including serum ALP. In our study ALP proved to be the most consistently elevated enzyme in proven cases of liver metastasis. Imaging studies play a crucial role in the detection of liver metastasis and prognosis.[8] The imaging studies which detect exact number, regional distribution, size of metastases and the volume of the remaining liver is crucial to determine resectability.[9,10] A multi-modality approach is recommended since no single modality can detect all liver metastases

CONCLUSION

From this crosssectional study it can be concluded that the majority of liver secondaries occur from GI malignancies and they are mostly from colo-rectal malignancy. They are usually adeno carcinoma. Enzyme estimation is a good indicator of metastatic liver disease .In combination with radiological investigation they are virtually. diagnostic of metastasis even in absence of liver biopsy. Enzymes especially serum alkaline phosphatase and gamma glutamyl transpeptidase are useful indicators of hepatic metastasis.When used in combination with imaging modalities they may prove to be the best screening tools for detecting hepatic metastasis. Further studies comparing and correlating the predictive values of various modalities including enzymes, imaging and scintigraphy will be required to find out the best combination of modalities to screen for liver metastasis.

REFERENCES

1. Kusheri ., Grace, Darzi , Rowley-clinical surgery text book
2. Reichling JJ, Kaplan MM. Clinical use of serum enzymes in liver diseases. Dig Dis Sci. 1988;33:1601–1614
3. H. Schreve 0. T. Terpstra, L. Ausemat, J. S. Lamerist, A. J. van Seijent and J. Jeekel
4. Detection of liver metastases. A prospective study comparing liver enzymes, scintigraphy, ultrasonography and computed tomography. Br. J. Surg. 1984, Vol. 71, December, 947-949
5. Wulkan RW, Leijnse B. Alkaline phosphatase and cholestasis. *Ann Clin Biochem* 1986;23:405-12

6. Maldonado O, Demasi R, Maldonado Y, et al. Extremely high levels of alkaline phosphatase in hospitalized patients. J ClinGastroenterol. 1998;27:342–345.
7. Hugier M, Lacaine F. Hepatic metastases in gastrointestinal cancer. Arch Surg 1981; 116:399-401.
8. Tartter PI, Slater G, Gelernt I, et al. Screening for liver Metastases from colorectal cancer with carcinoembryonic antigen and alkaline phosphatase. Ann Surg 1981; 193:357- 360.
9. Klompje J, Petrelli NJ, Herrera L, Mittelman A. The prognostic value of preoperative alkaline phosphatase for resection of solitary liver metastasis from colorectal carcinoma. Eur J SurgOncol. 1987;13(4):345–347
10. Xu LH, Cai SJ, Cai GX, Peng WJ. Imaging diagnosis of colorectal liver metastasis. World J Gastroenterol. 2011 Nov 14;17(42):4654-9.
11. Sica GT, Ji H, Ros PR. CT and MR imaging of hepatic metastases. AJR Am J Roentgenol 2000; 174: 691-698