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Original Article

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Comparision of the Characteristics of Familial and Sporadic Cases in Patients with Gastric Cancer

[1]Şevket Arslan, [2]Mahmut İlhan

ABSTRACT

In this study, it was aimed to find the percentage of the non-familial and familial cases and comparison of their characteristic susing 2004 Canadian criteria in our cancer patients. The data from the files of 200 patients with histopathologically proven gastric cancer registered in our Medical Oncology Clinic were evaluated between January 2001 and December 2005. In our study, the ratio of familial cases is 10%. The mean ages of the patients are 56.44±0.78 in non-familial group and 53.30±2.90 in familial group. There were 113 males (62.77%), 67 females (37.23%) in non-familial group and 14 males (70%), 6 females (30%) in familial group. Histological types in familial and non-familial groups are; intestinal type 23.8% (n:3) and 75.23% (n:82); diffuse type 76.92% (n:10) and 24.77% (n:27) (p<0.01), respectively. The rate of cancers in localized stages are 5% (n:1) and 26,67% (n:48); where as the rates of advanced-stage cancers were 95% (n:19) and 73.33% (n:132) (p<0.01) in familial and non-familial groups respectively. Non-familial patients were 9.38% (n:12) Hp negative and 90.62% (n:116) were Hp positive where as familial cases were 100% (n:13) Hp positive (p<0.01). Blood groups in familial and non-familial groups are; Group A were 33.33% (n=2) and 58.46% (n:38); group B were 16.67% (n:1) and 10.77% (n:7), group O were 50% (n:3) and 29.23% (n:19) respectively. One patient (1.54%) in non-familial group was AB positive. Endoscopic screening should strongly be suggested in cases of unexplained upper abdominal complaints, especially for those people living in rural area in Van region.

Key words: *Gastric cancer, familial, sporadic.*

Mide Kanserli Hastalarda Familyal ve Sporadik Vakaların Özelliklerinin Karşılaştırılması

ÖZET

Bu çalışmada; mide kanserli hastalarımızda 2004 Kanada kriterleri göz önüne alınarak familiyal ve nonfamilyal vakaların oranının saptanması ve özelliklerinin karşılaştırılması amaçlandı. Ocak 2001 ile Aralık 2005 tarihleri arasında YYÜ Medikal Onkoloji Bilim Dalında poliklinik kayıdı olan histopatolojik tanısı konulmuş 200 mide kanserli hastanın dosya verileri değerlendirildi ve hasta ve/veya yakınları ile görüşüldü. Familyal özellik gösteren vaka oranı %10 oranında saptanmış olup hastaların yaş ortalamaları nonfamilyal grupta 56.44±0.78 yıl; familyal grupta 53.30±2.90 yıl olarak tespit edilmiştir. Nonfamilyal grupta 113 kişi (%62.77) erkek, 67 kişi (%37.23) kadın, familyal grupta 14 kişi (%70) erkek, 6 kişi (%30) kadın cinsiyette idi. Histolojik tipleri familyal ve nonfamilyal grupta sırasıyla %23.8 (n:3) ve %75.23 (n:82) intestinal tip; %76.92 (n:10) ve %24.77 (n:27) diffüz tip idi (p<0.01). Kanser evreleri familyal ve nonfamilyal vakalarda sırasıyla %5 (n:1) ve %26.67 (n:48) lokalize; %95 (n:19) ve %73.33 (n:132) ilerlemiş evredeydi (p<0.01). Helicobacterpylori (Hp) durumu; nonfamilyal grupta %9,38 (n=12) Hp negatif ve %90.62 (n:116) Hp pozitif; familyal grupta %100 (n:13) Hp pozitif idi (p<0.01). Kan grupları familyal ve nonfamilyal gruplarda sırasıyla %33.33 (n:2) ve %58.46 (n:38) A kan grubu; %16.67 (n:1) ve %10.77 (n:7) B kan grubu; %50 (n:3) ve %29.23 (n:19) O kan grubu idi. Nonfamilyal vakalarda %1.54 (n:1) AB kan grubu idi. Van yöresinde özellikle kırsal kesim şartlarında yaşayan insanlarda üst abdomen ile ilgili şikayetlerde endoskopik tarama ısrarla tavsiye edilmelidir.

Anahtar kelimeler: *Mide kanseri, ailesel, sporadik*

[1]Necmettin Erbakan University Medical Faculty, Division of Immunology and Allergic Disease, Konya, Turkey, [2]Special Avrasya Hospital, Medical Oncology, Istanbul, Turkey

Correspondence: *Şevket Arslan,*
Necmettin Erbakan University Medical Faculty, Division of Immunology and Allergic Disease, Konya, Turkey 42075 Konya-TURKEY
Tel: 00. 90. 332 223 6500 Fax: 00. 90. 332 223 6181
E-mail: arslansevket@hotmail.com

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INTRODUCTION

The gastric cancer (GC) has a high rate of morbidity and mortality among various cancers worldwide. It is the second leading cause of cancer death in both sexes worldwide (1). It is the third most commonly occurring cancer (8.2% of all cancers) in our country. Gastric cancer is reported that the most common form of cancer causes of high mortality in Eastern Anatolia (1,2). The understanding causes of GC has been made progressin the last 10 years. But, the etiopathological mechanism of human GC remains unclear, most researchers believe that the pathogenesis of this cancer is a multifactorial, multistage and multistepprocess. However, the epidemiological and histopathological studies have shown that infection with gastric bacterium Helicobacter pylori (HP) plays a role in the etiology of GC (3,4). The gastric cancers are sporadic and familial clustering is observed in about 10% of the cases. Guilford et al reported three Maori kindred with early onset, multigenerational, diffuse gastric cancer, in which germline mutations of the E-cadherin (CDH1) gene were identified by genetic linkage analysis and mutation screening in 1999 (7).

The families from other ethnicities were identified sharing similar features and the inaugural meeting of the International Gastric Cancer Linkage Consortium (IGCLC) was held to determine the diagnostic criteria and to provide guidelines for the clinical management of families with familial GC (5,6,7). Recently, the molecular mechanisms underlying familial GC have been studied intensively and in last decades, GC mortality rate has decreased globally (6,8). Gastric cancer is most common encountered in men and is the second most frequently in women in Eastern Anatolia (1,9).In our daily observations, GC in has been found to be more some families. Therefore, in this study, our GC patients who that with familial and non-familial cases identified in a kohort and their properties were compared.

MATERIALS AND METHODS

Study Population

The study took place in the division of Medical Oncology clinic at Yuzuncu Yil University Faculty of Medicine in Turkey, from January 2001 and December 2005. We obtained retrospectively clinic records of patients with GC who were diagnosed with histopathology. Inaddition, patients and/or their relatives were interviewed. Interview of the study was provided by the primary investigator.

In this study definition of familial gastric cancer in 2004 Canadian criteria (10) was used. Patients meeting these criteria were analyzed.

2004 Canadian criteria:

1.Two or more documented cases of diffuse gastric cancer (DGC) in first degree relatives, with at least one diagnosed before age 50.

1A.Two or more cases of GC, with at least one DGC diagnosed before age 50.

2. Three or more documented cases of DGC in first degree relatives, diagnosed at any age.

2A. Three or more cases of GC, diagnosed at any age, with at least one documented case of DGC.

3. Isolated individual diagnosed with DGC at less than 45 years of age.

4. Isolated individual diagnosed with both DGC and lobular breast cancer (no other criteria met).

5. One family member diagnosed with DGC and another with lobular breast cancer (no other criteria met).

6. One family member diagnosed with DGC and another with colon cancer(no other criteria met.

7. Intestinal gastric cancer.

The questionnaire was used to determine familial factors. At the beginning of this questionnaire; patient's name, surname, address, telephone number, Medical Oncology clinic file number has been saved.

Questionnaire form:

1.Who was performed with questionnaire?

a. It was performed with patient.

b. It was performed with patients' relatives (which patients' relatives)

c. It was performed with patients and their relatives (which patients' relatives)

2. Do you have cancer in first-degree relatives?

H: 0 (No)

E: 1 (Yes, there is the same type of cancer), E: 2 (Yes, there is different types of cancer)

S. 3 (doubtful)

B: 4 (unknown)

3. Who were caught the cancer in first-degree relatives?

Mom: 1

Father: 2

Children: 3 (How many children suffering from cancer?)

Siblings: 4 (How many brothers and sisters suffering from cancer?)

4. Do you have cancer in second-degree relatives?

H: 0 (No)

E: 1 (Yes, there is the same type of cancer), E: 2 (Yes, there are different types of cancer)

S. 3 (doubtful)

B: 4 (unknown)

5. Who were caught the cancer in second-degree relatives?

a. Mother's sister: 1

b. The children of the mother's sister: 2

c. Father's sister: 3

d. The children of father's brother: 4

The data on the outpatient files of all patients were investigated. Moreover, patients and/or their families were also interviewed. The interviews were performed by the primary researcher of this study. The familial gastric cancer was defined according to the 2004 Canadian Criteria (10). In determination of familial factors, a questionnaire of 12 main items was used. At the beginning of this questionnaire; name, surname, address, telephone number and medical oncology file number of all patients were recorded. First 8 items were the data of the patients, while the last 4 were the summary of these data.

Other than the presence of familial gastric cancer, by investigating outpatient files of all patients with gastric cancer, some more parameters including age, gender (male, female), histological type of cancer (diffuse, intestinal), cancer stage (local, advanced= local progressive + metastatic), localization of cancer (proximal= les, cardia, fundus; distal= corpus, antrum, pylori and both proximal and distal), the Helicobacter pylori (Hp) status (positive, negative) and blood groups (A, B, AB and O) of all patients were also recorded.

Table 1. *The meanage of patients*

Stomach Cancer Groups	*n:200*	*%*	*mean±SD (min-max)*
Non-familial	*180*	*90*	*56.44±0.78 (22-80)*
Familial	*20*	*10*	*53.3±2.90 (40-86)*
Total	*200*	*100*	*56.13±0.76 (22-86)*

RESULTS

In this consecutive cohort of 200 cases, 20 (10%) of the cases were showing familial characteristics according to the 2004 revised multi-national Canadian Criteria while 180 (90%) of the cases were not showing familial characteristics. In our study, 10% (n:20) of the cases were deserving E-cadherin mutation analysis. The tables according to these criteria including age, gender, histological tissue type, cancer stage, cancer localization, Hp status and blood groups of patients are shown below. According to 2004 Canadian criteria; the mean age of patients included in the study were determined as 56.44±0.784 years in non-familial group, while it was 53.30±2.90 among familial cases (Table 1). The gender distribution of patients was 113 (62.77%) male, 67 (37.23%) female in non-familial group whereas 14 (70%) patients were male and 6 (30%) were female in familial group.

In evaluation of histological types of cancers; 82 (75.23%) patients had intestinal type and 27 (24.77%) patients had diffuse type in non-familial group while in familial group 3 (23.08%) were intestinal type and 10 (76.92%) were diffuse type. The cancer stage of included patients were localized in 48 (26.67%) patients and advanced in 132 (73.33%) patients among non-familial group even though 1 (5%) patient had localized and 19 (95%) patients had advanced disease in familial group. The localization of cancer was proximal in 54 patients (30%), distal in 115 patients (63.89%) and both proximal and distal in 11 (6.11%) patients in the non-familial group. On the other hand, in familial group 5 (25%) patients had proximally located, 13 (65%) patients had distally located and 2 (10%) patients had bot proximally and distally located disease (Table 2).

In evaluation of Hp status of patients; in non-familial group 12 (9.38%) patients were negative and 116 (90.62%) were positive while in familial group all assessed 13 (100%) patients were Hp positive .The blood group distribution of included patients were as follows; 38 (58.46%)

patients were carrying A blood group, 7 (10.77%) were in B blood group, 1 (1.54%) was in AB blood group and 19 (29.23%) were in 0 blood group in non-familial group. On the other hand, among patients in familial group, 2 (33.33%) were carrying A blood group, 1 (16.67%) was in B blood group and 3 (50%) were carrying 0 blood group (Table 3).

DISCUSSION

Gastric cancer (GC) is the 2nd most common cause of deaths due to cancer in all over the world. In developed and developing all countries, gastric cancer is more commonly seen among man (1). Five-to ten percent of GC are reported to be familial (5,6). In our country, any studies about the familial GC is not present, yet. In this study among GC patients; according to the 2004 revised multinational Canadian Criteria among familial cases 70% of patients were male and 30% of patients were female while in non-familial group 62,77 % were male and 37,23% were female.

In Eastern Anatolia region, GC is commonly reported in between the ages of 50-70 years (1,9). The risk of GC, before the age of 30 years is extremely rare (11). In our study, the mean age of non-familial cases was 56,44±0.78 years which was compatible with the literature; however the mean age of familial cases was 53,30±2.90 years which was higher than the previously reported values in literature.

The first data about the association of Hp with gastric carcinoma has been determined by the epidemiologic studies (12). The Hp prevalence on gastric mucosa around the carcinoma in gastrectomy material of advanced GC is close to the Hp prevalence on gastric mucosa of gastric ulcer or chronic gastritis. Helicobacter Pylori is the microorganism that causes atrophic gastritis and/or concomitant intestinal metaplasia which are also known as GC precursors (3,4,12). In an investigation of EUROGAST study group, on 17 different populations in 11 European countries, Japan and USA, the risk of gastric cancer development was determined as 6 times increased among Hp positive patients compared with negative ones (13). As gastric cancer, Hp infection was also more commonly reported in developing countries (14). In investigations around the Van region, for many years, Hp prevalence was not determined to be very high in GC. In our region; Turkdogan et al (11) have reported 57% of Hp positivity among 384 gastric cancer patients. In our study, Hp was positive in 90,62% and negative in 9,38% of cases in non-familial group and Hp positivity was determined as 100% in familial group. This higher value of us in Hp prevalence was thought to be probably due to the lower number of cases in our study compared with the previous studies in Van region.

The role of genetic factors in gastric cancer was first determined with the finding of association of blood groups with chronic gastritis. It has been suggested that, the patients with the A blood group carry more risk in regards to the GC compared with the people with other blood groups (15). In our study, among non-familial cases 58,46% were carrying A blood group, 10,77% were in B blood group, 1,54% were in AB blood group and 19 29,23% were carrying 0 blood group. On the other hand, among patients of familial group, 33,33% were carrying A blood group, 16,67% was in B blood group and 50% were carrying 0 blood group whereas there was no patients with AB blood group in familial cases. In this study we have determined that 0 blood group was more common in familial group, however owing to the low number of cases, larger studies are warranted in familial GC patients to determine the effects of blood groups. Five-to-ten percentage of GC is familial (16). Hemminki and Jiang (17), investigated 10,2 million cases of which was comprehending more than 34 thousands GC cases, and determined the familial risk as 5-10% among GC patients. In our study we also have determined the familial features with the ratio of 10 % among gastric cancer patients, which was compatible with the literature.

Both familial and sporadic GC are the results of mul-

***Table 2**. The localization of cancer patients*

Stomach Cancer Groups	Proximal		Distal		Proximal+Distal		Total	
	n	%	n	%	n	%	n	%
Non-familial	54	30	115	63.89	11	6,11	180	100
Familial	5	25	13	65	2	10	20	100
	z=0,49	p=0.626	z=0,10	p=0.921	z=0,56	p=0.575		

tiple genetic and epigenetic differentiations that cause the transformation of normal gastric epithelial cells into malign neoplasm. E-cadherin gene is commonly found in mutated form in many malignancies such as breast, thyroid, prostate, colon and GC (6,18,19). Familial tendency is more commonly reported in diffuse gastric cancer than intestinal type. The risk of GC among the relatives of patients with diffuse type gastric cancer increases 7 times while it increases 1,4 times among the relatives of patients with intestinal type gastric cancer. Because of this reason, suggesting screening and preventive treatments is appropriate to the family members of patients with gastric cancer (20). In our study histological types of 122 GC cases were determined; among those in non-familial group 75,23% were intestinal type and 24,77% were diffuse type. On the other hand, among familial cases, 23,08% were intestinal type and 76,92% were diffuse type. Our findings were in parallel with the previous reports. In a study, it has been determined that 36% of GC were localized in antrum, 21% in esophago-cardiac junction, 42% in corpus, 0.7% in fundus while 4% were diffuse (1). Turkdogan et al (11) had determined that 36% of gastric cancers were localized in antrum, 36% in corpus, 20% in cardia and 8% were diffuse. In our study, the localization of cancer was proximal in 30%, distal in 63,89% and both proximal and distal in 6,11% of patients in the non-familial group. On the other hand, in familial group 25% of patients had proximally located, 65% of patients had distally located and 10% of patients had both proximally and distally located disease. Our results were compatible with the previous studies.

Generally GC is diagnosed at later stages. The lesions do not provide obvious symptoms till the advanced stages. Usually the patient is at advanced stages (stage 3 or 4) when the gastric cancer is diagnosed. Although 40% of gastric cancers are diagnosed at early stages in Japan, this ratio is about 15% in Europe (21). Similarly in our study, many of patients were at advanced stages for instance; in non-familial group 26,67% of cases were localized and 73,33% were advanced while among familial cases 5% were determined as localized and 95% were advanced. In conclusion, the necessity of determination of cases with the family history of gastric cancer and informing them about the genetic studies and early screening of gastric cancer and especially in a region like Van region, which has the highest prevalence of gastric cancer in Turkey, endoscopic screening of family members of gastric cancer patients over the age of 35 years and living in rural areas and moreover education of both the doctors and community on this topic is considered. By this way, the cases with the high risk of gastric cancer may be diagnosed earlier and the survival rates of gastric cancer patients may be elongated.

REFERENCES

1. *Tuncer I, Uygan I, Kosem M, Ozen S, Ugras S, Turkdogan K. Demographic and histopathologic features of Upper Gastrointestinal Cancer observed in Van region and surrounding areas. Van J Med 2001;8:1.*
2. *Alıcı S, Izmirli M, Dogan E. Epidemiologic evaluation of cancer patients admitted toYuzuncu Yıl UniversityFaculty of Medicine, Department of Medical Oncology. Turkish J Oncol 2006;2:87-97.*
3. *Sriamporn S, Setiawan V, Pisani P, et al. Gastric Cancer: the Roles of Diet, Alcohol Drinking, Smoking and Helicobacter pylori in Northeastern Thailand. Asian Pac J Cancer Prev 2002;3:345-52.*
4. *Roder DM. The epidemiology of gastric cancer. Gastric Cancer 2002;5:5-11.*
5. *Blair V, Martin I, Shaw D, et al. Hereditary diffuse gastric cancer: diagnosis and management. Clin Gastroenterol Hepatol 2006;4:262-75.*
6. *Suriano G, Yew S, Ferreira P, et al. Characterization of a recurrent germline mutation of the E-cadherin gene: implications for genetic testing and clinical management. Clin Cancer Res 2005;11:5401-9.*
7. *Guilford P, Hopkins J, Harraway J, et al. E-cadherin germline mutations in familial gastric cancer. Nature 1998;392:402-5.*
8. *Bacani JT, Soares M, Zwingerman R, et al. CDH1/E-cadherin germline mutations in early-onset gastric cancer. J Med Genet 2006;43:867-72.*

Table 3*. The blood groups of cancer patients*

Stomach Cancer Groups	Ablood groups		Bblood groups		ABblood groups		Oblood groups	
	n	%	n	%	n	%	n	%
Non-familial	38	58.46	7	10.77	1	1.54	19	29.23
Familial	2	33.33	1	16.67	0	0	3	50
	z=1.24	p=0.213	z=0.38	p=0.71	z=1.01	p=0.314	z=0.98	p=0.327

9. Turkdogan MK, Akman N, Tuncer I, et al. Epidemiological aspects of endemic upper gastrointestinal cancers in Eastern Turkey. Hepato-Gastroenterology 2005;52:496-500.

10. Brooks-Wilson AR, Kaurah P, et al. Germline E-cadherin mutations in hereditary diffuse gastric cancer: assessment of 42 new families and review of genetic screening criteria. J Med Genet 2004;41:508-17.

11. Konturek JW. Discovery by Jaworski of Helicobacter pylori and its pathogenic role in peptic ulcer, gastritis and gastric cancer. J Physiol Pharmacol 2003;54:23-41.

12. Webb PM, Forman D. Helicobacter pylori as a risk factor for cancer. Baillieres Clin Gastroenterol 1995;9:563-82.

13. Jenab M, McKay JD, Ferrari P, et al. CDH1 gene polymorphisms, smoking, Helicobacter pylori infection and the risk of gastric cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST). Eur J Cancer 2008;44:774-80.

14. Parsonnet J. The incidence of Helicobacter pylori infection. Aliment Pharmacol Ther 1995;9:45-51.

15. You WC, Ma JL, Liu W, et al. Blood type and family cancer history in relation to precancerous gastric lesions. Int J Epidemiol 2000;29:405-7.

16. Barber M, Fitzgerald RC, Caldas C. Familial gastric cancer-aetiology and pathogenesis. Gastric Cancer 2006;20:721-34.

17. Hemminki K, JiangY. Familial and second gastric carcinomas: A Nation wide epidemiologic study from Sweden. Cancer 2002;94:1157-65.

18. Pedrazzani C, Corso G, Marrelli D, Roviello F. E-cadherin and hereditary diffuse gastric cancer. Surgery 2007;142:645-57.

19. Graziano F, Humar B, Guilford P. The role of the E-cadherin gene (CDH1) in diffuse gastric cancer susceptibility: from the laboratory to clinical practice. Ann Oncol 2003;14:1705-13.

20. Chen JD, Kearns S, Porter T, Richards FM, Maher ER, Teh BT. MET mutation and familial gastric cancer. J Med Genet 2001;38:26.

21. Hohenberger P, Gretschel S. Gastric cancer. Lancet 2003;362:305-15.