ORIGINAL RESEARCH PAPER

Pathology

KEY WORDS: Gastric Carcinoma,MDR-1

A HISTOPATHOLOGICAL STUDY AND MDR -1 EXPRESSION IN GASTRIC CARCINOMA

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ABSTRACT

Introduction : Gastric carcinoma is one of the common cause for cancer related mortality.There are three genes related to drug resistance,Multi drug resistance gene (MDR), Multi drug resistance Protein(MRP) and the lung resitance Protein (LRP).
Material and Methods:30 gastrectomy specimens from surgical department received.5 microns thick section cut.Stained with hematoxyllin and Eosin (H &E), Immunohistochemical study carried out using MDR-1 antibodies.
Conclusion: 18 out of 30 cases show positivity for MDR-1 gene expression.

Introduction:

Gastric cancer lincidence varies with geography..Gastric cancer is more common in lower socioeconomic groups, also in individuals with mucosal atrophy and intestinal metaplasia.Most of the patients are managed by either surgery or Chemotherapy[1,2]. Advances have been made in the field of Chemotherpy for a wide range of malignancies. However some types of cancers develop resistance to certain chemotherapeutic agents. Many types of drug resistnace have been reported in literature (Devita et al 1989)[3]. There are three genes related to drug resistance,Multi drug resistance gene(MDR), Multi drug resistance Protein(MRP) and the lung resitance Protein (LRP) Of these genetically determined muti drug resistance is best characterized and more common Among this MDR-1 gene is responsible for resistance of tumors to a wide variety of structurally and functionally unrelated chemotherapeutic agents[4]. The MDR-1 gene encodes for a 170 kd glycoprotein called which can be expressed in both normal and tumor tisssues. MDR-1 expressed in tissue can be detected by various methods like Western blot, IHC and PCR. Despite the multitude of chemotherapeutic agents available,gastric carcinoma has been proven to be highly refractory to chemotherapy.

Material and methods:

This study was conducted in Government Mohan Kumarama ngalam Medical College,Salem for a period of 2 years from January 2014 to December 2015.During that period 30 cases of total gastrectomy specimens were received from the surgical department. Taken bits from representative areas and submitted for processing.3-5 microns thick sections were cut and stained with Hematoxyllin and eosin.Histopathological diagnosis made according to WHO classification.Then Immunohistochemical study was carried out by using MDR-1 antibodies.

Observation and results:

The age of the patients included in this study ranges from 47 years to 72 years.There were 18 males and 12 females.

Histological subtype	No of cases	MDR positive cases
Tubular	5	3
Papillary	4	3
Mucinous	3	2
Adenosquamous	1	1
Small cell	1	1
Undifferentiated	14	5
Unclassified	3	3
Total	30	18

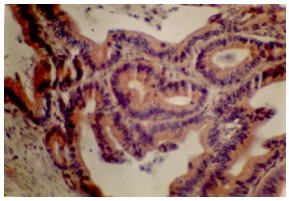

Fig 1:Well differentiated Adenocarcinoma shows diffuse MDR-1 Positivity.

The tumor was considered positive for p-glycoprotein if >5% of neoplastic cells exhibit immunoreactivity.In this study 18 out of 30 cases show MDR positivity i.e.60% of cases.The percentage of cells showing positivity in these tumors ranged from10% to 60 %(1+ to 3+ positivity)The positivity was cytoplasmic and was diffuse or granular in appearance.The intensity of positivity in these tumors varied from week to strong.

Discussion:

Gastric carcinoma is one of the leading causes of cancer death worldwide. Most patients diagnosed in advanced stage. Surgical treatment achieves poor survival due to locoregional recurrences. Different chemotherapeutic regimes employed achieve <15% complete response due to drug resistance. The over expression of MDR -1 gene explained the reason for poor results obtained with chemotherapeutic regimen.IHC is a reliable method detecting MDR-1 expression in tissues[8].

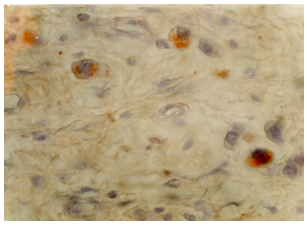

Fig 2:Shows Poorly Differentiated Adenocarcinoma Focal positivity for MDR

In our study shows positivity for MDR-1 is 60% with monoclonal antibody with p-glycoprotein which correlates with Lacueva et al[8]

This study shows p- glycoprotein expression with grade of carcinoma revealed highest percentage of positivity in grade II carcinoma and the lowest in grade IV carcinoma. Dhar et al[4] Fuji et al[5] reported the higher expression of differentiated tumors.

The expression of p glycoprotein in relation to cumulative survival rate in carcinoma of the stomach has been studied by Fujii et al[5]. Most chemotherapeutic ns regimens used against gastric carcinoma include anthracyclines whose effectiveness can be impaired by presence of p-glycoprotein. Since the effect of p-glycoprotein can be reversed by the use of certain modulating agents,it may be essential to detect the presence of this protein in gastric carcinoma[8].

Conclusion:

Demonstration of this gene product in tumors is particularly significant as it act as an efflux pump for the anthracycline group of drugs which are used in the treatment of these neoplasms[10,11]. Chemosensitization by certain modulating agents like verapamil reverses the drug efflux activity and holds promise for improving

the treatment outcome.Correlation of p-glycoprotein positivity with poor cumulative survival rate has been reported and the presence of this protein found to be useful prognostic indicator.

Bibliography

1. Alexander D,Yamamoto T,Kato S,Kasai S Histopathological assessment of multi drug resistance in gastric cancer.Expresion of p-glycoprotein, multigrug resistance-Associated protein and lung resistance protein Surg Today 1999;29(5):401
2. Chan HSL,Bradley G,Garipey et al A sensitive method for Immuno cytochemical detection of p-Glycoprotein in Multi drug resistant human ovarian carcinoma cell lines. Lab invest.1988,59:870,975
3. Devita VT,Hellman S,Rosengerg SA Principles and practice of oncology.Cancer 3 rd edition page No 276-300,1989
4. Dhar DK,Nagasue N,Yoshimura H et al overexpression of p-glycoprotein in unrelated AFP-producing gastric carcinoma J.Surg.Oncol,1995,6050-54
5. Fujii H,Tanigawa N,Muraoka,Shimamatsuya T,Tanaska T.Clinical significance of Multi drug resistance and p-glycoprotein expression in patients with gastric carcinoma J SUg.On 1995,58 -(1),page No 63-69
6. Gerlach JH,Endicott JA,Juraka PF et al Homology between p-glycoprotein and a bacterial transport protein suggests a model for Multi drug resistance ,1986:324:485-489
7. Hotta T,Tanimura H.T Sumoda T.Iwanashi M.et al p-glycoprotein expression and chemosensivity in highly purified fresh human gastrointestinal cancer cells. Hepatogastroenterology,1999:46(25):316-321
8. Lacueva e Fj,Terauel A,Calpeno R,Medrano J,Perez—Vazquez MT Detection of p -glycoproteinin frozen and paraffin embedded gastric adenocarcinoma tissues using a panel of monoclonal antibodies Histopathology1998,32(4) 328-334
9. Mizoguchi T.Yaamada K.et al Expression of MDR-1 gene in human gastric and Colorectal carcinoma J.Natl Cancer 1990 :82(21) page 1679-1683.
10. Yahandha AM,Adler KM,Fischer GA et al A phase I trial of etoposide with Cyclosporine as a modulator of multidrug resistance Jour. Clinical Oncology 1992, 10:1624-34
11. Gao Z Advances in the research on multi drug resistance genes Zhonghua Bing Li1996 june 25 (3)185-87