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The Incidence of Epstein Barr Virus Antibodies in Hodgkins Lymphoma

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Abstract:

The association of Epstein Barr Virus (EBV) with Hodgkins lymphoma (HL) seems to depend on many factors such as geographical area , histological subtype and age. The present study included (30) patients having HL (18 males and 12 females) with age ranged 25 – 53 years, where histopathological sections reviewed. A second group regarded as control group complained of non malignant disorders (25)patients with age ranged (20 -55) years was identified that VCA –lgG and EA-lgG were significantly higher (p 0.05) in HL group compared with control group. EBV positive is more prevalent in mixed cellularity subtype (56.6%) of all cases examined.The significant association between EBV and HL that was found further strengthens the suggestion that all cases of HL should be assessed for EBV status by immunohistochemistry because its presence may have a significant impact on prognosis and response to therapy.

Introduction:

The hypothesis that the pathogenesis of Hodgkins Lymphoma (HL) involves an infectious agent has been considered since it was described by Thomas Hodgkins in 1832. This is suggested primarily by its clinical features of night sweats, fever and lymphadenopathy, as well as histological features resembling an inflammatory granuloma (1). Epstein–Barr virus (EBV), a member of herpes group infects many normal individuals through the B–lymphocytes. Since its discovery as the first tumor virus, EBV has been implicated in the development of wide range of B-cell lymphoproliferative disorders including Burkitts' lymphoma, HL and lymphoma arising in immunocomprised individuals (post-transplant and HIV –associated lymphoproliferative disorders) (2,3,4).

The association of EBV with HL seems to depend on factors such as country of residence, histologic subtype, gender, age and ethnicity. The increased incidence of EBV-positive HL in developing countries could result from the existence of an underlying immunosuppression. Similar to that was observed in African Burkitts' lymphoma patients infected with malaria (5,6).

The evidence that EBV is associated with HL was provided by the detection of raised antibodies titers to EBV antigens in patients with HL when compared with other lymphomas
And further that those raised values preceded the development of HL by several years (7,8).
In addition, the relative risk of developing HL in individuals with history of infectious mononucleosis, relative risk to those with no previous history was shown to range between 2.0 and 5 .0 (9,10).

In this preliminary study,we studied the incidence of antibodies to EBV antigens in adult patients with HL.

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Material and Methods:

The present study was conduded at January 2011 to the end of august 2011 on patients with Hodgkin`s lymphoma (HL) attending nuclear medicine hospital in Baghdad .

Thirty patients with (HL) with age range (25 -53) years (18 males and 12 females) that were treated by chemotherapy and /or radiotherapy.

The histopathological subtype of the disease was reviewed

by examining their histopathological slides. A control group was taken from (25) patients who complaint from non malignant disorders with age ranged from (20-50) years (14) females and (11) males was also included in this study.
Venous blood was taken (4 ml) from each group , putting in clot activator tubes .

The following tests (viral capsid antigen) (VcA) IgM (EB virus), VCA IgG, early antigen (EA)IgM and (EA)-IgG ,were performed using enzyme linked immunosorbent assay (ELISA)

The mentioned above tests were done according to the instructions of the kit provided by cortez diagnostics.
Ethical approval for our study was not required by the this hospital as experiment carried out

did not relate to patients privacy or treatment .
The statistical data were analyzed with SPSS for windows version (17.0).
P-value <0.05 was considered significant .

Results:

Our data showed that 20 patients out of 30 patients with HL showed positive result of VCA IgG (66.6%)(cuttof value 1.02) with mean value of (1.24+-0.3) compared with control group that only 2 patients have VCA AgG positive with mean value of (0.73+-0.27) with ($p<0.05$). in case of VCA IgM only 3 patient with HL have positive results compared with only 2 patients of control group non significant difference was noticed. Regarding EA IgG a significant difference was found in HL compared with control groups (see table 1).

Table (1): mean levels of EBV titer in the HL and control group.

HL	control group
VCA IgG 1.24 +- 0.3	0.73 +- 0.27 ($p<0.05$)
VCA IgM 0.8 +- 0.23	0.79 +- 0.31 N.S
EA IgG 1.32 +- 0.35	0.82 +- 0.04 ($p<0.05$)
EA IgM 0.77 +- 0.27	

The distribution of EBV among subtypes of HL showed (56.6%) of cellularity of all HL group as shown in table (2).

Table (2): EBV distribution in different subtypes of HL

	EBV- negative	EBV- positive
Mixed cellularity type	3	17
Nodular sclerosis	2	1
Lymphocytic predominant	2	1
Lymphocytic depleted	3	1
Total	10	20

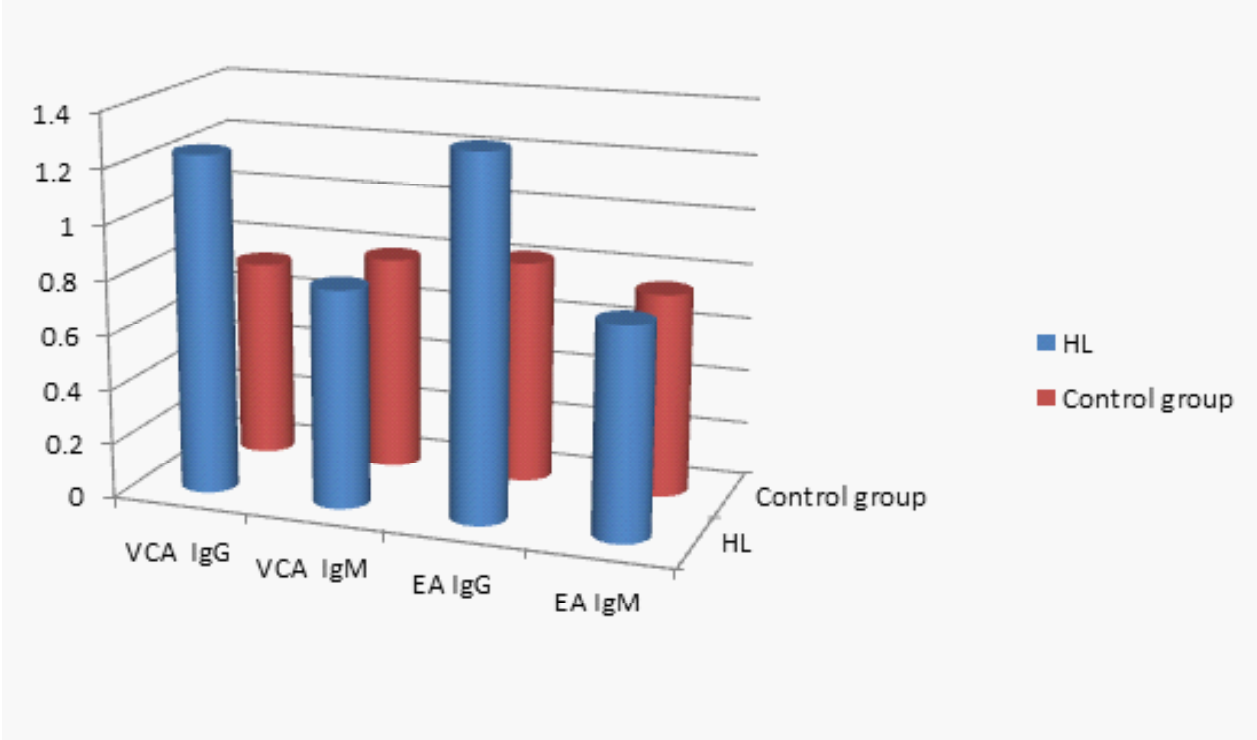

Figure (1) shows the mean levels of EBV in the HL and Control groups.

Discussion:

The sets of our findings concern elevated antibodies against the major determinants of EBV. These include that HL patients as a group had significantly higher VCA-lgG in comparison to control group who generally were patients with other non malignant diseases. Moreover, the result obtained from the present study revealed that EA-lgG were significantly higher in HL patients compared to the control group. These findings are similar to that reported by Goldman, Henle., Johannsonet, Levin, Deschryver, and Henderson in which the most common findings were that HL patients had elevated titers of VCA-lgG also elevated titers of EA-lgG antibodies (1, 2, 3, 4, 5, 6).

The first evidence that EBV might be associated with HL was provided by the detection of raised antibodies titers to EBV antigens in patients with HL when compared with patients with other malignancies (7). EBV could either play a direct role in the pathogenesis of HL possibly by triggering the pathogenic mechanism(s) or it could reflect the presence of an inherited or acquired depression of immunoregulation that is prelude both malignant and to reactivation of EBV (8).

It is well known that not all subtypes of HL harbor EBV to the same degree. We reported that (20) cases out of (30) patients of HL are belong to mixed cellularity type, as shown in table (2). Seventeen patient out of twenty cases of mixed cellularity having VCA-lgG positive results which represented (56.6%) of all cases HL examined group.

Our data findings is similar to that reported by a study in Jordan that EBV was seen in (65%) of mixed cellularity subtype (9). Moreover in United Arab Emirates national study revealed that EBV was seen predominantly in mixed cellularity subtype (10).

However, in Egypt (100%) of mixed cellularity subtype having EBV positive results (11).

The ability to identify prognostic factors raises the possibility of optimizing treatment in HL EBV tumor cell presence is associated with better survival in young patients and poorer survival in older patients with HL independent of other factors (12). Moreover, a variety of strategies have been investigated for treating EBV- associated tumor specifically and several of these have been generated some intriguing successes(13).

From the mentioned results there is a significant association between EBV and HL. Further studies using immunohistochemsitry are highly indicated because its presence may have significant impact on prognosis and response to therapy.

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ترافق وجود الاجسام المضادة لفايروس الابشتيان بار هربس عند المصابين بسرطان اللمفوما نوع هوجكن

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الخلاصة :

ان ارتباط فيروس ايبيشتاين – بار مع سرطان هوجكن يعتمد على عدة عوامل منها الموقع الجغرافي , وتحت النوع النسيجي والعمر .تضمنت الدراسة الحالية (30) شخصا مصابا بمرض سرطان هوجكن (18 ذكرا و 12 أنثى) تتراوح اعمارهم (25 – 53) سنه. تمت دراسة الشرائح النسيجية لمعرفة النوع. أما مجموعة السيطرة فتم اختبار (25) شخصا ممن يعانون من امراض غير سرطانية . وكانت اعمارهم تتراوح بين (55-20) سنة. وجد ان مضادات(Viral Capsid A-tigen lgG) ومضادات (Early Antigen IgG) اعلى وبنسب معنوية احصائية من مجموعة السيطرة. كذلك وجد ان مزيج الخلايا تحت النوع يحمل الاضداد لفيروس ايبيشتاين – بار بنسبة (56.6%) وجد ان هنالك علاقة معنوية بين وجود الاضداد للفيروس المذكور ومرض هوجكن . نقترح بان تكون هنالك دراسات مستقبلية لمعرفة الفيروس المذكور بواسطة طرق مناعيه كيمياوية نسيجية وذلك لأهميتها من ناحية نوع العلاج المستخدم وتطور المرض.