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Gastric lymphoma diagnosis in Lithuania over the last 10 years

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Gastric lymphoma amounts to 1–5% of all gastric malignances. Contrary to gastric adenocarcinoma, gastric lymphoma does not show a decreasing trend.

The aim of this study is to analyze possible changes in the patterns of diagnosed gastric malignancies, particularly lymphomas, as the imunohistochemical (IH) method employing lymphoid markers has been introduced into clinical practice in Lithuania 10 years ago.

Materials and methods: Gastric lymphomas and carcinomas were selected from all gastric malignancies registered in databases of the Lithuanian Cancer Registry in 1993–2003; the differentiation grade was taken into account. During this period, gastric malignancies were diagnosed in 11823 cases (133 gastric lymphomas and 8579 gastric carcinomas with histological confirmation). Gastric malignancies traditionally are diagnosed using endoscopical examinations combined with biopsy and histopathological examination. In 1996, the IH method was introduced in clinical practice in Lithuania, and this allowed us to improve the diagnosis of gastric lymphomas. The same methods and their combinations with the IH method using lymphoid and other markers (LCA, CD3, CD8, CD20, CD5, Cyclin D1, Ki67, CK8, CK116) were used for diagnosing gastric lymphoma.

Results: The number of gastric lymphomas diagnosed in Lithuania has increase from 7 cases in 1993 to 15 cases in 1998 and 11 cases in 2003. Gastric lymphoma counts for 1.6% of all histologically confirmed gastric malignancies. The number of lymphomas detected imunohistochemically increased from 30% in 2000 to almost 70% in 2003 together with the number of IH markers used. Our data show that most of gastric lymphomas in the period 2000–2003 when we used WHO classification were B cell lymphomas, followed by marginal zone cell lymphomas (62.9%, 39/62); this corresponds to data from other countries. The most common subtype of B-cell lymphoma was diffuse large B-cell lymphoma (DLBCL) (45.2%, 28/62).

Key words: primary gastric lymphoma, imunohistochemical (IH) method, lymphoma classification, diffuse large B-cell lymphoma (DLBCL)

INTRODUCTION

Over the last decade the incidence of gastric malignancies has been decreasing both in the world and in Lithuania. Primary gastric lymphoma amounts to 1–5% of all gastric malignances (1). Contrary to gastric adenocarcinoma, gastric lymphoma does not show a decreasing trend. Changing patterns of gastric malignanciens are important for treatment strategies of these lesions (2–4). The incidence rate of gastric lymphoma in European countries is similar, except the histological subtype of diffuse large B-cell lymphoma (DLBCL), and amounts to 33–80% from all gastric lymphomas. The aim of this study was to assess the incidence of primary gastric lymphoma after the immunohistochemical method with lymphoid markers has been introduced in Lithuania 10 years ago. The method is helpful to identify diffuse large B-cell (DLBCL) as well as other lymphomas.

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MATERIALS AND METHODS

Gastric lymphomas and carcinomas were selected from all gastric malignancies registered in databases of the Lithuanian Cancer Registry in 1993–2003; the differentiation grade was taken into account. During this period gastric malignancies were diagnosed in

11823 cases including 133 gastric lymphomas and 8579 gastric carcinomas (5539 with differentiated and 1708 poorly differentiated). Gastric malignancies traditionally are diagnosed endoscopical examinations with biopsy, with a subsequent histopathological investigation. Endoscopically, gastric lymphoma looks like a polypoid or ulcerated mass; its appearance does not differ much from gastric carcinoma. In 1996, the IH method was introduced into clinical practice in Lithuania, and this allowed us to improve the diagnostics of gastric lymphomas. The same methods and their combinations with the IH method with lymphoid and other markers (LCA, CD3, CD8, CD20, CD5, Cyclin D1, Ki67, CK8, CK116) were used for diagnosing gastric lymphoma. Since 2000, to assess the distribution of primary gastric lymphomas, special diffuse large B-cell lymphoma (DLBCL) is classified in Lithuania according to the WHO (World Health Organization) classification.

RESULTS

The results of this population-based study show that the gastric lymphomas diagnosed in Lithuania has increased from 7 cases in 1993 to 11 cases in 2003. For this period, gastric lymphoma accounts for 1.6% (133/8579) of all histologically confirmed gastric malignancies. The number of lymphomas detected imunohistochemically gradually increased from 30% (7/21) in 2000 to almost 70% (7/11) in 2003, together with the number of IH markers used (see Table 1). The diagnosis of the specific types of gastric lymphomas in comparison with NOS increased from 57.1% (12/21) in 2000 to 81.8% (9/11) in 2003. Our data show that most of gastric lymphomas for the period 2000–2003 when we used the WHO classification are B cell lymphoma, followed by marginal zone cell lymphoma (62.9%, 39/62); this corresponds to data from other countries (see Table 2). The most common subtype of B-cell lymphoma was diffuse large B-cell lymphoma (DlBCL) – 45.2% (28/62).

Table 1. **Usage of immunohistochemistry for diagnosing gastric lymphomas**

Item	Year of diagnosis					
	1998	1999	2000	2001	2002	2003
New cases	15	9	21	18	12	11
Among them:						
IH detected Lymphomas	3	8	7	10	9	7
number of different IH markers used	4	5	6	9	8	11

Table 2. **Specific types and lymphomas NOS 2000–2003 in NCP**

Category	Year of diagnosis			
	2000	2001	2002	2003
Lymphoma NOS	12	7	2	2
Specific types of lymphomas	9	11	10	9
Among them:				
DLBCL	6	8	8	6
B SLL	3	1	–	–
Marginal zone MALT	–	2	2	3

DISCUSSION

According to the results of this study, gastric lymphomas count for 1.6% of all gastric malignancies. A study in Lithuania showed that in 1994–1999 only 0.9% of gastric neoplasms were lymphomas (5). The same results has been shown by a recent study made at two National Health Institutes in Mexico City. It revealed a remarkable increase in the frequency of gastric lymphoma (9.3% and 10.3%). For comparison, two studies performed in Mexico in 1960 and 1966 found that only 1.9% and 1% of gastric neoplasms were lymphomas (1). From 1993 to 2004, 133 gastric lymphomas were diagnosed at the National Center of Pathology (NCP). It is hard to classify properly the specific types of gastric lymphomas until 2000 or even for 2001. The Kiel classification or the Working Formulation of lymphomas' classification was used until 1997 and sometimes until 1999 or even 2000 at the NCP. Almost all of the 44 gastric lymphomas diagnosed in 1993–1997 were defined as lymphosarcomas or as lymphoblastic lymphosarcomas. Only one small B cell lymphocytic, one follicular and three Hodgkin's lymphomas were detected during this period. It should be noted that the term lymphoblastic lymphosarcoma was applied to every lymphoma with large cells (centroblastic according to Kiel), thus the majority of the gastric lymphomas diagnosed in 1993–1997 seem to be diffuse large B cell lymphomas (DLBCL). On the other hand, the term lymphosarcoma might mean any type of the diffuse lymphoma-B small lymphocytic lymphoma (B SLL), mantle cell or marginal zone B cell lymphoma and finally DLBCL (see Figs. 1 and 2). The term centrocytic / centroblastic lymphoma from the Kiel classification emerged at the NCP in 1998. This class of lymphomas covers four cases from 15 gastric lymphomas in 1998. The others are two DLBCL and nine not otherwise specified (NOS) lymphomas.

The Revised European American Classification of Lymphoid Neoplasm (REAL) was proposed in 1994. It became familiar at the NCP in 1999. This year was a transition period during which the Kiel classification / Working For-

Table 3. **Clinicopathological studies of primary gastric DLBCL lymphomas**

Study [Ref]	Year	Number of subjects	DLBCL cases (%)	Type
Recent	2000–2003	62	28(45.2)	Population-based
Barreda B et al.	[2] 1995–2000	169	137(81.1)	Clinical-based
Gospodarovicz M.	[11] 1967–1996	149	122(81. 9)	Clinical-based
Ranaldi R et al.	[12] 1976–1996	152	53(34.9)	Population-based
Ullrich A et al.	[13] 1998–2000	94	31(33.0)	Population-based

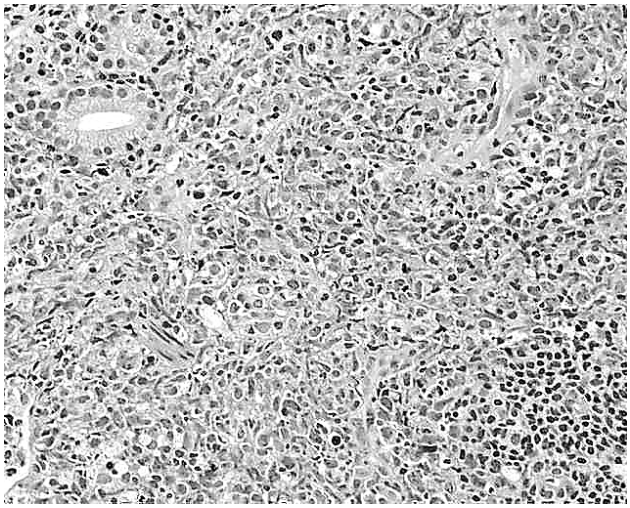

Fig. 1. Diffuse large B cell lymphoma: polymorphous lymphoid cells between gastric glands. ´200, HE.

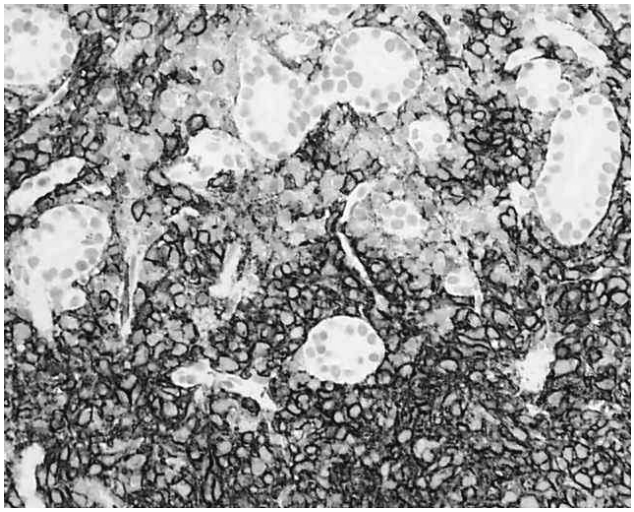

Fig. 2. Diffuse large B cell lymphoma: CD 20 positive (brown) B cells between gastric glands with destruction of the glands. Imunohistochemistry. ´200.

mulation was replaced by the REAL classification. Therefore in 1999 we had two centrocytic / centroblastic, two DLBCL and five lymphoma NOS from nine gastric lymphomas.

Despite availability of the IH methods and the introduction of the new classifications, especially REAL, there were many not otherwise specified lymphomas in the year 2000 (12 from 21 gastric lymphomas). The other gastric lymphomas diagnosed in 2000 were six DLBCL and three diffuse small B cell lymphomas. The newest WHO classification, based on the REAL classification, was published in 2001. Since this year we observe a gradual decrease of the frequency of diagnosed NOS lymphomas and an increase of the number of diagnosed lymphomas of specified types (6–8). The imunohistochemical (IH) method at the NCP was introduced in 1996 and allowed us to improve the diagnosing of gastric lymphomas. Initially only three lymphoid markers (LCA, CD 20 and CD 45RO), were in use and hematological IH markers were used very sporadically until 1999. For example, in 1998 the diagnosis of only three lymphomas from 15 gastric lymphomas were proved imunohistochemically. In one case only common epithelial (CK 116) and common leucocytic antibodies (LCA) were used. At present, the NCP has about 70 IH markers, 26 hematological markers among them. The IH method in diagnosing gastric lymphoma helps to identify the type of endoscopically diagnosed gastric malignancy (9, 10). Our data show that most of gastric lymphomas for the period 2000–2003 when we used the WHO classification are the B cell lymphomas, followed by marginal zone cell lymphoma (62.9%, 39/62). The most common subtype of B-cell lymphoma was diffuse large B-cell lymphoma (DLBCL) – 45.2%. Other studies show similar findings (2,11–13). The clinicopathological results on primary gastric (DLBCL) lymphomas in the present study and from other countries are shown in Table 3. Our population-based study is in good agreement with other population-based studies (45.2% *versus* 34.9% and 33.0% of DLBCL), but differs from clinical bases that show a higher proportion (more that 80%) of DLBCL. The effect of the adequate treatment of gastric lymphomas with regard to their histopahotological type should be studied in Lithuania in the future.

CONCLUSIONS

1. The number of diagnosed gastric lymphomas has increased in Lithuania over the last decade. This tumor accounts for 1.6% of all morphologically confirmed gastric malignancies.

2. The proportion of the imunohistochemically detected lymphomas gradually increased from 30% in 2000 to almost 70% in 2003 together with the number of IH markers used. The most common subtype of B-cell lymphoma was diffuse large B-cell lymphoma (DLBCL) – 45.2%.

2. The IH method with lymphoid and other markers used for the final diagnosis of gastric lymphoma was important in the differential diagnosis of gastric malignancies and will be helpful in improving the identification of the subtypes of gastric lymphomas and in achieving better treatment results.

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PIRMINIØ SKRANDÞIO LIMFOMØ DIAGNOSTIKA PER PASTARUOSIUS 10 METØ LIETUVOJE

Santrauka

Ávadas. Skrandþio limfomos sudaro apie 1–5% visø skrandþio piktybiniø navikø. Skirtingai nuo vëþio, sergamumas skrandþio limfoma maþëja ir yra panaðus Europos ðalyse. Ðio darbo tikslas – iðnagrinëti sergamumà pirmine skrandþio limfoma Lietuvoje atsiþvelgiant á prieð 10 metø ðalyje ádiegtà imunohistocheminá metodà. **Medþiaga ir metodai**. Skrandþio piktybiniø navikø bei limfomos atvejai Lietuvos vëþio registre buvo atrinkti 1993–2003 m. pagal ávairiø tipø registruotø navikø diferenciacijà. Ðiuo periodu buvo diagnozuoti 11823 piktybiniai navikai, áskaitant 133 skrandþio limfomas, 8579 histologiðkai patvirtinti skrandþio vëþio atvejai. Skrandþio piktybiniai navikai buvo diagnozuojami endoskopu paëmus biopsijà ir atlikus patohistologinius tyrimus. 1996 m. á Lietuvos medicinos praktikà buvo ádiegtas imunohistocheminis metodas (IH), kuris labai pagerino skrandþio limfomø diagnostikà. Endoskopiná metodà derindami su imunohistocheminiu metodu, taip pat naudodamiesi ávairiais limfoidiniais bei kitais markeriais (LCA, CD3, CD8, CD20, CD5, Cyclin D1, Ki67, CK8, CK116) nustatydavome galutinæ skrandþio limfomos diagnozæ. **Rezultatai**. Ðio darbo rezultatai rodo, kad diagnozuotø skrandþio limfomø daugëja: nuo 7 atvejø 1993 m. iki 11 atvejø 2003 metais. Ið viso skrandþio limfomos Lietuvoje sudaro 1,6% visø histologiðkai patvirtintø piktybiniø navikø. Diagnozuotø skrandþio limfomø dalis panaudojus IH markerius þenkliai iðaugo – nuo 30% (7/21) 2000 m. iki 70% (7/11) 2003 metais. Ðio darbo duomenimis, didesnæ skrandþio limfomø dalá sudaro didelës difuzinës B làsteliø limfomos – 45,2% (28/62). Mûsø atlikto darbo duomenys sutampa su analogiðkø uþsienio darbø duomenimis.