RECOMMENDATIONS

1- Human leukocyte antigen- G should be done on a wider scale of AML patients to confirm its relation to unfavourable risk patients.

2- Further studies should be performed to assess HLA-G role in context with other genetic and epigenetic factors that affect the prognosis of AML patients.

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SUMMARY

Acute myeloid leukemia (AML) is a clonal stem cell malignancy in which immature hematopoietic cells proliferate and accumulate in bone marrow, peripheral blood, and other tissues. This process results in inhibition of normal hematopoiesis, and the clinical features of bone marrow failure. AML accounts for 90%of all acute leukemias in adults.

Human leukocyte antigen G (HLA-G) is a non-classic major histocompatibility complex class I gene encoding for a protein showing restrictive distribution and lower polymorphism. Membrane-bound HLA-G isoforms are expressed by extravillous cytotrophoblast cells, fetal capillary endothelial cells, endovascular cells, and thymic epithelium cells. They can also be detected in tumoral pathologies such as melanomas, breast, renal, and lung carcinomas gliomas, and cutaneous lymphomas.

HLA-G has been suggested to provide tumor cells with an effective pathway to escape from anti-tumor immune responses and to be involved in promoting beneficial tolerance in several settings, such as autoimmunity and organ transplantation, and in contributing to detrimental tolerance in viral infections and cancer. Few studies had been performed on HLA-G expression in different types of leukemia patients; however, data are limited and conclusions remain controversial. In addition, this molecule might be a promising target for future immune therapeutic approaches based on its immune tolerant functions and its highly specific expression for malignant transformation.

The present study aimed at determining the role of soluble HLA-G in AML patients and to study its prognostic significance. The study was performed on 30 patients and 15 healthy controls of matched age and sex. The mean value of age in group A was 48.5 ± 16.98 years, in group B was 50.1 ± 17.5 years and in group C was 49.8 ± 19.5 years. Males in group A were 7 (46.67%), in group B were 6 (40%) and in group C were 8(53.33%). Females in group A were 8(53.33%), in group B were 9(60%) and in group C were 7 (46.67%). M4 was the commonest subtype in both

groups (6 cases, 40%). The mean value of sHLA-G levels in group A was 329.8 ± 57.54 ng/L, in group B was 451.15 ± 163.99 ng/L and in group C was 551.63 ± 109.08 ng/L. There was statistically significant difference in sHLA-G levels between the three studied groups ($P<0.05$), being significantly higher in relapsed than new AML cases. The cutoff value of sHLA-G was 368.84, this value showed sensitivity of 100.0% and specificity of 62.0%. There was no statistically significant difference between sHLA-G as regards age, gender and WBCs ($P >0.05$) while there was statistically significant difference between, sHLA-G and bone marrow blasts percentage ($P<0.05$). There was statistically insignificant difference between sHLA-G and different FAB subtypes with the highest mean values was observed in M6 (605.3±116.5) while the lowest mean value was observed in M2 (365.2±98.9). ($P =0.685$). There was statistically insignificant difference between sHLA-G and response to therapy ($P = 0.158$).

الملخص

تعتبر اللوكيميا الميلود ية الحادة من السرطانات التى تنشأ من الخلايا الجذعية المسرطنة و تحتوى على خلايا بدائيه لها القدرة على التكاثر و التراكم في نخاع العظم و في الدم و انسجه اخرى مما يؤدى الى نقص الخلايا الطبيعيه في نخاع العظم و ظهور اعراض فشل النخاع. و تمثل اللوكيميا الميلودية حوالى 90% من كل الوكيميا الحادة في البالغين.

الانتيجين الملائم النسيجي-جي يعتبر من مجموعه المورثات 1 غير النمطية و ينتج بروتين ذو انتشار وتعدد شكلي محدود. وقد وجد الانتجين الملائم –جي على الزغب الخارجية لخلايا التروفوبلاست و الشعيرات الدموية الجنينية و خلايا البطان الوريدي و خلايا الثايموسية الغشائية. و قد وجد ايضا في الخلايا السرطانية مثل خلايا الميلانوما و خلايا سرطان الثدي و الكلى و الرئة و اورام المخ و اورام الليمفاوية الجلدية.

و يشكل الجزئي للانتيجين الملائم النسيجي وظائف مناعية مختلفة من خلال تثبيط عمل الخلايا المناعية و برغم من ان اهميته ظهرت من التقبل المناعي بين الام و الجنين الا انه ظهر كاحد العوامل التى تساعد خلايا السرطان من تجنب التفاعلات المناعية مما يؤدي الى تقبل خلايا السرطان او حتى الخلايا المصابة بالفروسات الى جانب ظهور اهميته مع امراض اخرى مثل الامراض المناعية و زرع الاعضاء. توجد ابحاث قليلة عن العلاقة بين الانتيجين الملائم النسيجي-جي وانواع اللوكيميا المختلفة ولكن النتائج محدودة و متنوعة. ولكن قد يكون ذو فائدة مستقبلية فى استخدام العلاج المناعى فى علاج الاورام

وكان هذا البحث يهدف الى دراسة دور الانتيجين الملائم النسيجي – جي في لوكيميا النقوى الحادة ودراسة قيمته التنبؤية وقد ا شتملت الدراسة على 30 مريضا مصابين بالوكيميا النقوية الحادة و 15 عينة ضابطة متوافقه من حيث العمر و النوع. وكان متوسط الاعمار في المجموعه الاولى 48.5 ± 16.98 سنة و المجموعة الثانية 17.5 ± 50.1 بينما كان فى المجموعة الثالثة 19.5 ± 49.8 سنة. و بلغت نسبة الاناث في المجموعة الاولى 53.3% و في الثانية 60% و الثالثة 46.67%. و لوحظ ان اكثرانواع اللوكيميا شيوعا كان M4. و لم يتواجد اختلاف بين المورثات بين مجموعه المرضى المنتكسة و حديثى التشخيص. وبلغ مستوى الانتيجين الملائم النسيجي جي في المجموعه الاولى 57.54 ± 329.8 ng/L وفي المجموعة الثانية 163.99 ± 451.15 ng/L و فى المجموعة الثالثة 109.08 ± 551.63 ng/L. و قد وجد اختلاف ذو دلالة احصائيه بين هذه القيم فى مجموعه المرضى المنتكسة و مجموعة حديثى التشخيص بالمقارنة بالمجموعة الضابطة ($p<0.05$) .
واتضح من الدراسة ان الحد الفاصل لنسبة الانتجين كان عند القيمة 368.84 حيث بلغ مدى حساسية التشخيص نسبة 100% و الخصوصية 62%. و عند تحليل الانتجين و علاقته ببقيه العوامل لوحظ الاتي: وجدت علاقة ذات دلالة احصائية بينه و بين نسبة الخلايا السرطانية في نخاع العظم ($P<0.05$) .الا انه لم تتواجد اى علاقه بينه و بين سن المرضى أو جنس المريض أو عدد كرات الدم البيضاء في الدم ($p>0.05$). كما انه لم تتواجد اى علاقه بينه و نوع اللوكيميا النقوى الحادة وكان مستوى الانتيجين أعلى فى النوع M6 (605.3±116.5) بينما

كانت اقل قيمة له فى النوع(98.9±365.2) M2 بالمقارنة بالانواع الاخرى (P =0.685) . كما انه لم تتواجد اى علاقه ذات دلالة احصائية بينه و بين مدى استجابته للعلاج (P=0.158).

دراسة مستوى الانتيجين الملائم النسيجى- جى المرسل عند مرضى اللوكيميا الميلودية الحادة

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إيفاء جزئيا للحصول على درجة

الماجستير في أمراض دم

كلية الطب

جامعة الإسكندرية

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الاكاديمية الطبية العسكرية

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رسالة

مقدمة إلى كلية الطب- جامعة الإسكندرية

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الماجستير في أمراض دم

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